ISSN 2220-3206 (online)

World Journal of *Psychiatry*

World J Psychiatry 2024 February 19; 14(2): 194-333

Published by Baishideng Publishing Group Inc

World Journal of Psychiatry

Contents

Monthly Volume 14 Number 2 February 19, 2024

World Journal of Psychiatry

Monthly Volume 14 Number 2 February 19, 2024

Contents

ABOUT COVER

Editorial Board Member of *World Journal of Psychiatry*, Hector Wing Hong Tsang, PhD, OTR, Chair Professor and Head, Department of Rehabilitation Sciences, Interim Director of Mental Health Research Centre, The Hong Kong Polytechnic University, Hong Kong 999077, China. hector.tsang@polyu.edu.hk

AIMS AND SCOPE

The primary aim of *World Journal of Psychiatry* (*WJP*, *World J Psychiatry*) is to provide scholars and readers from various fields of psychiatry with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

WJP mainly publishes articles reporting research results and findings obtained in the field of psychiatry and covering a wide range of topics including adolescent psychiatry, biological psychiatry, child psychiatry, community psychiatry, ethnopsychology, psychoanalysis, psychosomatic medicine, *etc*.

INDEXING/ABSTRACTING

The *WJP* is now abstracted and indexed in Science Citation Index Expanded (SCIE, also known as SciSearch®), Current Contents/Clinical Medicine, Journal Citation Reports/Science Edition, PubMed, PubMed Central, Reference Citation Analysis, China Science and Technology Journal Database, and Superstar Journals Database. The 2023 Edition of Journal Citation Reports® cites the 2022 impact factor (IF) for *WJP* as 3.1; IF without journal self cites: 2.9; 5-year IF: 4.2; Journal Citation Indicator: 0.52; Ranking: 91 among 155 journals in psychiatry; and Quartile category: Q3.

RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: *Yu-Xi Chen*; **Production Department Director:** *Xu Guo*; **Editorial Office Director:** *Jia-Ping Yan*.

NAME OF JOURNAL
World Journal of Psychiatry

ISSN
ISSN 2220-3206 (online)

LAUNCH DATE
December 31, 2011

FREQUENCY
Monthly

EDITORS-IN-CHIEF
Ting-Shao Zhu

EDITORIAL BOARD MEMBERS
https://www.wjgnet.com/2220-3206/editorialboard.htm

PUBLICATION DATE
February 19, 2024

INSTRUCTIONS TO AUTHORS
https://www.wjgnet.com/bpg/gerinfo/204

GUIDELINES FOR ETHICS DOCUMENTS
https://www.wjgnet.com/bpg/GerInfo/287

GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH
https://www.wjgnet.com/bpg/gerinfo/240

PUBLICATION ETHICS
https://www.wjgnet.com/bpg/GerInfo/288

PUBLICATION MISCONDUCT
https://www.wjgnet.com/bpg/gerinfo/208

ARTICLE PROCESSING CHARGE
https://www.wjgnet.com/bpg/gerinfo/242

STEPS FOR SUBMITTING MANUSCRIPTS
https://www.wjgnet.com/bpg/GerInfo/239

ONLINE SUBMISSION
https://www.f6publishing.com

World Journal of Psychiatry

Submit a Manuscript: https://www.f6publishing.com

World J Psychiatry 2024 February 19; 14(2): 194-198

DOI: 10.5498/wjp.v14.i2.194

ISSN 2220-3206 (online)

EDITORIAL

Keep in mind sex differences when prescribing psychotropic drugs

Marianna Mazza, Domenico De Berardis, Giuseppe Marano

Specialty type: Psychiatry

Provenance and peer review: Invited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

Grade A (Excellent): 0
Grade B (Very good): B
Grade C (Good): C, C
Grade D (Fair): 0
Grade E (Poor): 0

P-Reviewer: Joseph MA, Oman; Seeman MV, Canada

Received: October 8, 2023
Peer-review started: October 8, 2023
First decision: November 30, 2023
Revised: December 2, 2023
Accepted: January 2, 2024
Article in press: January 2, 2024
Published online: February 19, 2024

Marianna Mazza, Giuseppe Marano, Department of Neurosciences, Fondazione Policlinico Universitario A Gemelli IRCCS, Università Cattolica del Sacro Cuore, Rome 00168, Italy

Domenico De Berardis, Mental Health, NHS, ASL 4 Teramo, Teramo 64100, Italy

Corresponding author: Marianna Mazza, MD, PhD, Assistant Professor, Department of Neurosciences, Fondazione Policlinico Universitario A Gemelli IRCCS, Università Cattolica del Sacro Cuore, Largo A Gemelli 8, Rome 00168, Italy. mariannamazza@hotmail.com

Abstract

Women represent the majority of patients with psychiatric diagnoses and also the largest users of psychotropic drugs. There are inevitable differences in efficacy, side effects and long-term treatment response between men and women. Psychopharmacological research needs to develop adequately powered animal and human trials aimed to consider pharmacokinetics and pharmacodynamics of central nervous system drugs in both male and female subjects. Healthcare professionals have the responsibility to prescribe sex-specific psychopharmacotherapies with a priority to differentiate between men and women in order to minimize adverse drugs reactions, to maximize therapeutic effectiveness and to provide personalized management of care.

Key Words: Women; Psychopharmacology; Psychotropic drugs; Sex differences

Core Tip: It has been largely demonstrated that women are the majority of patients with psychiatric diagnoses and also the largest users of psychotropic drugs. There are differences between men and women receiving psychotropic drugs, in terms of response, efficacy, side effects, long-term treatment outcome. There is still a lack of psychopharmacological research focusing on these differences in male and female patients. This editorial focuses on the important issue of deeply understanding the pharmacokinetics and pharmacodynamics of central nervous system drugs with a priority to differentiate between men and women in order to provide personalized management of care.

Citation: Mazza M, De Berardis D, Marano G. Keep in mind sex differences when prescribing psychotropic drugs. *World J Psychiatry* 2024; 14(2): 194-198
URL: https://www.wjgnet.com/2220-3206/full/v14/i2/194.htm
DOI: https://dx.doi.org/10.5498/wjp.v14.i2.194

INTRODUCTION

Nothwithstanding both biological research and clinical experience have largely demonstrated that pathophysiological dissimilarities between men and women significantly influence the pharmacokinetics and pharmacodynamics of psychotropic drugs, most central nervous system drugs are prescribed to women and men at the same doses[1]. Sex differences in neural and behavioral outcomes have been described in the majority of neuroimaging studies evaluating the response to antidepressants, antipsychotics, sedative-hypnotics, stimulants and mood stabilizers[2]. Sex differences exist in every major part of the brain[3], hormones and neurosteroids affect the brains of men and women differentially and dissimilar biological mechanisms may underlie sex differences in responsiveness to stress[4].

Gender psychopharmacology is a complex field of study: Not only biological and physiological differences have a pivotal importance, but also all those factors that contribute to the formation of the individual, such as psychological behaviour, social role, cultural characteristics contribute significatively. Personalized medicine could become the future, designing suitable drugs or providing more appropriate doses, with different administration intervals. Men and women use drugs and other health interventions differently, for biological reasons, as they get sick differently (for example, men seem to have higher pain tolerance and more lethal conditions, whereas women have a stronger immune response but more disabling chronic conditions) and socio-cultural reasons, as they have different attitudes toward health and care[5]. Besides, men and women respond differently to pharmacotherapies, because the drugs are absorbed and eliminated differently or because there are differences in the sensitivity and distribution of the targets on which these substances act. Gender differences in drug response are based on pharmacokinetic and pharmacodynamic variations, such as bioavailability, volume of distribution and binding to plasma proteins. There are also differences in metabolization and drug excretion: Women produce less creatinine, have a lower glomerular filtrate volume than men, and there is a tendency for women to accumulate drugs. On average, men have larger body sizes that result in larger distribution volumes and faster total clearance of most medications in men compared to women. Greater body fat in women (until older ages) may increase distribution volumes for lipophilic drugs[6].

Over the course of life, women undergo several hormonal changes connected, for example, to the onset and end of the menstrual cycle as well as pregnancy and the post-partum period. Pregnancy and lactation modify all pharmacokinetic parameters, due to changes in the volume of distribution. Besides, the placenta is a drug-metabolizing organ and the enzymes in the placenta are different from those in the liver[5].

WOMEN AND PSYCHOTROPIC DRUGS: FUTURE PERSPECTIVES OF RESEARCH

Women represent the majority of patients with psychiatric diagnoses and also the largest users of psychotropic drugs, especially antidepressants[7,8]. More women than men take multiple medications, and are more vulnerable to a number of adverse drug reactions. The reasons for this increased risk include gender-related differences in pharmacokinetic, immunological and hormonal factors (Figure 1). Among these differences, variation in levels and changes in sex steroids that subsequently interact with neurotransmitters, lower lean body mass compared to men, reduced hepatic clearance, different activity of cytochrome P450 enzymes with consequent different rates of metabolization, as well as conjugation, absorption, protein binding and renal elimination should be considered[9]. Besides, important issues regard the increased risk of QT prolongation at electrocardiogram with certain drugs compared with men even at equivalent serum concentrations and specific cutaneous reactions due to possible gender differences in T cell activation and proliferation (Figure 2). The prevalence of side effects in women is moderated by readiness to report, pain threshold, nature of the side effect, adherence to prescription, therapeutic alliance, genetic differences. It can be argued how both sex-related than gender-related factors (lifestyle factors, communication styles, health information-seeking behaviour, differences in social roles, and medication prescribing and adherence) could also lead to gender-specific differences in the occurrence, perception and reporting of adverse drug reactions. For example, women and men may perceive symptoms differently; women seem to search more actively for health information than men; there are often differences in the dose of drugs or duration of therapies prescribed to women as compared to men[10].

There is an increase of the rates of individuals reporting the use of any psychiatric medications over the last few decade, and in particular rates of antidepressant, benzodiazepine and antipsychotic use seem to be higher in females[11]. Although these data witness the advancements of medicine and the improvement of the quality of life of psychiatric patients, the other side of the coin is represented by the inevitable consideration of differences in efficacy, side effects and long-term treatment response between males and females, probably related, almost in part, to sex differences in how these drugs act on the brain and are metabolized and excreted. In addition, reproductive-aged women have repetitive variations in sex hormones with each monthly cycle that influence the onset, chronicity, and outcome of a variety of psychiatric illnesses[12].

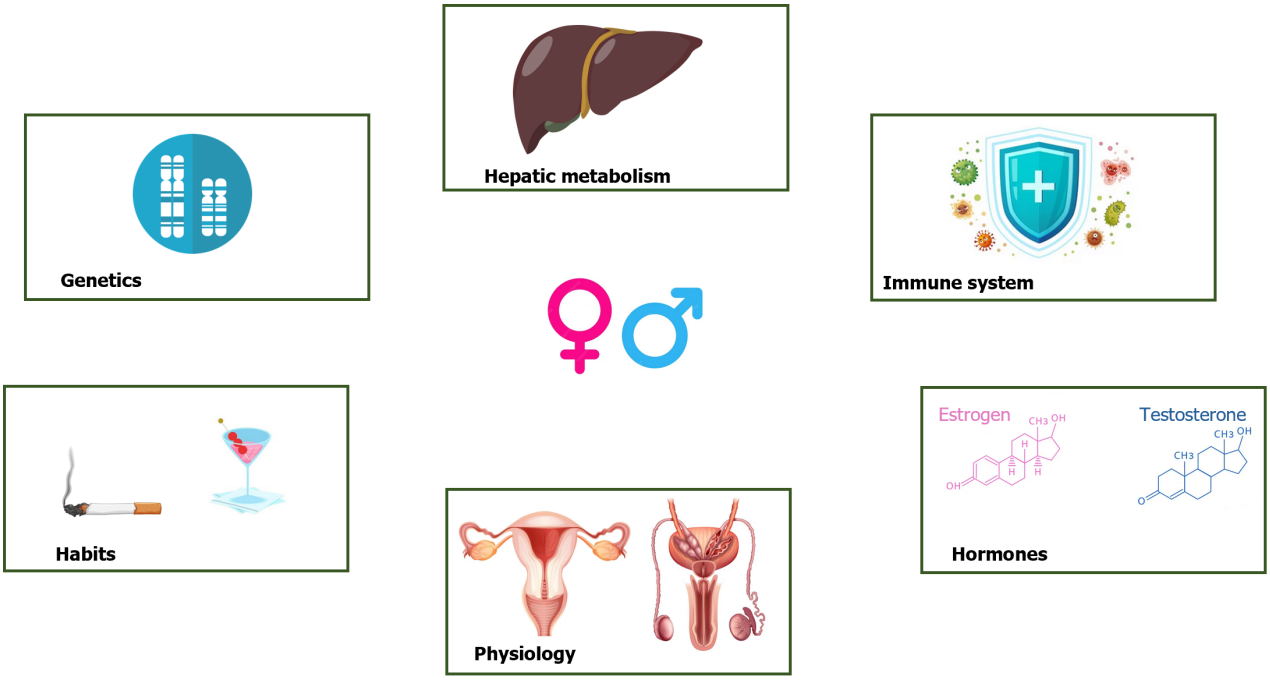

Figure 1 Gender differences in pharmacokinetics and pharmacodynamics.

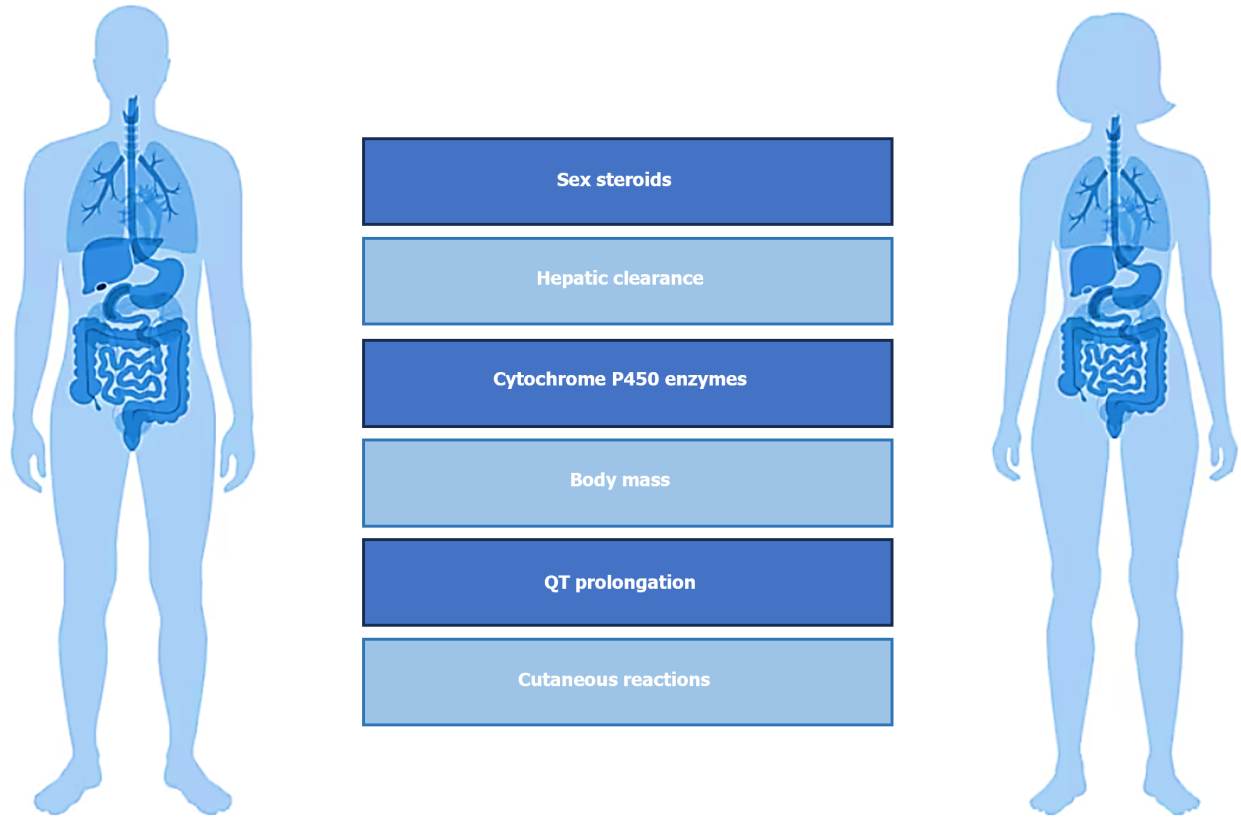

Figure 2 Factors influencing gender-based drug response.

The complexity of women's hormonal physiology translates into mood instability related to the menstrual cycle, the manifold physiological changes of pregnancy, and, finally, the extremely complicated phase of menopause. Levels of sex hormones throughout the menstrual cycle are associated with the activation of specific hepatic enzymes and the rate of clearance of certain drugs, while the main differences between men and women in drug kinetics disappear at menopause due to the progressive decline in the production of estrogen and progesterone[7].

The specificity of psychopharmacological treatment in women arise from sex-related mechanisms of pharmacodynamics and pharmacokinetics up to peculiarities in terms of absorption, distribution, metabolization, and excretion. For example, in the prescription of antipsychotics, like olanzapine and clozapine, the effective dose for a woman might need to be lower than guidelines recommend for men on average (men with psychosis often require higher dosages of antipsychotic drugs related to their greater liver enzymatic clearance), while some antipsychotic side effects, weight gain for instance, are more worrisome for women than for men. After menopause, women need an increase in their antipsychotic dose, due to the decline of endogenous estrogen levels; other reproductive stages in women's lives require special prescribing considerations as well[13-15].

Notwithstanding the number of trials enrolling women has increased following the instructions of Food and Durg Administration, women are still less represented in clinical trials because both pharmacokinetics and pharmacodynamics of a drug can be influenced by menstrual cycle phases, hormonal fluctuations, use of oral contraceptives and hormonal therapy, and life events such as pregnancy and lactation.

Clinicians should always keep in mind sex differences when prescribing psychotropic drugs and there must be adequate academic and scientific information on the potential impact of sex-related factors that affect pharmacokinetics and pharmacodynamics processes. This topic results critical in order to ensure drug safety and efficacy for females and males, and for informing clinical product monographs and consumer information.

There is a need of adequately powered psychopharmacological researches aimed to consider both male and female subjects in animal and human studies. In addition, clinical trials should necessarily analyze sex-related differences in results. Evaluation of the effects of sex can help to explain seemingly contradictory findings of pharmacological studies. In future researches, it could be interesting to deepen sex-specific differences in response to antidepressant therapy[16], to compare the clinical trajectory of women and men with treatment-resistent depression treated with similar augmentation strategies[17], to test different psychotropic drugs aiming to individuate which may have a greater efficacy on women than men[18] or to better evaluate sex differences in studies examining the role of the glutamate system in psychiatric disease[19]. Not only women often use drugs differently and respond to drugs differently, but they can also have unique obstacles to effective treatment (for example not being able to find child care or being prescribed treatment that has not been adequately tested on women)[20]. Although men are more likely than women to use almost all types of illicit drugs, there is evidence that women may be more susceptible to craving and relapse[21], therefore, influencing psychopharmacological treatment in terms of comorbidity and compliance with therapy. It could be useful to identify more precisely which gender-related psychosocial factors, environmental factors (chemical pollutants, cigarette smoking or oral contraceptives, nutritional variables) and psychological factors, in terms of patients' beliefs, attitudes and expectations, that can affect the efficacy of a prescribed pharmacotherapy, and this issue results particularly applicable to centrally acting drugs.

CONCLUSION

Studying and recognizing differences between both sexes is the first step in ensuring equity and appropriateness of care. Sex is a key variable that cannot be neglected to optimize psychopharmacological treatment and to improve the efficacy and safety of drug use[22]. The development of sex-specific psychopharmacological research should aim to create a link between researchers and physicians for careful evaluation of biological, physiological, and pathological differences between men and women for the purpose of an increasing level of personalized medicine. On one hand, it is imperative to better identify the most urgent priorities and to increase awareness and knowledge about the mechanisms underlying the differences. On the other hand, it is crucial to stimulate the development of scientific and regulatory pathways that ensure that male and female populations are studied specifically and selectively.

Neuropsychopharmacology research should necessarily and primarily consider sex as a biological variable in order to reduce costs and improve benefits, reproducibility of results and rigor of methodology. Treatment guidelines should always take into account sex-related factors and their influence on pharmacokinetics and pharmacodynamics processes as well as the occurrence of adverse drug reactions and events. Healthcare professionals have a responsability to understand the pharmacokinetics and pharmacodynamics of central nervous system drugs with a priority to differentiate between men and women in order to minimize the adeverse drugs reactions, to maximize the therapeutic effectiveness, to provide personalized management of care of patients and to contribute to the development of sex-specific psychopharmacotherapies.

FOOTNOTES

Author contributions: Mazza M, De Berardis D, and Marano G designed the research study and wrote the manuscript; and all authors have read and have approved the final manuscript.

Conflict-of-interest statement: All the authors report no relevant conflicts of interest for this article.

Country/Territory of origin: Italy

ORCID number: Marianna Mazza 0000-0002-3007-8162; Domenico De Berardis 0000-0003-4415-5058; Giuseppe Marano 0000-0001-7058-4927.

S-Editor: Wang JJ
L-Editor: A
P-Editor: Chen YX

REFERENCES

1 **Romanescu M**, Buda V, Lombrea A, Andor M, Ledeti I, Suciu M, Danciu C, Dehelean CA, Dehelean L. Sex-Related Differences in Pharmacological Response to CNS Drugs: A Narrative Review. *J Pers Med* 2022; **12** [PMID: 35743692 DOI: 10.3390/jpm12060907]
2 **Duffy KA**, Epperson CN. Evaluating the evidence for sex differences: a scoping review of human neuroimaging in psychopharmacology research. *Neuropsychopharmacology* 2022; **47**: 430-443 [PMID: 34732844 DOI: 10.1038/s41386-021-01162-8]
3 **Cahill L**. Why sex matters for neuroscience. *Nat Rev Neurosci* 2006; **7**: 477-484 [PMID: 16688123 DOI: 10.1038/nrn1909]
4 **Bolea-Alamanac B**, Bailey SJ, Lovick TA, Scheele D, Valentino R. Female psychopharmacology matters! Towards a sex-specific psychopharmacology. *J Psychopharmacol* 2018; **32**: 125-133 [PMID: 29405799 DOI: 10.1177/0269881117747578]
5 **Crimmins EM**, Shim H, Zhang YS, Kim JK. Differences between Men and Women in Mortality and the Health Dimensions of the Morbidity Process. *Clin Chem* 2019; **65**: 135-145 [PMID: 30478135 DOI: 10.1373/clinchem.2018.288332]
6 **Schwartz JB**. The influence of sex on pharmacokinetics. *Clin Pharmacokinet* 2003; **42**: 107-121 [PMID: 12537512 DOI: 10.2165/00003088-200342020-00001]
7 **Estancial Fernandes CS**, de Azevedo RCS, Goldbaum M, Barros MBA. Psychotropic use patterns: Are there differences between men and women? *PLoS One* 2018; **13**: e0207921 [PMID: 30475871 DOI: 10.1371/journal.pone.0207921]
8 **Boyd A**, Van de Velde S, Pivette M, Ten Have M, Florescu S, O'Neill S, Caldas-de-Almeida JM, Vilagut G, Haro JM, Alonso J, Kovess-Masféty V; EU-WMH investigators. Gender differences in psychotropic use across Europe: Results from a large cross-sectional, population-based study. *Eur Psychiatry* 2015; **30**: 778-788 [PMID: 26052073 DOI: 10.1016/j.eurpsy.2015.05.001]
9 **Rademaker M**. Do women have more adverse drug reactions? *Am J Clin Dermatol* 2001; **2**: 349-351 [PMID: 11770389 DOI: 10.2165/00128071-200102060-00001]
10 **de Vries ST**, Denig P, Ekhart C, Burgers JS, Kleefstra N, Mol PGM, van Puijenbroek EP. Sex differences in adverse drug reactions reported to the National Pharmacovigilance Centre in the Netherlands: An explorative observational study. *Br J Clin Pharmacol* 2019; **85**: 1507-1515 [PMID: 30941789 DOI: 10.1111/bcp.13923]
11 **Johansen ME**. Psychiatric Medication Users by Age and Sex in the United States, 1999-2018. *J Am Board Fam Med* 2021; **34**: 732-740 [PMID: 34312266 DOI: 10.3122/jabfm.2021.04.200596]
12 **Kornstein SG**, Clayton AH. Women's Mental Health. *Psychiatr Clin North Am* 2023; **46**: xiii-xixv [PMID: 37500256 DOI: 10.1016/j.psc.2023.04.016]
13 **Li R**, Ma X, Wang G, Yang J, Wang C. Why sex differences in schizophrenia? *J Transl Neurosci (Beijing)* 2016; **1**: 37-42 [PMID: 29152382]
14 **Seeman MV**. The Pharmacodynamics of Antipsychotic Drugs in Women and Men. *Front Psychiatry* 2021; **12**: 650904 [PMID: 33897500 DOI: 10.3389/fpsyt.2021.650904]
15 **Mazza M**, Caroppo E, De Berardis D, Marano G, Avallone C, Kotzalidis GD, Janiri D, Moccia L, Simonetti A, Conte E, Martinotti G, Janiri L, Sani G. Psychosis in Women: Time for Personalized Treatment. *J Pers Med* 2021; **11**: 1279 [PMID: 34945748 DOI: 10.3390/jpm11121279]
16 **Sramek JJ**, Murphy MF, Cutler NR. Sex differences in the psychopharmacological treatment of depression. *Dialogues Clin Neurosci* 2016; **18**: 447-457 [PMID: 28179816 DOI: 10.31887/DCNS.2016.18.4/ncutler]
17 **Moderie C**, Nuñez N, Fielding A, Comai S, Gobbi G. Sex Differences in Responses to Antidepressant Augmentations in Treatment-Resistant Depression. *Int J Neuropsychopharmacol* 2022; **25**: 479-488 [PMID: 35167671 DOI: 10.1093/ijnp/pyac017]
18 **Ma L**, Xu Y, Wang G, Li R. What do we know about sex differences in depression: A review of animal models and potential mechanisms. *Prog Neuropsychopharmacol Biol Psychiatry* 2019; **89**: 48-56 [PMID: 30165122 DOI: 10.1016/j.pnpbp.2018.08.026]
19 **Wickens MM**, Bangasser DA, Briand LA. Sex Differences in Psychiatric Disease: A Focus on the Glutamate System. *Front Mol Neurosci* 2018; **11**: 197 [PMID: 29922129 DOI: 10.3389/fnmol.2018.00197]
20 **National Institute on Drug Abuse**. Sex and Gender Differences in Substance Use. [cited 4 September 2023]. Available from: https://nida.nih.gov/publications/research-reports/substance-use-in-women/sex-gender-differences-in-substance-use
21 **Kennedy AP**, Epstein DH, Phillips KA, Preston KL. Sex differences in cocaine/heroin users: drug-use triggers and craving in daily life. *Drug Alcohol Depend* 2013; **132**: 29-37 [PMID: 23357742 DOI: 10.1016/j.drugalcdep.2012.12.025]
22 **Allevato M**, Bancovsky J. Psychopharmacology and women. In: RennóJ, Valadares G, Cantilino A, Mendes-Ribeiro J, Rocha R, da Silva AG. Women's mental health: A clinical and evidence-based guide. Switzerland: Springer Nature, 2020: 227-239

World Journal of Psychiatry

Submit a Manuscript: https://www.f6publishing.com

World J Psychiatry 2024 February 19; 14(2): 199-203

DOI: 10.5498/wjp.v14.i2.199

ISSN 2220-3206 (online)

EDITORIAL

Therapeutic approach to emotional reactions accompanied with thermal skin injury – from basic to epidemiological research

Bojana Krstic, Milos Krstic, Dragica Selakovic, Nemanja Jovicic, Gvozden Rosic

Specialty type: Psychiatry

Provenance and peer review: Invited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

Grade A (Excellent): 0
Grade B (Very good): 0
Grade C (Good): 0
Grade D (Fair): D
Grade E (Poor): 0

P-Reviewer: Liu XQ, China

Received: October 9, 2023
Peer-review started: October 9, 2023
First decision: December 6, 2023
Revised: December 15, 2023
Accepted: January 24, 2024
Article in press: January 24, 2024
Published online: February 19, 2024

Bojana Krstic, Milos Krstic, Dragica Selakovic, Gvozden Rosic, Department of Physiology, Faculty of Medical Sciences, University of Kragujevac, Kragujevac 34000, Serbia

Nemanja Jovicic, Department of Histology and Embryology, Faculty of Medical Sciences, University of Kragujevac, Kragujevac 34000, Serbia

Corresponding author: Gvozden Rosic, MD, PhD, Full Professor, Department of Physiology, Faculty of Medical Sciences, University of Kragujevac, Svetozara Markovica 69, Kragujevac 34000, Serbia. grosic@medf.kg.ac.rs

Abstract

In this editorial, we discuss the status of a therapeutic approach to emotional reactions accompanying thermal skin injuries. Burns are considered a major health problem, as well as an economic and social problem, with potentially devastating and life-changing consequences. They affect a wide range of patients with different damage mechanisms, varied depths, and localizations of the burns. The most common are thermal burns, with more than 11 million occurrences annually according to the World Health Organization data. Thermal skin injuries are among the most tragic and catastrophic injuries, almost unsurpassed in terms of severity, morbidity, and mortality, as well as functional, aesthetic, social, economic, and psychological consequences. Burn survivors face stress, anxiety, depression, low self-esteem, body deformity, social isolation, unemployment, financial burden, and family problems. The advances in acute burn care have allowed researchers and physicians to pay more attention to other effects of burns, focusing on psychological consequences in particular. Apart from the significant improvements in routine protocols, it seems useful to take care of psychological disturbances that occur simultaneously but may emerge as the most lasting outcome of those injuries. In that sense, various standards and additional approaches may be involved to achieve overall recovery.

Key Words: Thermal skin injury; Anxiety; Depression; Psychological consequences of burns

Core Tip: This editorial aimed to allow updated principle information considering the psychological consequences of burns by means of their medical, social, and economic significance in the population. Also, it aimed to bring some new insight into the potential therapeutic advances using alternative and adjuvant therapies. In that manner, we offered some evidence for the benefits of using a new methodology in the treatment of one of the most lasting consequences induced by thermal skin injury.

Citation: Krstic B, Krstic M, Selakovic D, Jovicic N, Rosic G. Therapeutic approach to emotional reactions accompanied with thermal skin injury – from basic to epidemiological research. *World J Psychiatry* 2024; 14(2): 199-203
URL: https://www.wjgnet.com/2220-3206/full/v14/i2/199.htm
DOI: https://dx.doi.org/10.5498/wjp.v14.i2.199

INTRODUCTION

Epidemiological data

Burns represent injuries to the skin and local tissue occurring as a consequence of energy transfer from a heat source to the body, thus causing an increase in the local tissue temperature. The increase of the tissue temperature above a certain threshold leads to irreversible cellular injury, interrupting metabolic processes[1]. According to the basic characteristics of the etiological agent, burns, as a medical entity, are divided into thermal, electrical, chemical, and radiation injuries. The most common are thermal burns, which make up about 86% of all burns. These burns could be caused by flame, hot liquid, or steam, as well as by direct contact with a hot object. Approximately 4% of burns are caused by electricity, 3% by chemical substances, and 7% could be classified as other types of burns. Burns are a major health problem, as well as an economic and social problem, with potentially devastating and life-changing consequences[2]. According to the World Health Organization data, more than 11 million burns occur annually, with the majority taking place in underdeveloped and developing countries due to various environmental factors (old buildings, lower safety standards, absence of smoke detectors, faulty electricity, *etc.*).

Classification according to population categories

There is a wide range of patients affected by burns, and their mechanisms of damage, burn depth, and localizations of burns are varied as well. The degree of damage depends on the power of the heat source, the duration of the heat effect, the method of injury, the age of the patient, the location of the burn, and the overall patient's health condition. According to the diagnostic criteria, burns can vary from small wounds treated on an outpatient basis to very large injuries that require specific protocols, including treatment in specialized centres. The treatment of severe burns includes prevention of progression to multiorgan system failure, which is usually accompanied by long stays in hospitals and long-term follow-up (to avoid risk from functional and psychosocial consequences). In total, more than 6% of all burn victims undergo specialized therapeutic protocols, yet with a devastating overall mortality rate[3]. Burn injuries affect the whole population, regardless of gender and age, although some studies suggest that these injuries are more common in men. Studies have shown certain patterns, indicating that males most often get burns outside the home (outdoors and at the workplace), whereas females are most frequently injured at home, and children usually get burns when they are not under the supervision of adults at home[4]. The morbidity and mortality risk of these injuries is also influenced by the population structure. Studies demonstrated that the highest rates of burn-related injuries and fatalities occur among the populations of young children, under 4 years of age and also senior adults over 60 years of age[5]. This kind of trauma is particularly important in children populations due to the long period of disability. A surveillance study in low and middle-income countries demonstrated that 17% of children with this kind of trauma experienced disability longer than 6 wk, while in 8% lifelong disability lifelong disability is predicted[6].

SOCIAL CHALLENGES AND ECONOMIC IMPACT OF THERMAL SKIN INJURIES

This is an important public health issue with a significant disease burden, not only in terms of serious morbidity and mortality but also with a large economic impact. Between 7 and 12 million people who sustain burn injuries (and require medical treatment) are absent from school or work for longer periods[7]. Studies have shown that the average number of days off work after burn trauma was close to 60, thus indicating the high economic burden that burn trauma causes. Patients' return to active duty, such as work or school, are important outcome after burn trauma since work is not only a source of income but also evidence of integration and participation in the community. All regions are affected by the incidence and mortality of this kind of trauma globally, yet middle and lower-income areas have the highest occurrence rates, probably due to living conditions, infrastructure, lack of advanced safety measures and access to medical care. Survival rates after severe burns have increased significantly in recent decades, especially in developed countries, due to better treatment of burn shock, more active surgical approaches, more effective infection control, and immune and metabolic status. War operations should also be mentioned when discussing this type of injury as thermal injuries are a significant source of morbidity and mortality in times of war. They constitute 5% to 20% of all injuries and 4% of all

deaths in military personnel. These numbers are doubled in the civilian population[8,9]. The complexity and outcomes of treatment are significantly influenced by the lack of adequate medical care, as well as the specific psychological aspect that accompanies war situations.

THE PSYCHOLOGICAL IMPACT OF THERMAL SKIN INJURIES

Burns are injuries of great medical, scientific, and economic importance and can affect and worsen the physical and mental health of survivors and present significant social challenges, especially for those with more extensive burns[10]. Thermal skin injuries are among the most tragic and catastrophic injuries, almost unsurpassed in terms of severity, morbidity, and mortality, as well as consequences that are functional, aesthetic, social, economic, and psychological. The psychological impact on the patient's health is very pronounced in these injuries. Understanding of trauma-related psychological complications has only recently been directed to burn care. There are several psychopathologic effects related to burn trauma. The range is wide, from acute stress disorder, within the first 30 d, to posttraumatic stress disorder, a reaction that persists longer than 30 days following an incident, to major depressive disorder[11,12]. A long stay in the hospital, intense pain, loss of function, fear of the reaction of the environment, the struggle to accept a new way of life, and many other factors lead to different emotional reactions in burned patients, who are a particularly vulnerable population. Burn survivors face stress, anxiety, depression, body deformity, low self-esteem, and unemployment followed by financial burdens. Social isolation and private, family problems also occur frequently. Burn survivors find it extremely difficult to live with visible scars in a modern society that values physical features and attractiveness. These consequences can lead to body image disaffection, which can cause social anxiety, social withdrawal, and depressive disorder[13]. Anxiety is a common response in burn recovery and to the treatments necessary to heal burned tissue, although the origin of anxiety can be related to the trauma itself. It was noted that most patients with superficial burns suffered from mild anxiety, while patients with deeper burns tended to suffer from severe anxiety. Burn survivors may also be at increased risk for depression due to impairment or loss of function, changes in physical appearance, difficulty managing pain, or time away from social interactions due to prolonged hospitalization and physical rehabilitation. Disfigurement of socially visible areas such as the face and dissatisfaction with the appearance of the body after a burn were found to be associated with the development and maintenance of psychological distress and lower self-esteem. For burn patients, even the common challenges of everyday life may present psychological stress. A previously familiar environment, due to physical and psychological limitations, can seem new and lead to helplessness, hopelessness, and loneliness. The realization that life may not return to the way it was before the injury, could lead to a series of negative feelings, which may result in various psychological disorders[14]. One-third of burn patients experienced a stress disorder, including post-traumatic stress disorder, according to previously published data[15]. Patients with moderate burns can also have psychological consequences, not only severe ones, which can occur even more than a year after the trauma. The emotional trauma caused by burns can affect all areas of a person's life: put stress on relationships, lead to depression or substance abuse, and even put additional strain on their physical health. There is a very high risk of death in burn patients in the first year after the burn, strongly correlated with trauma and mental illness. Burn survivors have a notable need for mental health care, and due to the known and prolonged effect of burn trauma on mental health, patients cannot be considered cured right after the physical healing of the wound[11].

THE PSYCHOLOGICAL CARE FOR BURN PATIENTS

The advances in acute burn care have allowed researchers and physicians to pay more attention to some of the other effects of burns, particularly the psychological consequences. However, planning for physical and psychological rehabilitation after major burns should begin at the time of admission. Recently, great progress has been made in the recognition and treatment of psychological complications caused by these injuries. There has even been a linguistic change in nomenclature, with patients previously categorized as "burn victims" now being referred to as "burn trauma survivors" [16]. An initial focus on physical limitations in burn treatment is necessary, but treatment must also address the psychological trauma that may last longer than physical limitations. Coordinating psychological care for burn patients is challenging, and just as physical recovery occurs in stages, psychological needs vary over time. As the reaction to a burn is very complex, so is the approach to its treatment. This is why burn treatment is a multidisciplinary approach, as the focus is on restoring functionality both physically and mentally. To return to a normal life, patients need an adequate influence on the emotional reactions caused by the burn injury[17]. Along with the conventional approach that involves antidepressants, anxiolytics, and cognitive behavioral therapy, new therapeutic approaches are emerging to address scarring, mental health, and quality of life. New forms of treatment have the effect of improving the outcome of burns both acutely and in the long term, therefore proposing the additional therapeutic protocols, as potentially beneficial.

THE ADJUNCTIVE THERAPEUTIC APPROACHES IN BURN PATIENTS

Among others, hyperbaric oxygen therapy (HBO) has long been used as an adjunctive therapy to promote wound healing. In addition to the benefits that HBO has on the wound healing process, several studies have shown that HBO reduces neuropathic pain caused by burns. Previously published data show that administration of HBO can induce

tolerance to ischemia through the regulation of antioxidative enzymes, suggesting that administration of HBO could also prevent impairment of cognitive functions[18]. In addition, numerous studies stated that antioxidant supplementations for burn patients significantly promote faster wound healing, shorten hospital stays, reduce mortality rate, and decrease the incidence of infection in all cases. At the same time, the administration of antioxidants and trace elements significantly enhances the rate of recovery, prevents complications, and reduces the mortality rate, thus affecting the psychological consequences of burns[19].

CONCLUSION

Taken altogether, the multidimensional importance of thermal injuries and their widespread consequences implies the necessity for a multidisciplinary approach to their treatment. Aside from the significant improvement in routine protocols, it seems useful to take care of simultaneously occurring psychological disturbances that may appear as the most lasting outcome of those injuries. In that sense, future investigations of potential therapeutic protocols to treat thermal skin injury, including both standard and additional protocols, should include the estimation of their action in the brain regions involved in emotional regulations to achieve overall recovery.

FOOTNOTES

Author contributions: Krstic B, Selakovic D, Rosic G designed the overall concept and outline of the manuscript; Krstic M and Jovicic N contributed to the discussion and design of the manuscript; Krstic B, Krstic M, Selakovic D, Jovicic N, Rosic G contributed to the writing, and editing the manuscript, and review of the literature.

Conflict-of-interest statement: Bojana Krstic, Milos Krstic, Dragica Selakovic, Nemanja Jovicic and Gvozden Rosic have nothing to disclose.

Country/Territory of origin: Serbia

ORCID number: Gvozden Rosic 0000-0003-2003-4358.

S-Editor: Lin C
L-Editor: A
P-Editor: Zheng XM

REFERENCES

1 **Ong BB**, Milne N. Milne, Injury, Fatal and Nonfatal: Burns and Scalds. In: Encyclopedia of Forensic and Legal Medicine. 2nd ed. Payne-James J, Byard RW, editors. Amsterdam: Elsevier, 2016: 173-181 [DOI: 10.1016/B978-0-12-800034-2.00220-2]

2 **Brink C**, Isaacs Q, Scriba MF, Nathire MEH, Rode H, Martinez R. Infant burns: A single institution retrospective review. *Burns* 2019; **45**: 1518-1527 [PMID: 30638666 DOI: 10.1016/j.burns.2018.11.005]

3 **Walker NJ**, King KC. Acute and Chronic Thermal Burn Evaluation and Management. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 [PMID: 28613481]

4 **Stokes MAR**, Johnson WD. Burns in the Third World: an unmet need. *Ann Burns Fire Disasters* 2017; **30**: 243-246 [PMID: 29983673]

5 **Forjuoh SN**. Burns in low- and middle-income countries: a review of available literature on descriptive epidemiology, risk factors, treatment, and prevention. *Burns* 2006; **32**: 529-537 [PMID: 16777340 DOI: 10.1016/j.burns.2006.04.002]

6 **Hyder AA**, Sugerman DE, Puvanachandra P, Razzak J, El-Sayed H, Isaza A, Rahman F, Peden M. Global childhood unintentional injury surveillance in four cities in developing countries: a pilot study. *Bull World Health Organ* 2009; **87**: 345-352 [PMID: 19551252 DOI: 10.2471/blt.08.055798]

7 **James SL**, Lucchesi LR, Bisignano C, Castle CD, Dingels ZV, Fox JT, Hamilton EB, Henry NJ, McCracken D, Roberts NLS, Sylte DO, Ahmadi A, Ahmed MB, Alahdab F, Alipour V, Andualem Z, Antonio CAT, Arabloo J, Badiye AD, Bagherzadeh M, Banstola A, Bärnighausen TW, Barzegar A, Bayati M, Bhaumik S, Bijani A, Bukhman G, Carvalho F, Crowe CS, Dalal K, Daryani A, Nasab MD, Do HT, Do HP, Endries AY, Fernandes E, Filip I, Fischer F, Fukumoto T, Gebremedhin KBB, Gebremeskel GG, Gilani SA, Haagsma JA, Hamidi S, Hostiuc S, Househ M, Igumbor EU, Ilesanmi OS, Irvani SSN, Jayatilleke AU, Kahsay A, Kapoor N, Kasaeian A, Khader YS, Khalil IA, Khan EA, Khazaee-Pool M, Kokubo Y, Lopez AD, Madadin M, Majdan M, Maled V, Malekzadeh R, Manafi N, Manafi A, Mangalam S, Massenburg BB, Meles HG, Menezes RG, Meretoja TJ, Miazgowski B, Miller TR, Mohammadian-Hafshejani A, Mohammadpourhodki R, Morrison SD, Negoi I, Nguyen TH, Nguyen SH, Nguyen CT, Nixon MR, Olagunju AT, Olagunju TO, Padubidri JR, Polinder S, Rabiee N, Rabiee M, Radfar A, Rahimi-Movaghar V, Rawaf S, Rawaf DL, Rezapour A, Rickard J, Roro EM, Roy N, Safari-Faramani R, Salamati P, Samy AM, Satpathy M, Sawhney M, Schwebel DC, Senthilkumaran S, Sepanlou SG, Shigematsu M, Soheili A, Stokes MA, Tohidinik HR, Tran BX, Valdez PR,

Wijeratne T, Yisma E, Zaidi Z, Zamani M, Zhang ZJ, Hay SI, Mokdad AH. Epidemiology of injuries from fire, heat and hot substances: global, regional and national morbidity and mortality estimates from the Global Burden of Disease 2017 study. *Inj Prev* 2020; **26**: i36-i45 [PMID: 31857422 DOI: 10.1136/injuryprev-2019-043299]

8 **Roeder RA**, Schulman CI. An overview of war-related thermal injuries. *J Craniofac Surg* 2010; **21**: 971-975 [PMID: 20613571 DOI: 10.1097/SCS.0b013e3181e1e802]

9 **Rizzo JA**, Pruskowski KA, Le T, Gurney J, Rowan MP, Chung KK, Cancio LC. Comparison of military and civilian burn patients admitted to a single center during 12 years of war. *Burns* 2019; **45**: 199-204 [PMID: 30253961 DOI: 10.1016/j.burns.2018.08.026]

10 **Goei H**, Hop MJ, van der Vlies CH, Nieuwenhuis MK, Polinder S, Middelkoop E, van Baar ME; 'Dutch Burn Repository group' consists of. Return to work after specialised burn care: A two-year prospective follow-up study of the prevalence, predictors and related costs. *Injury* 2016; **47**: 1975-1982 [PMID: 27085837 DOI: 10.1016/j.injury.2016.03.031]

11 **Chokshi SN**, Powell CM, Gavrilova Y, Wolf SE, Ozhathil DK. A Narrative Review of the History of Burn-Related Depression and Stress Reactions. *Medicina (Kaunas)* 2022; **58** [PMID: 36295556 DOI: 10.3390/medicina58101395]

12 **Dalal PK**, Saha R, Agarwal M. Psychiatric aspects of burn. *Indian J Plast Surg* 2010; **43**: S136-S142 [PMID: 21321649 DOI: 10.4103/0970-0358.70731]

13 **Jain M**, Khadilkar N, De Sousa A. Burn-related factors affecting anxiety, depression and self-esteem in burn patients: an exploratory study. *Ann Burns Fire Disasters* 2017; **30**: 30-34 [PMID: 28592931]

14 **Bhatti DS**, Ul Ain N, Zulkiffal R, Al-Nabulsi ZS, Faraz A, Ahmad R. Anxiety and Depression Among Non-Facial Burn Patients at a Tertiary Care Center in Pakistan. *Cureus* 2020; **12**: e11347 [PMID: 33304682 DOI: 10.7759/cureus.11347]

15 **Sadeghi-Bazargani H**, Maghsoudi H, Soudmand-Niri M, Ranjbar F, Mashadi-Abdollahi H. Stress disorder and PTSD after burn injuries: a prospective study of predictors of PTSD at Sina Burn Center, Iran. *Neuropsychiatr Dis Treat* 2011; **7**: 425-429 [PMID: 21857783 DOI: 10.2147/NDT.S23041]

16 **Jeschke MG**, van Baar ME, Choudhry MA, Chung KK, Gibran NS, Logsetty S. Burn injury. *Nat Rev Dis Primers* 2020; **6**: 11 [PMID: 32054846 DOI: 10.1038/s41572-020-0145-5]

17 **Roshangar L**, Soleimani Rad J, Kheirjou R, Reza Ranjkesh M, Ferdowsi Khosroshahi A. Skin Burns: Review of Molecular Mechanisms and Therapeutic Approaches. *Wounds* 2019; **31**: 308-315 [PMID: 31730513]

18 **Niinikoski JH**. Clinical hyperbaric oxygen therapy, wound perfusion, and transcutaneous oximetry. *World J Surg* 2004; **28**: 307-311 [PMID: 14961187 DOI: 10.1007/s00268-003-7401-1]

19 **Sahib AS**, Al-Jawad FH, Alkaisy AA. Effect of antioxidants on the incidence of wound infection in burn patients. *Ann Burns Fire Disasters* 2010; **23**: 199-205 [PMID: 21991225]

World Journal of Psychiatry

Submit a Manuscript: https://www.f6publishing.com

World J Psychiatry 2024 February 19; 14(2): 204-209

DOI: 10.5498/wjp.v14.i2.204

ISSN 2220-3206 (online)

EDITORIAL

Climate change, ambient air pollution, and students' mental health

Jing-Xuan Wang, Xin-Qiao Liu

Specialty type: Psychiatry

Provenance and peer review: Invited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

Grade A (Excellent): 0
Grade B (Very good): 0
Grade C (Good): C
Grade D (Fair): 0
Grade E (Poor): 0

P-Reviewer: Wood AM, United Kingdom

Received: November 29, 2023
Peer-review started: November 30, 2023
First decision: December 23, 2023
Revised: December 29, 2023
Accepted: January 23, 2024
Article in press: January 23, 2024
Published online: February 19, 2024

Jing-Xuan Wang, Xin-Qiao Liu, School of Education, Tianjin University, Tianjin 300350, China

Corresponding author: Xin-Qiao Liu, PhD, Associate Professor, School of Education, Tianjin University, No. 135 Yaguan Road, Jinnan District, Tianjin 300350, China.
xinqiaoliu@pku.edu.cn

Abstract

The impact of global climate change and air pollution on mental health has become a crucial public health issue. Increased public awareness of health, advancements in medical diagnosis and treatment, the way media outlets report environmental changes and the variation in social resources affect psychological responses and adaptation methods to climate change and air pollution. In the context of climate change, extreme weather events seriously disrupt people's living environments, and unstable educational environments lead to an increase in mental health issues for students. Air pollution affects students' mental health by increasing the incidence of diseases while decreasing contact with nature, leading to problems such as anxiety, depression, and decreased cognitive function. We call for joint efforts to reduce pollutant emissions at the source, improve energy structures, strengthen environmental monitoring and governance, increase attention to the mental health issues of students, and help student groups build resilience; by establishing public policies, enhancing social support and adjusting lifestyles and habits, we can help students cope with the constantly changing environment and maintain a good level of mental health. Through these comprehensive measures, we can more effectively address the challenges of global climate change and air pollution and promote the achievement of the United Nations Sustainable Development Goals.

Key Words: Climate change; Ambient air pollution; Mental health; Energy structure; Public policy; Sustainable development

Core Tip: Global climate change and air pollution are becoming increasingly important issues in the field of public health and are exerting complex impacts on mental well-being. Extreme climate events and air pollution not only disrupt living environments, triggering the emergence of psychological conditions such as "ecological anxiety" but also exacerbate anxiety, depression, and other psychological problems. In response to this challenge, nations should begin to reduce pollutant emissions and improve energy structures, and society needs to strengthen environmental regulations and establish supportive public policies. Additionally, individuals should maintain good mental health and collectively contribute to achieving the United Nations Sustainable Development Goals.

Citation: Wang JX, Liu XQ. Climate change, ambient air pollution, and students' mental health. *World J Psychiatry* 2024; 14(2): 204-209
URL: https://www.wjgnet.com/2220-3206/full/v14/i2/204.htm
DOI: https://dx.doi.org/10.5498/wjp.v14.i2.204

INTRODUCTION

To address a series of social, economic, and environmental issues faced worldwide, the United Nations has proposed the Sustainable Development Goals, which call for urgent action to address climate change and its impacts, ensure healthy lifestyles, and promote the well-being of people of all ages. The Sustainable Development Goals emphasize the urgency of maintaining the environment and human health at a global level. Recently, Hu *et al*[1] explored the impact of meteorological factors and air pollution on depression incidence. Their study revealed that both meteorological factors and the air pollutant nitrogen dioxide influence daily hospitalization rates among individuals with depression, and there is an interaction between meteorological factors and environmental air pollution. The findings of Hu *et al*[1] offer important references for further analyzing the relationships among climate change, environmental air pollution, and mental health.

In recent years, with the continuous increase in energy consumption and greenhouse gas emissions, air pollution has become more severe, and the climate is continually changing, leading people worldwide to increasingly suffer from the impacts of extreme weather events[2]. Issues such as resource scarcity, poor living conditions, and displacement are becoming increasingly prominent. In some areas, people suffer from serious disease due to environmental pollution, which not only causes considerable disturbances in their lives but also poses a great threat to their mental health. In the face of climate change and environmental issues, negative emotions such as depression, anxiety, and stress frequently occur. The learning environment of students is destabilized by extreme weather, physical health problems are caused by air pollution, and media reports on environmental pollution create a sense of existential crisis, leading to a continuous increase in psychological distress. These factors have a profound negative impact on students' daily academic lives. This has led to the realization that, in addition to traditional factors such as genetics[3], childhood environment[4], personal personality[5], and peer relationships[6], the impact of climate change and environmental air pollution on students' mental health cannot be ignored. How to maintain a healthy psychological state is currently a concern. A healthy psychological state can help students realize their personal potential, cope with various pressures in daily work and life, and reduce the adverse effects of negative emotions on the body[7]. Improvements in mental health can enhance people's quality of life, public health, and productivity[8]. Furthermore, students with good mental health are more likely to actively participate in social activities, which has a profound impact on social and economic development. Therefore, good mental health is very important for students' personal growth, economic progress, and sustainable social development.

THE IMPACT OF CLIMATE CHANGE ON MENTAL HEALTH

Global climate change, characterized by extreme weather events such as floods, droughts, hurricanes, and blizzards, leads to the destruction of living environments and poses threats to physical and mental health. Events such as injuries, deaths of loved ones, and illness increase the likelihood of mental disorders[9,10]. "Ecological anxiety" and "ecological grief" also affect people's mental health[11,12].

Different types of extreme weather events negatively impact mental health in varying ways. In the aftermath of floods or hurricanes, individuals are susceptible to illnesses such as colds, coughs, rashes, and gastrointestinal infections. From a neurobiological perspective, traumatic experiences associated with flooding can lead to overactivation of the brain's stress response system, impacting the long-term balance of neurotransmitters such as serotonin and norepinephrine[13,14]. Increasing environmental temperatures may lead to an increase in the incidence of personal attacks, homicides[15,16], and suicide[17]. In Bern, Switzerland, for every 10 °C increase in the average daily temperature due to global warming, the risk of mental health disorders increases linearly by 4%[18]. When the average Wet Bulb Globe Temperature index reaches 35 °C, overheating can occur in temperature-sensitive areas of the brain and thyroid hormones are inhibited, leading to functional hypothyroidism, which affects psychological functions and emotional regulation[19]. When temperatures exceed 26.7 °C, the number of hospitalizations for mental health disorders increases[20]. For people with existing mental health issues, heatwaves can exacerbate underlying psychiatric and behavioral disorders, increasing their risk of death by more than three times[21,22]. Research conducted by Hackbarth *et al*[23] demonstrated that individuals who

experience meteorological disasters often face drastic lifestyle changes and resource shortages. These challenges lead not only to a scarcity of material resources but also to a weakened sense of community belonging and disturbances in individual self-identity, thereby increasing the risk of posttraumatic stress disorder. Additionally, a study by Rataj *et al* [24] indicated that residents of low- and middle-income countries are more susceptible to the impacts of extreme weather events.

Moreover, extreme weather causes transportation difficulties, and restrictions on individual activities disrupt the normal lives and social activities of students, easily triggering anxiety and leading to a sense of social isolation. This anxiety and social isolation further exacerbate mental health issues[25]. The frequent occurrence of extreme weather events, which can be sudden and unpredictable, leads to uncertainty and fear about the future. This sense of hopelessness and powerlessness can lead to escapism, negatively impacting mental health. The environmental deterioration caused by climate change may force people to relocate, losing their original social networks and community ties[26], which leads to instability in students' learning environments and adversely affects their mental health.

THE IMPACT OF AMBIENT AIR POLLUTION ON MENTAL HEALTH

The detrimental effects of air pollution on mental health cannot be overlooked. Air pollution is currently one of the most impactful environmental health risks worldwide. It arises not only from industrial emissions and vehicle exhaust but also from agricultural activities and household burning. As a major environmental issue, air pollution substantially impacts people's physical and mental health[27]. The World Health Organization (WHO) reports that 91% of the global population lives in places where the air quality exceeds WHO guideline limits, with 4.2 million premature deaths caused by environmental air pollution. Air pollutants are considered one of the most critical risk factors affecting mental health [28].

On the one hand, air pollution contains numerous toxic substances, such as fine particulate matter ($PM_{2.5}$), NO_2, and SO_x, posing a direct threat to human health and leading to respiratory and cardiovascular diseases[29]. Epidemiological studies have shown that air pollutants such as $PM_{2.5}$ and PM_{10} are associated with an increased risk of mental health issues. Short-term exposure to these environmental particulates can lead to an increase in symptoms of mental health problems, such as depression and anxiety[30]. Particulate matter can travel through the respiratory tract to the brain, causing inflammation. This inflammation can lead to changes in brain activity and pathological function, ultimately affecting cognitive ability. Prolonged exposure to high concentrations of air pollution may cause neurodegenerative changes and increase the risk of mental and behavioral disorders[31]. Air pollution affects mental health levels by increasing the incidence and severity of diseases.

On the other hand, according to the biophilia hypothesis, humans have an inherent inclination to connect with nature and other life forms. In highly urbanized areas or environments that lack green spaces, air pollution reduces students' contact with nature, which may lead to issues such as anxiety, depression, and cognitive decline[32]. Due to limited outdoor activities, students' social interactions are impacted, which may lead to a decline in social skills, an increase in feelings of loneliness, and a weakening of community cohesion. This social isolation not only affects individuals' emotional states but can also impact the stability of social relationships. Regular physical activity has been suggested to have a positive effect on reducing anxiety and depression in students, as well as improving mood and self-esteem[33]. Air pollution also leads to a lack of regular physical exercise for many people, directly impacting their physical health and, consequently, their mental health. In addition to its general impact on students' mental health, air pollution has a more severe effect on specific groups. Men, rural residents, and individuals with lower income and education levels may be more susceptible to the negative effects of air pollution due to their specific socioeconomic status and environmental exposure[34,35]. Long-term exposure of children to pollutants can affect brain development and function, leading to learning disabilities, attention deficits, and memory loss[36]. The impact of air pollution on children may have adverse effects on the future education of the country.

CONCLUSION

With the current global trend of climate warming, we are facing an increasingly severe environmental and health crisis. To effectively address this global health crisis, it is imperative to take measures in the following areas to maintain students' mental health.

First, it is crucial to reduce pollutant emissions at the source, improve energy structures, enhance energy efficiency, and strengthen environmental monitoring and governance. The fundamental causes of meteorological changes and air pollution are the extensive greenhouse gas emissions generated during the industrialization process, mainly from burning fossil fuels. The urban heat island effect, exacerbated by rapid urbanization, also intensifies climate change. In daily life, the widespread use of private vehicles and the application of fertilizers and pesticides in agriculture contribute substantially to greenhouse gas emissions. Therefore, it is necessary to reduce pollutant emissions at their source; accelerate the transition from fossil fuels to renewable energy sources such as solar power, wind power, and hydropower; and promote high-quality socioeconomic development through green initiatives. Relevant societal sectors need to promote green building standards and technologies to reduce building energy consumption and mitigate the urban heat island effect while enhancing environmental monitoring and governance. Additionally, the public should be encouraged to increase their awareness of environmental protection, adopt healthier lifestyles, reduce greenhouse gas emissions, and implement more environmentally friendly production and consumption patterns to alleviate the negative impact of the

environment on mental health.

Second, attention must be given to students' mental health issues. By establishing public policies and strengthening social support, we can help students build resilience, reduce the psychological impact of climate change and environmental pollution and ensure students' growth and learning in a healthy environment. Public policies play a crucial role in increasing awareness of mental health and reducing environmental pollution. Additionally, social support systems are key for providing sociopsychological health services and maintaining individual mental health, assisting students in coping with psychological distress and enhancing overall mental well-being. Implementing material use interventions in educational environments can effectively alleviate mental health issues among students[37]. Support from families, friends, and communities can also help students cope with the stress and challenges brought about by environmental changes. A crucial aspect of addressing the potential negative psychological impacts of climate change is building resilience. Relevant authorities should guide professional rescuers to help students develop psychological resilience and utilize their social networks.

Finally, students need to adjust their lifestyles and habits to cope with the constantly changing environment and maintain a good level of mental health. Artificial intelligence-assisted screening for psychiatric risks can help students maintain sound mental health[38]. Good mental health enables students to adapt better to environmental changes. Individuals with healthy mental states are more adept at accepting lifestyle changes brought about by environmental degradation and maintaining a positive and optimistic attitude during the adaptation process. Mental health is closely linked to physical health, and physical exercise plays a vital role in maintaining mental well-being. Exercise not only increases hormone levels, such as those of endorphins and brain-derived neurotrophic factors, which reduce stress, but also helps alleviate mood disorders[39]. The maintenance and improvement of mental health are related to the intensity and frequency of physical exercise, and frequent high-intensity physical exercise is beneficial for maintaining mental health[40]. In adverse weather conditions, interactive sports games, such as simulated football, tennis, and running, can be played through electronic devices to maintain the continuity of physical activity. Moreover, maintaining normal social activities is equally important for students' mental health.

In summary, in the face of climate change and environmental challenges, maintaining and promoting individual mental health among students is crucial. Comprehensive measures are needed, ranging from reducing greenhouse gas emissions to providing mental health services. These actions are not only key to achieving students' mental health and well-being but also vital components of promoting overall sustainable social development. Through such integrated approaches, we can more effectively confront the challenges posed by global climate change and air pollution, fulfilling the vision of the United Nations Sustainable Development Goals related to health and climate action and thus contributing to building a healthier, more sustainable future.

FOOTNOTES

Author contributions: Liu XQ designed the study, and Liu XQ and Wang JX wrote the manuscript; All the authors contributed equally to this work and have approved the final manuscript.

Conflict-of-interest statement: All the authors report no relevant conflicts of interest for this article.

Country/Territory of origin: China

ORCID number: Xin-Qiao Liu 0000-0001-6620-4119.

S-Editor: Li L
L-Editor: A
P-Editor: Li L

REFERENCES

1 **Hu T**, Xu ZY, Wang J, Su Y, Guo BB. Meteorological factors, ambient air pollution, and daily hospital admissions for depressive disorder in Harbin: A time-series study. *World J Psychiatry* 2023; **13**: 1061-1078 [PMID: 38186723 DOI: 10.5498/wjp.v13.i12.1061]

2 **Lawrance EL**, Thompson R, Newberry Le Vay J, Page L, Jennings N. The Impact of Climate Change on Mental Health and Emotional Wellbeing: A Narrative Review of Current Evidence, and its Implications. *Int Rev Psychiatry* 2022; **34**: 443-498 [PMID: 36165756 DOI: 10.1080/09540261.2022.2128725]

3 **Al-Mubarak B**, Abouelhoda M, Omar A, AlDhalaan H, Aldosari M, Nester M, Alshamrani HA, El-Kalioby M, Goljan E, Albar R, Subhani S, Tahir A, Asfahani S, Eskandrani A, Almusaiab A, Magrashi A, Shinwari J, Monies D, Al Tassan N. Whole exome sequencing reveals inherited and de novo variants in autism spectrum disorder: a trio study from Saudi families. *Sci Rep* 2017; **7**: 5679 [PMID: 28720891 DOI: 10.1038/s41598-017-06033-1]

4 **Bomysoad RN**, Francis LA. Adverse Childhood Experiences and Mental Health Conditions Among Adolescents. *J Adolesc Health* 2020; **67**:

868-870 [PMID: 32576484 DOI: 10.1016/j.jadohealth.2020.04.013]
5 **Liu XQ**, Zhang YF, Gao WJ, Cao XJ. Developmental trajectories of depression, anxiety, and stress among college students: a piecewise growth mixture model analysis. *Humanit Soc Sci Commun* 2023; **10**: 736 [DOI: 10.1057/s41599-023-02252-2]
6 **Bradshaw CP**, Haynes KT. Building a science of partnership-focused research: forging and sustaining partnerships to support child mental health prevention and services research. *Adm Policy Ment Health* 2012; **39**: 221-224 [PMID: 22696183 DOI: 10.1007/s10488-012-0427-7]
7 **Fredrickson BL**, Levenson RW. Positive Emotions Speed Recovery from the Cardiovascular Sequelae of Negative Emotions. *Cogn Emot* 1998; **12**: 191-220 [PMID: 21852890 DOI: 10.1080/026999398379718]
8 **Herrman H**. The need for mental health promotion. *Aust N Z J Psychiatry* 2001; **35**: 709-715 [PMID: 11990880 DOI: 10.1046/j.1440-1614.2001.00947.x]
9 **Hayes K**, Blashki G, Wiseman J, Burke S, Reifels L. Climate change and mental health: risks, impacts and priority actions. *Int J Ment Health Syst* 2018; **12**: 28 [PMID: 29881451 DOI: 10.1186/s13033-018-0210-6]
10 **Ebi KL**, Vanos J, Baldwin JW, Bell JE, Hondula DM, Errett NA, Hayes K, Reid CE, Saha S, Spector J, Berry P. Extreme Weather and Climate Change: Population Health and Health System Implications. *Annu Rev Public Health* 2021; **42**: 293-315 [PMID: 33406378 DOI: 10.1146/annurev-publhealth-012420-105026]
11 **Cunsolo A**, Ellis NR. Ecological grief as a mental health response to climate change-related loss. *Nat Clim Chang* 2018; **8**: 275-281 [DOI: 10.1038/s41558-018-0092-2]
12 **Palinkas LA**, Wong M. Global climate change and mental health. *Curr Opin Psychol* 2020; **32**: 12-16 [PMID: 31349129 DOI: 10.1016/j.copsyc.2019.06.023]
13 **Zhong S**, Yang L, Toloo S, Wang Z, Tong S, Sun X, Crompton D, FitzGerald G, Huang C. The long-term physical and psychological health impacts of flooding: A systematic mapping. *Sci Total Environ* 2018; **626**: 165-194 [PMID: 29339262 DOI: 10.1016/j.scitotenv.2018.01.041]
14 **Crane K**, Li L, Subramanian P, Rovit E, Liu J. Climate Change and Mental Health: A Review of Empirical Evidence, Mechanisms and Implications. *Atmosphere (Basel)* 2022; **13** [PMID: 37727770 DOI: 10.3390/atmos13122096]
15 **Stevens HR**, Beggs PJ, Graham PL, Chang HC. Hot and bothered? Associations between temperature and crime in Australia. *Int J Biometeorol* 2019; **63**: 747-762 [PMID: 30830288 DOI: 10.1007/s00484-019-01689-y]
16 **Younan D**, Li L, Tuvblad C, Wu J, Lurmann F, Franklin M, Berhane K, McConnell R, Wu AH, Baker LA, Chen JC. Long-Term Ambient Temperature and Externalizing Behaviors in Adolescents. *Am J Epidemiol* 2018; **187**: 1931-1941 [PMID: 29788079 DOI: 10.1093/aje/kwy104]
17 **Pervilhac C**, Schoilew K, Znoj H, Müller TJ. [Weather and suicide: Association between meteorological variables and suicidal behavior-a systematic qualitative review article]. *Nervenarzt* 2020; **91**: 227-232 [PMID: 31468092 DOI: 10.1007/s00115-019-00795-x]
18 **Bundo M**, de Schrijver E, Federspiel A, Toreti A, Xoplaki E, Luterbacher J, Franco OH, Müller T, Vicedo-Cabrera AM. Ambient temperature and mental health hospitalizations in Bern, Switzerland: A 45-year time-series study. *PLoS One* 2021; **16**: e0258302 [PMID: 34637463 DOI: 10.1371/journal.pone.0258302]
19 **Norloei S**, Jafari MJ, Omidi L, Khodakarim S, Bashash D, Abdollahi MB, Jafari M. The effects of heat stress on a number of hematological parameters and levels of thyroid hormones in foundry workers. *Int J Occup Saf Ergon* 2017; **23**: 481-490 [PMID: 27882829 DOI: 10.1080/10803548.2016.1246122]
20 **Hansen A**, Bi P, Nitschke M, Ryan P, Pisaniello D, Tucker G. The effect of heat waves on mental health in a temperate Australian city. *Environ Health Perspect* 2008; **116**: 1369-1375 [PMID: 18941580 DOI: 10.1289/ehp.11339]
21 **Bouchama A**, Dehbi M, Mohamed G, Matthies F, Shoukri M, Menne B. Prognostic factors in heat wave related deaths: a meta-analysis. *Arch Intern Med* 2007; **167**: 2170-2176 [PMID: 17698676 DOI: 10.1001/archinte.167.20.ira70009]
22 **Schmeltz MT**, Gamble JL. Risk characterization of hospitalizations for mental illness and/or behavioral disorders with concurrent heat-related illness. *PLoS One* 2017; **12**: e0186509 [PMID: 29036206 DOI: 10.1371/journal.pone.0186509]
23 **Hackbarth M**, Pavkov T, Wetchler J, Flannery M. Natural disasters: an assessment of family resiliency following Hurricane Katrina. *J Marital Fam Ther* 2012; **38**: 340-351 [PMID: 22512296 DOI: 10.1111/j.1752-0606.2011.00227.x]
24 **Rataj E**, Kunzweiler K, Garthus-Niegel S. Extreme weather events in developing countries and related injuries and mental health disorders - a systematic review. *BMC Public Health* 2016; **16**: 1020 [PMID: 27682833 DOI: 10.1186/s12889-016-3692-7]
25 **Deglon M**, Dalvie MA, Abrams A. The impact of extreme weather events on mental health in Africa: A scoping review of the evidence. *Sci Total Environ* 2023; **881**: 163420 [PMID: 37054787 DOI: 10.1016/j.scitotenv.2023.163420]
26 **Salcoğlu E**, Başoğlu M, Livanou M. Psychosocial determinants of relocation in survivors of the 1999 earthquake in Turkey. *J Nerv Ment Dis* 2008; **196**: 55-61 [PMID: 18195642 DOI: 10.1097/NMD.0b013e31815fa52e]
27 **Landrigan PJ**. Air pollution and health. *Lancet Public Health* 2017; **2**: e4-e5 [PMID: 29249479 DOI: 10.1016/S2468-2667(16)30023-8]
28 **Mallet J**, Huillard O, Goldwasser F, Dubertret C, Le Strat Y. Mental disorders associated with recent cancer diagnosis: Results from a nationally representative survey. *Eur J Cancer* 2018; **105**: 10-18 [PMID: 30388660 DOI: 10.1016/j.ejca.2018.09.038]
29 **Yohannes AM**, Willgoss TG, Baldwin RC, Connolly MJ. Depression and anxiety in chronic heart failure and chronic obstructive pulmonary disease: prevalence, relevance, clinical implications and management principles. *Int J Geriatr Psychiatry* 2010; **25**: 1209-1221 [PMID: 20033905 DOI: 10.1002/gps.2463]
30 **Song J**, Zheng L, Lu M, Gui L, Xu D, Wu W, Liu Y. Acute effects of ambient particulate matter pollution on hospital admissions for mental and behavioral disorders: A time-series study in Shijiazhuang, China. *Sci Total Environ* 2018; **636**: 205-211 [PMID: 29704715 DOI: 10.1016/j.scitotenv.2018.04.187]
31 **Calderón-Garcidueñas L**, Franco-Lira M, Henríquez-Roldán C, Osnaya N, González-Maciel A, Reynoso-Robles R, Villarreal-Calderon R, Herritt L, Brooks D, Keefe S, Palacios-Moreno J, Torres-Jardón R, Medina-Cortina H, Delgado-Chávez R, Aiello-Mora M, Maronpot RR, Doty RL. Urban air pollution: influences on olfactory function and pathology in exposed children and young adults. *Exp Toxicol Pathol* 2010; **62**: 91-102 [PMID: 19297138 DOI: 10.1016/j.etp.2009.02.117]
32 **Xue T**, Zhu T, Zheng Y, Zhang Q. Declines in mental health associated with air pollution and temperature variability in China. *Nat Commun* 2019; **10**: 2165 [PMID: 31092825 DOI: 10.1038/s41467-019-10196-y]
33 **Herbert C**, Meixner F, Wiebking C, Gilg V. Regular Physical Activity, Short-Term Exercise, Mental Health, and Well-Being Among University Students: The Results of an Online and a Laboratory Study. *Front Psychol* 2020; **11**: 509 [PMID: 32528333 DOI: 10.3389/fpsyg.2020.00509]
34 **Forastiere F**, Stafoggia M, Tasco C, Picciotto S, Agabiti N, Cesaroni G, Perucci CA. Socioeconomic status, particulate air pollution, and daily mortality: differential exposure or differential susceptibility. *Am J Ind Med* 2007; **50**: 208-216 [PMID: 16847936 DOI: 10.1002/ajim.20368]
35 **Wang R**, Liu J, Qin Y, Chen Z, Li J, Guo P, Shan L, Li Y, Hao Y, Jiao M, Qi X, Meng N, Jiang S, Kang Z, Wu Q. Global attributed burden of

death for air pollution: Demographic decomposition and birth cohort effect. *Sci Total Environ* 2023; **860**: 160444 [PMID: 36435245 DOI: 10.1016/j.scitotenv.2022.160444]

36 **Watts N**, Amann M, Arnell N, Ayeb-Karlsson S, Belesova K, Boykoff M, Byass P, Cai W, Campbell-Lendrum D, Capstick S, Chambers J, Dalin C, Daly M, Dasandi N, Davies M, Drummond P, Dubrow R, Ebi KL, Eckelman M, Ekins P, Escobar LE, Fernandez Montoya L, Georgeson L, Graham H, Haggar P, Hamilton I, Hartinger S, Hess J, Kelman I, Kiesewetter G, Kjellstrom T, Kniveton D, Lemke B, Liu Y, Lott M, Lowe R, Sewe MO, Martinez-Urtaza J, Maslin M, McAllister L, McGushin A, Jankin Mikhaylov S, Milner J, Moradi-Lakeh M, Morrissey K, Murray K, Munzert S, Nilsson M, Neville T, Oreszczyn T, Owfi F, Pearman O, Pencheon D, Phung D, Pye S, Quinn R, Rabbaniha M, Robinson E, Rocklöv J, Semenza JC, Sherman J, Shumake-Guillemot J, Tabatabaei M, Taylor J, Trinanes J, Wilkinson P, Costello A, Gong P, Montgomery H. The 2019 report of The Lancet Countdown on health and climate change: ensuring that the health of a child born today is not defined by a changing climate. *Lancet* 2019; **394**: 1836-1878 [PMID: 31733928 DOI: 10.1016/S0140-6736(19)32596-6]

37 **Liu XQ**, Guo YX, Wang X. Delivering substance use prevention interventions for adolescents in educational settings: A scoping review. *World J Psychiatry* 2023; **13**: 409-422 [PMID: 37547731 DOI: 10.5498/wjp.v13.i7.409]

38 **Cao XJ**, Liu XQ. Artificial intelligence-assisted psychosis risk screening in adolescents: Practices and challenges. *World J Psychiatry* 2022; **12**: 1287-1297 [PMID: 36389087 DOI: 10.5498/wjp.v12.i10.1287]

39 **Chavda VP**, Vuppu S, Mishra T, Stojanovska L, Apostolopoulos V. Importance of mental health and exercise in the tough time of viral outbreaks. *Maturitas* 2023; **176**: 107751 [PMID: 37002055 DOI: 10.1016/j.maturitas.2023.03.004]

40 **Ai X**, Yang J, Lin Z, Wan X. Mental Health and the Role of Physical Activity During the COVID-19 Pandemic. *Front Psychol* 2021; **12**: 759987 [PMID: 34744938 DOI: 10.3389/fpsyg.2021.759987]

World Journal of Psychiatry

Submit a Manuscript: https://www.f6publishing.com

World J Psychiatry 2024 February 19; 14(2): 210-214

DOI: 10.5498/wjp.v14.i2.210

ISSN 2220-3206 (online)

EDITORIAL

Catatonia: A deep dive into its unfathomable depths

Peter Phiri, Gayathri Delanerolle, Oliver Hope, Tharangini Murugaiyan, Geoffrey Dimba, Shanaya Rathod, Zukiswa Zingela

Specialty type: Psychiatry

Provenance and peer review: Invited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

Grade A (Excellent): 0
Grade B (Very good): B, B
Grade C (Good): 0
Grade D (Fair): 0
Grade E (Poor): 0

P-Reviewer: Pitton Rissardo J, United States; Zhang JW, China

Received: December 7, 2023
Peer-review started: December 7, 2023
First decision: December 17, 2023
Revised: December 22, 2023
Accepted: January 18, 2024
Article in press: January 18, 2024
Published online: February 19, 2024

Peter Phiri, Gayathri Delanerolle, Oliver Hope, Shanaya Rathod, Research & Innovation Department, Southern Health NHS Foundation Trust, Southampton SO30 3JB, United Kingdom

Peter Phiri, School of Psychology, Faculty of Environmental and Life Sciences, University of Southampton, Southampton SO17 1BJ, Hampshire, United Kingdom

Tharangini Murugaiyan, Acute Inpatients Services, Southern Health NHS Foundation Trust, Basingstoke RG24 9RH, United Kingdom

Geoffrey Dimba, Home Treatment Team, South West, Surrey and Borders Partnerships NHS Foundation Trust, Guildford GU2 7XL, Surrey, United Kingdom

Zukiswa Zingela, Faculty of Health Sciences, Nelson Mandela University, Summerstrand 6001, Gqeberha, South Africa

Corresponding author: Peter Phiri, BSc, PhD, RN, Academic Research, Director, Research Fellow, Research & Innovation Department, Southern Health NHS Foundation Trust, Botley Road, Southampton SO30 3JB, United Kingdom. peter.phiri@southernhealth.nhs.uk

Abstract

This editorial addresses catatonia, a complex neuropsychiatric syndrome characterised by a spectrum of psychomotor disturbances. The editorial seeks to clarify the ambiguous aspects of catatonia, integrating recent research findings, including global studies and diagnostic advancements. It discusses catatonia's clinical manifestations, prevalence, and associated psychiatric and medical conditions, with particular emphasis on its frequent co-occurrence with schizophrenia and mood disorders. The prevalence of catatonia, which varies across psychiatric populations, is illustrated by a significant study conducted in Nelson Mandela Bay, South Africa. This study provides valuable insights into the effectiveness of the Bush-Francis Screening Instrument compared to the Diagnostic and Statistical Manual 5 criteria in diagnosing catatonia. The editorial evaluates treatment approaches, primarily focusing on benzodiazepines and electroconvulsive therapy, and discusses emerging therapeutic strategies. It underscores the importance of robust diagnostic frameworks and early intervention in managing catatonia, as recommended by the latest evidence-based consensus guideline. Furthermore, it suggests future research directions, particularly in exploring the neurobiological and genetic factors of catatonia, to enhance our understanding and improve treatment outcomes. This editorial succinctly aims to demystify catatonia and provide valuable insights for clinicians and researchers in mental health care.

Key Words: Catatonia; Schizophrenia; Neuropsychiatry; Benzodiazepines; Electroconvulsive therapy; Bush-Francis screening instrument; Diagnosis

Core Tip: This editorial illuminates the complex nature of catatonia, emphasising its varied psychomotor symptoms. It highlights challenges in diagnosis, noting the effectiveness of the Bush-Francis screening instrument over the Diagnostic and Statistical Manual 5 criteria, and discusses the syndrome's prevalence and associations with disorders like schizophrenia and mood disorders. Furthermore, it critically examines mainstay treatments such as benzodiazepines and electroconvulsive therapy and advocates for strong diagnostic criteria and prompt intervention. It calls for further research into catatonia's neurobiological and genetic aspects, aiming to advance mental health care outcomes.

Citation: Phiri P, Delanerolle G, Hope O, Murugaiyan T, Dimba G, Rathod S, Zingela Z. Catatonia: A deep dive into its unfathomable depths. *World J Psychiatry* 2024; 14(2): 210-214
URL: https://www.wjgnet.com/2220-3206/full/v14/i2/210.htm
DOI: https://dx.doi.org/10.5498/wjp.v14.i2.210

INTRODUCTION

Catatonia, a complex and multifaceted neuropsychiatric condition, manifests through a range of psychomotor abnormalities from hypoactivity to hyperactivity. Its deep entanglement with various psychiatric and medical disorders not only underscores its clinical importance but also complicates its comprehension and treatment. This editorial delves into the diverse aspects of catatonia, encompassing its clinical manifestations, prevalence, distinctive characteristics, and evolving therapeutic approaches. The aim is to demystify catatonia's complexities and offer a clearer understanding of this intriguing condition. By synthesizing the latest research and clinical insights, this review strives to present a thorough and nuanced view of catatonia, ultimately enriching our knowledge and treatment strategies in mental health care.

PRESENTATION

Catatonia exhibits a spectrum of psychomotor abnormalities, encompassing hyperactivity states to hypo-activity manifestations. The classical portrayal of catatonia encompasses catalepsy, waxy flexibility, and stupor, alongside other symptoms like mutism, negativism, and echophenomena[1]. Catatonia has been historically correlated with schizophrenia, and was classed as a subtype of schizophrenia, however catatonic symptoms are also seen in bipolar disorder, major depressive disorder[2], and a range of neurological conditions, both acquired, like encephalitis, and congenital, like autism spectrum disorder[3], as well as other systemic conditions, most frequently autoimmune and inflammatory diseases. Withdrawal syndromes from multiple classes of psychoactive medications have also been associated with catatonia, including benzodiazepines, a mainstay of the treatment of catatonia, and other gamma-aminobutyric acid (GABA) agonists.

PREVALENCE

The prevalence of catatonia portrays a varied landscape, with estimates ranging between 7% to 38% among psychiatric populations, with certain subgroups, showing particularly increased prevalence rates in those with mood disorders or psychosis, learning differences, learning disabilities and cognitive impairment[4,5].

Within the African context, Zingela *et al*'s notable study conducted in Nelson Mandela Bay, South Africa, unveiled a prevalence rate of 18.3% within an acute mental health unit[6]. The authors argued that a wide-ranging prevalence rates, from less than 10% to just above 60%, accentuated the crucial role of effective diagnostic tools in ascertaining accurate prevalence rates.

CHARACTERISTICS

Although, the etiological underpinnings of catatonia remain elusive, it is often associated with a myriad of psychiatric and medical conditions. While no definitive causative process has been identified, potential contributory factors include genetic predispositions, changes in regional activity of areas of the brain, especially those to do with movement initiation

and perception of movement, significant life changes, and certain medical conditions like autoimmune diseases, stroke, encephalitis, delirium, and metabolic abnormalities[2,7].

In schizophrenia, catatonia - which represents itself through complicated disturbances in movement and psychomotor behaviour, is one of six classified types of abnormal motor functions. It envelops a range of motor behaviours including decreased, increased, and abnormal movements, disturbances of volition, and autonomic instability. The intertwined relationship between schizophrenia, mood disorders, other mental disorders and catatonia unveils a layer of complexity, further enriching the clinical tableau of catatonia[8]. The neurobiological framework of catatonia is hypothesised to be rooted in the dysfunction of GABA and glutamate neurotransmitter systems[8,9]. A characteristic pattern is that of hypo and hyperactivity in regions of the brain including the premotor cortex, orbitofrontal cortex and supplementary motor cortex[10]. Differing levels of electrical stimulation to these areas have been shown to disrupt the formation of motor impulses, or the perception of motor function, leading to a paralysis without distress, further correlating the pattern with catatonia[11].

DIAGNOSIS

The diagnosis of catatonia entails a meticulous physical examination, predominantly assessing for waxy flexibility, catalepsy and other hallmark signs of catatonia. The Bush-Francis Catatonia Rating Scale (BFCRS) a 23 items scale rated on a Likert scale of 0-3, and serves as a vital tool for diagnosing catatonia, involving observations of patient behaviour during normal conversation, aggressive head scratching to check for imitation, and several other diagnostic maneuvers [12], as examples, Sienaert *et al*[13] identified seven rating scales in assessing catatonia in clinical settings, namely the Modified Rogers Catatonia Scale, the Rogers Catatonia Scale, the Northoff Catatonia Rating Scale (NCRS), the Braunig Catatonia Rating Scale (BCRS), the Kanner Scale and of course, the Bush Francis Catatonia Rating Scale. Of these, the BFCRS, NCRS and BCRS were identified for their reliability in varied populations[13]. Zingela *et al*[6,14] utilised three diagnostic instruments, namely the Bush Francis Screening Instrument (BFCSI), the BFCRS, and the Diagnostic and Statistical Manual 5 (DSM-5), unearthing the superior efficacy of the BFCSI in identifying catatonia cases compared to the DSM-5, which missed nearly 64% of cases.

TREATMENT

The treatment paradigm for catatonia primarily revolves around addressing the underlying conditions whether associated with mental, physical or other disorders like delirium. Benzodiazepines, particularly lorazepam, emerge as the mainstay of catatonia treatment, administered through intravenous injections, however, caution must be exercised on patients presenting with delirium, it is noteworthy that even in cases of delirium, catatonia responds well to Lorazepam [1,15]. Electroconvulsive therapy (ECT) serves as an alternative, especially when benzodiazepines prove ineffective, with studies reporting an effectiveness range of 80%-100% in different catatonia cases[1]. A recent systematic review by Xiao *et al*[16] concluded that ECT, evidence from 13 systematic reviews and one meta-analysis on ECT, 12 case reports on repetitive transcranial magnetic stimulation and seven studies of cases using transient direct current stimulation demonstrated statistically significant improvements in patients after treatment[16].

EVIDENCE-BASED CONSENSUS GUIDELINES

The British Association for Psychopharmacology has developed an evidence-based consensus guideline on the management of catatonia[17] based on existing systematic reviews and primary literature. This comprehensive guidance provides coverage on the diagnosis, aetiology, clinical features, and epidemiology of catatonia. It offers detailed recommendations for clinical assessments, including history, physical examination, and various investigations (Table 1). The treatment section encompasses benzodiazepines, ECT, other pharmacological and neuromodulatory therapies, addressing specific needs for diverse patient groups such as children, adolescents, older adults, women in the perinatal period, individuals with autism spectrum disorder, and those with certain medical conditions.

RESEARCH

The enigmatic nature of catatonia necessitates a concerted research endeavour to explain its neurobiological, genetic, and environmental underpinnings. Rogers *et al*[17] also emphasises that clinical trials in this area are scarce, and most recommendations are based on small observational studies, case series, and reports, highlighting the need for more randomised controlled trials and prospective cohort studies. Moreover, evolving treatment modalities like N-methyl-D-aspartate receptor antagonists warrant further exploration to enhance the therapeutic arsenal against catatonia[16]. Xiao *et al*[16] highlighted that although ECT is recommended first line treatment the emerging field of non-invasive brain stimulation (NIBS) can be an alternative option. However, more methodological robust randomised controlled trials in NIBS are warranted.

Table 1 British Association of Psychopharmacology evidence-based consensus guidelines for the management of catatonia: Summary of key recommendations

Recommendation category	Details
General approach and first-line treatment	Emphasised use of GABA-ergic pharmacotherapies as first-line treatment; followed by recommendation for management of non-response, and considering underlying conditions, and potential complications
Other therapies	Use of ECT, evolving treatment modalities like N-methyl-D-aspartate receptor antagonists, dopamine precursors, agonists and reuptake inhibitors, dopamine receptor antagonists and partial agonists, anticonvulsants, anticholinergic agents, miscellaneous treatments; alternatives to ECT include repetitive transcranial magnetic stimulation and transcranial direct-current stimulation
Subtypes of catatonia and related conditions	Specific recommendations for periodic catatonia, malignant catatonia, neuroleptic malignant syndrome, and medication-induced catatonia
Special groups and situations	Considerations for children and adolescents, older adults, the perinatal period (including the safety of lorazepam and use of ECT), individuals with autism spectrum disorder, and those with certain medical conditions
Research priorities	Emphasises the need for more randomised controlled trials and prospective cohort studies to strengthen evidence base for management of catatonia

GABA: Gamma-aminobutyric acid; ECT: Electroconvulsive therapy.

CONCLUSION

The nuanced understanding of catatonia's prevalence and its varied presentation, especially in acute mental health settings, requires a holistic approach towards its diagnosis and management. The study conducted in Nelson Mandela Bay serves as an excellent model for utilizing rigorous diagnostic criteria to reveal the true prevalence of catatonia. Applying accurate diagnoses then enables developing specialized treatments targeting the condition. Research on novel treatment modalities is warranted.

FOOTNOTES

Author contributions: Phiri P designed the overall concept and outline of the manuscript, and wrote first draft; Delanerolle G, Hope O, Murugaiyan T, Dimba G, Rathod S, and Zingela Z contributed to this paper; and all authors reviewed and approved the final version of the manuscript.

Conflict-of-interest statement: Phiri P has received research grants from Novo Nordisk, Janssen Cilag, and other, educational from QMUL, other from John Wiley & Sons, other from Otsuka, outside the submitted work. Rathod S reports other from Janssen, Lundbeck, Boehringer and Otsuka outside the submitted work. All other authors report no conflict of interest. The views expressed are those of the authors and not necessarily those of the NHS, the National Institute for Health Research, the Department of Health and Social Care or the Academic institutions.

Country/Territory of origin: United Kingdom

ORCID number: Peter Phiri 0000-0001-9950-3254; Gayathri Delanerolle 0000-0002-9628-9245; Shanaya Rathod 0000-0001-5126-3503; Zukiswa Zingela 0000-0002-3425-1145.

S-Editor: Wang JJ
L-Editor: A
P-Editor: Zhang XD

REFERENCES

1 **Edinoff AN**, Kaufman SE, Hollier JW, Virgen CG, Karam CA, Malone GW, Cornett EM, Kaye AM, Kaye AD. Catatonia: Clinical Overview of the Diagnosis, Treatment, and Clinical Challenges. *Neurol Int* 2021; **13**: 570-586 [PMID: 34842777 DOI: 10.3390/neurolint13040057]
2 **Tandon R**, Heckers S, Bustillo J, Barch DM, Gaebel W, Gur RE, Malaspina D, Owen MJ, Schultz S, Tsuang M, van Os J, Carpenter W. Catatonia in DSM-5. *Schizophr Res* 2013; **150**: 26-30 [PMID: 23806583 DOI: 10.1016/j.schres.2013.04.034]

3 **Dell'Osso L**, Amatori G, Massimetti G, Nardi B, Gravina D, Benedetti F, Bonelli C, Luciano M, Berardelli I, Brondino N, De Gregorio M, Deste G, Nola M, Reitano A, Muscatello MRA, Pompili M, Politi P, Vita A, Carmassi C, Maj M. Investigating the relationship between autistic traits and symptoms and Catatonia Spectrum. *Eur Psychiatry* 2022; **65**: e81 [PMID: 36328964 DOI: 10.1192/j.eurpsy.2022.2334]

4 **Malone K**, Saveen S, Stevens CM, McNeil S. Successful Treatment of Catatonia: A Case Report and Review of Treatment. *Cureus* 2022; **14**: e26328 [PMID: 35911277 DOI: 10.7759/cureus.26328]

5 **Bhati MT**, Datto CJ, O'Reardon JP. Clinical manifestations, diagnosis, and empirical treatments for catatonia. *Psychiatry (Edgmont)* 2007; **4**: 46-52 [PMID: 20805910]

6 **Zingela Z**, Stroud L, Cronje J, Fink M, Van Wyk S. A prospective descriptive study on prevalence of catatonia and correlates in an acute mental health unit in Nelson Mandela Bay, South Africa. *PLoS One* 2022; **17**: e0264944 [PMID: 35259194 DOI: 10.1371/journal.pone.0264944]

7 **Serrat F**, Iglesias-Gónzalez M, Sanagustin D, Etxandi M, de Pablo J, Cuevas-Esteban J. Catatonia and Cognitive Impairments: A Systematic Review. *Front Psychiatry* 2022; **13**: 877566 [PMID: 35845445 DOI: 10.3389/fpsyt.2022.877566]

8 **Rasmussen SA**, Mazurek MF, Rosebush PI. Catatonia: Our current understanding of its diagnosis, treatment and pathophysiology. *World J Psychiatry* 2016; **6**: 391-398 [PMID: 28078203 DOI: 10.5498/wjp.v6.i4.391]

9 **Pavlidou A**, Walther S. Using Virtual Reality as a Tool in the Rehabilitation of Movement Abnormalities in Schizophrenia. *Front Psychol* 2020; **11**: 607312 [PMID: 33488466 DOI: 10.3389/fpsyg.2020.607312]

10 **Walther S**, Stegmayer K, Wilson JE, Heckers S. Structure and neural mechanisms of catatonia. *Lancet Psychiatry* 2019; **6**: 610-619 [PMID: 31196794 DOI: 10.1016/S2215-0366(18)30474-7]

11 **Fornia L**, Puglisi G, Leonetti A, Bello L, Berti A, Cerri G, Garbarini F. Direct electrical stimulation of the premotor cortex shuts down awareness of voluntary actions. *Nat Commun* 2020; **11**: 705 [PMID: 32019940 DOI: 10.1038/s41467-020-14517-4]

12 **Bush G**, Fink M, Petrides G, Dowling F, Francis A. Catatonia. I. Rating scale and standardized examination. *Acta Psychiatr Scand* 1996; **93**: 129-136 [PMID: 8686483 DOI: 10.1111/j.1600-0447.1996.tb09814.x]

13 **Sienaert P**, Rooseleer J, De Fruyt J. Measuring catatonia: a systematic review of rating scales. *J Affect Disord* 2011; **135**: 1-9 [PMID: 21420736 DOI: 10.1016/j.jad.2011.02.012]

14 **Zingela Z**, Stroud L, Cronje J, Fink M, van Wyk S. Assessment of catatonia and inter-rater reliability of three instruments: a descriptive study. *Int J Ment Health Syst* 2021; **15**: 82 [PMID: 34809692 DOI: 10.1186/s13033-021-00505-8]

15 **Unal A**, Altindag A, Demir B, Aksoy I. The Use of Lorazepam and Electroconvulsive Therapy in the Treatment of Catatonia: Treatment Characteristics and Outcomes in 60 Patients. *J ECT* 2017; **33**: 290-293 [PMID: 28640169 DOI: 10.1097/YCT.0000000000000433]

16 **Xiao H**, Meng Y, Liu S, Cao Y, Sun H, Deng G, Wang M, Zheng Y, Qiu C. Non-invasive brain stimulation for treating catatonia: a systematic review. *Front Psychiatry* 2023; **14**: 1135583 [PMID: 37260758 DOI: 10.3389/fpsyt.2023.1135583]

17 **Rogers JP**, Oldham MA, Fricchione G, Northoff G, Ellen Wilson J, Mann SC, Francis A, Wieck A, Elizabeth Wachtel L, Lewis G, Grover S, Hirjak D, Ahuja N, Zandi MS, Young AH, Fone K, Andrews S, Kessler D, Saifee T, Gee S, Baldwin DS, David AS. Evidence-based consensus guidelines for the management of catatonia: Recommendations from the British Association for Psychopharmacology. *J Psychopharmacol* 2023; **37**: 327-369 [PMID: 37039129 DOI: 10.1177/02698811231158232]

World Journal of Psychiatry

Submit a Manuscript: https://www.f6publishing.com

World J Psychiatry 2024 February 19; 14(2): 215-224

DOI: 10.5498/wjp.v14.i2.215

ISSN 2220-3206 (online)

FIELD OF VISION

Cognitive dissonance and mindset perturbations during crisis: "eco-socio-psycho-somatic" perspectives

Felix Tretter, Henriette Löffler-Stastka

Specialty type: Psychiatry

Provenance and peer review: Unsolicited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

Grade A (Excellent): A
Grade B (Very good): B
Grade C (Good): 0
Grade D (Fair): 0
Grade E (Poor): 0

P-Reviewer: Chakrabarti S, India; Jin S, China

Received: September 12, 2023
Peer-review started: September 12, 2023
First decision: December 6, 2023
Revised: December 8, 2023
Accepted: January 3, 2024
Article in press: January 3, 2024
Published online: February 19, 2024

Felix Tretter, Department of Systems Medicine and Healthcare Systems, Bertalanffy Center for the Study of Systems Science, Vienna 1040, Austria

Henriette Löffler-Stastka, Department of Psychoanalysis and Psychotherapy, Medical University Vienna, Vienna 1090, Austria

Corresponding author: Henriette Löffler-Stastka, MD, PhD, Dean, Director, Department of Psychoanalysis and Psychotherapy, Medical University Vienna, No. 18-20 Währinger Gürtel, Vienna 1090, Austria. henriette.loeffler-stastka@meduniwien.ac.at

Abstract

Mandatory and restrictive health regulations during the corona pandemic caused psychic disorders in many people, which even led to clinically relevant mental disorders. At the same time, there was gradually a polarization of opinions among the population. In order to improve future pandemic management, an integrative understanding of these psychosocial processes therefore seems useful. Here we start theoretically with the mental effects of inconsistencies of the information environment by referring to concepts such as the theory of cognitive dissonance. In a next step, we use the psychodynamic theory to understand the affective-motivational defense mechanisms underlying these cognitive states and processes. However, a broader theoretical framework of psychoanalysis seems to make sense, because self-referential processing also influences the style of thinking. For this reason, we use a more comprehensive psychological systems theoretical framework model to integrate these different perspectives. This integrative view refers in part to basic knowledge of health psychology regarding the resistance of unhealthy ways of thinking and behaviors and the possibilities for interventions for change. We then extend this model to a broader picture that also covers the relationship between men and their environment. This results in the perspective of a multidimensional socioecological theoretical framework, which as a heuristic reference model and related to other ecological approaches could also be helpful for various theoretical questions for public health, and could provide a better public understanding of health issues. In line with this perspective, we hypothesize that with regard to the coronavirus disease 2019 pandemic, the acceptance of public health narratives could be increased if a more consistent picture of the scientific descriptions and explanations of the pandemic - similar to the model proposed - could be provided, which would enable the understanding of the origin, course and countermeasures, and thus could have positive collective psycho-hygienic effects.

Key Words: Infodemic; Affective-cognitive dissonance; Systems model of the mind; Socioecological model

Core Tip: With the emergence of an increasingly fragmented and crisis-ridden world, sound containment and mentalization capacities are required. We provide a stepped multidimensional socioecological theoretical framework that serves as a heuristic reference model. The example of the pandemic crisis is transferable and related to other ecological approaches. Parameters for sustainable and enduring change processes are given.

Citation: Tretter F, Löffler-Stastka H. Cognitive dissonance and mindset perturbations during crisis: "eco-socio-psycho-somatic" perspectives. *World J Psychiatry* 2024; 14(2): 215-224
URL: https://www.wjgnet.com/2220-3206/full/v14/i2/215.htm
DOI: https://dx.doi.org/10.5498/wjp.v14.i2.215

INTRODUCTION

Commentary on the psychosocial macro world

At present, we seem to live in a persistent post-normal state of society, especially as many crises such as migration, pandemics, wars, and the climate crisis overlap. We are confronted with multiple, interdependent crises[1]. This situation challenges the competence of the sciences to understand the situation and develop coping strategies for the knowledge society, which must be communicated in an understandable way, taking into account both the internal consistencies of their narratives and structural characteristics of the affective-cognitive level of citizens.

As an example of a challenge for public health, we refer here to the corona pandemic, in particular by highlighting the problem of consistency of health information and the mechanisms for building resilient mindsets that also reflect the influence of the sociocultural environment. We gradually develop a comprehensive multilevel model in which we first start from observable cognitive dissonances, and then conceptually combine this level with the psychoanalytic view of the dynamics of affects and motivations that must be regulated by ego functions. Finally, by use of a systems theoretical model of the mind we link this psychological model to a broader social-ecological conceptual framework. We hypothesize that the aversive reactions of an increasing part of the population to public health measures are based on the individual experience of a "bad" relationship with an increasingly fragmented world, which in addition may also lead to an increasingly fragmented self in the respective psychosocial development of the people. We therefore believe that pandemic management and public health interventions in general could be more efficient if they take into account these psychosocial aspects of people as "situated subjects" and make greater use of transparent theory-based narratives.

Productive and counterproductive power of simple but contradictory narratives: In modern societies, communication is largely based on scientific information, even if it is transformed into other, simpler descriptive and also regulatory narratives. Here we understand a narrative as a text that encodes values and emotions in order to create meaning and to give people affective and cognitive orientations, and that legitimizes a certain collective behavior[2]. Narratives are also an important basis of "knowledge societies."

With regard to the corona pandemic, various narratives contributed to the "infodemic", as the World Health Organization called the huge corona-related psychosocial information environment[3]. Above all, the effects of the different health regulations such as general lockdowns and their on's and off's were internationally varying and not really comprehensible, *i.e.* scientifically satisfactory proven (*e.g.*, wearing masks while skiing, but not in shops). Such inconsistencies caused by politics and/or science arise above all from the temporary construction of messages consisting of one-sentence or even one-word narratives, which are also increasingly communicated incoherently, as is typical in postmodern societies[4]. Such narratives about the corona pandemic were modified within a few months: "There will be millions of deaths" was communicated in European countries in spring 2020 and new narratives emerged in spring/summer 2021, such as: "The pandemic is over". It called for "protecting vulnerable individuals", "protecting health care", and finally "getting vaccinated", as "the pandemic is a pandemic of the unvaccinated" (Fall 2021). When the rapidly spreading but not so pathogenic omicron variant appeared in December 2021, mandatory vaccinations were propagated. However, this public health program could not function effectively because this type of virus was spreading at a very rapid pace, and time was short to carry out the vaccinations. As a result, the motivation to vaccinate did not increase[5]. The radicalization of the skeptical part of the population also increased.

As a consequence, there was a change in the conditions of public opinion formation regarding corona: a new simple rationality emerged, which seemed to be scientifically evidence-based, but which was propagated with insufficient justifications, differentiations, and updates. After a while, resentment was articulated in the population and through subtle systemic ping-pong processes, social radicalization gradually took place. Put simply: The collective imperatives were accepted or rejected - "Let's follow the science" or "The Great Reset[6] is behind it"!

This phenomenon of polarization is often interpreted as a "reactance reaction", since slightly skeptical attitudes of citizens can change into a passive (or even active) opposition in interaction with the given view of politics, the media and the sciences. A first stage of a theoretical explanation for such attitude dynamics at the individual level could be the theory of cognitive dissonance as it will be explained later. First, however, basic social mechanisms of the splitting of individual and collective consciousness will be explained.

"Spiral of silence" and the need for social acceptance: First, we hypothesize that information inconsistencies in public health communications have been instrumental in the emergence of an increasingly aggressive polarization of the social atmosphere during the pandemic. For example, at the beginning of 2022, more and more people seemed to belong to the silent majority, who may have arisen *via* the mass media strategy of the "cancel culture"[7] and the sociopsychic mechanisms such as the "spiral of silence"[8]: The more dissenting opinions (and even questions) from the institutions occured, the more these people were silenced and spontaneously fell silent. And the more they remained silent, the more the opinion of the institutions prevailed, thus reinforcing the conformity of public opinion. With regard to this process, it must generally be assumed that, among other things, the contact-preventing lockdowns led to the fact that people's essential need for social acceptance could no longer be satisfied, although this need could be partially satisfied by the use of social media.

Due to the psychohygienic relevance of good human social relationships, we shall first examine the reciprocal relationship between the person and her social environment in the context of psychological findings of individual development (terms we use here are elaborated in Supplementary material).

Basic interactions between the psychosocial environment and individual development: In view of the reduced social dialogue associated with the implementation of mandatory restrictive measures to combat the pandemic, a polarization of the social climate became apparent: The good guys as followers and the bad guys as resisters. This increasingly developing division of society overshadowed the current cultural change of modern societies, which is characterized by an accelerated increase in differentiated but also disintegrated narratives at macro, meso, and micro levels ("disintegrated pluralism"). This fragmented character of the sociocultural environment[9] in turn favors the individual development of "dissociated personalities", and thus in this "fragmented acceleration society"[10] a fundamental "loss of (coherent) resonance" of the individuals[11] arises. In relation to borderline personality disorder, narcissism and identity, and authenticity[12-14], psychoanalysis, in particular, has provided a great deal of empirical and theoretical knowledge about such features of the psychosocial development of the individual (*e.g.*, in the context of the influential object relations theory based on developmental phases)[15]. We want to shed light on these aspects here by starting with the theory of cognitive dissonance, which we then combine with psychoanalysis, and finally outlining a human-ecological point of view.

Theoretical framework models for a psychological understanding of the individual coping with the infodemic

In terms of the interrelationship between the structure of the social world and the evolving personality structure, we see a correspondence between the inconsistencies of the infodemic and the fragility of basic affective-cognitive[16,17] schemata of the individual: if the individual's current experiences exhibit a high degree of inconsistency, the resulting affective-cognitive structures are restructured towards a more stable constellation[18] (theory of cognitive dissonance)[19]. Moreover, such adaptations can be understood by defense mechanisms as identified by psychoanalysis (*e.g.*, rationalizing, suppressing). Finally, we use the structural model[20] and self-theory[21] of psychoanalysis by referring to systemic models of the mental (essential theoretical terms we use here are explained in Supplementary material).

Cognitive dissonance: We begin with the information environment of the individual, *i.e.* the social cognitive sphere. In this context, the psychopathological relevance of the need for orientation as identified by Grawe[22] can be assumed in principle: if a set of cognitions does not match their affective charges, a cognitive dissonance occurs with a negative basic emotionality, which enhances the need for orientation. We also assume that this intrinsic affective-cognitive imbalance occurs when the individual is in a state of information overload during affective-cognitive information uptake. The overload results from and during the construction of a cognitive schema that interacts with the basic internal affective-cognitive schema previously established by the individual development. If the need for orientation is not satisfied by the environment, the affective-cognitive balance of the person is restored by mainly unconscious mechanisms.

At first glance, the acute harmonization dynamics can now be successfully described by the theory of "cognitive dissonance"[19,23,24], which explains the quasi-automatic balancing[25,26] of inconsistent cognitive structures[27] (Supplementary material). Consequently, the concept of cognitive dissonance can be applied to cognitions during the pandemic. The cognitions were singular but emotionally charged narratives that practically fit together, such as skepticism about vaccinations and the options of conspiracy theories (Figure 1). A system of relations in the form of a "negative triad," consisting of the person experiencing both coronavirus disease 2019 (COVID-19) and vaccination negatively, leads to a dissonant unstable constellation (left triangle; three negative relations). An additional affective-cognitive element such as "The great reset," which is not liked but is believed to propagate also vaccination, stabilizes the entire system (right-angled triangle; two negative relations in triads have positive enhancing effects). Although this example has some shortcomings in terms of oversimplification, it is helpful for understanding resistance to change of opinions and attitudes.

Now the question arises why and how the respective stabilizing element emerges and where it comes from. Here we hypothesize that a fragmented and disintegrated internal model of the world and the self acts as an affective-cognitive reference structure stored in (implicit) long-term memory for the current information processing and causes the stabilization or destabilization of topic-specific and current affective-cognitive information, which is likely to form mainly in working memory and short-term memory. Thus, a stable "self" is likely to have a higher tolerance for inconsistent

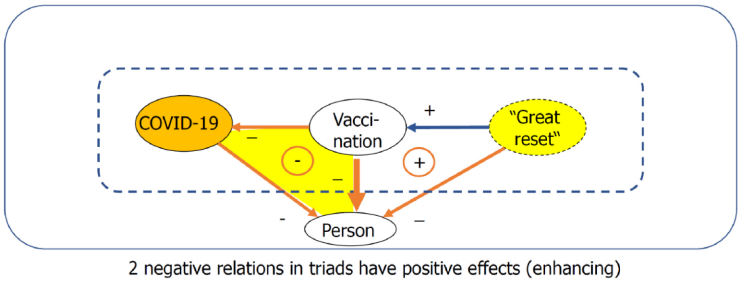

Figure 1 A hypothetical cognitive scheme of people with vaccine resistance stabilizing through conspiracy narratives ("The Great Reset"). See the text for more information. COVID-19: Coronavirus disease 2019.

external information.

It should be noted here too that the well-known resistance to changes of such mindsets is a central issue in health issues in context of public health. This is a challenge in addiction psychology and implies motivational interventions by therapists[28,29]. In line with this microtheory, it must be acknowledged that a broader conceptual framework of theoretical psychology is useful, as health psychologist Robert West has shown with regard to smoking[30]. In addition to the cognitive level, West also emphasizes the importance of the affective-motivational level of the mental, and he points to the need for a differentiated integrative model of general psychology (PRIME model), a topic recently highlighted by the authors[17]. Here, we first follow the traditional theory-integrating path of psychoanalysis, namely the developmental psychological perspective of object relations theory[31].

Developmental fragility of the affective-cognitive reference structure: According to the object relations theory (Supplementary material), at the beginning of psychological development there is initially no internal reference structure for the affective-cognitive order that fits the environment: Elements of conscious experience are classified separately and only polarized as "good" and "bad" experiences (Figure 2). In addition, at this stage of development, there is a lack of stable affective-cognitive object relations that distinguish the self and the environment[32] sufficiently. This structure therefore resembles a psychotic personality structure[31].

For some individuals, the lifelong interaction between two basic dimensions of human experience of relations - connectedness with others *vs* self-determination - is deficient and leads to a high vulnerability of human-environment relationships[33,34]. In this understanding, with a view to the evolving process of interaction with meaningful others[31], the cumulative and socially engrammed self-representations can be understood as a "constant frame of reference" embedded in the self. It serves as a benchmark with future social cognitions associated with affects[21,35]. Social engrams[36] and empathic behavior[37] have been shown to influence higher-order cognition and modulate negative experiences and memories, in part by facilitating learning new ones[38].

Following the object relations theory[31], it is now assumed that the basic reference structure for the current affective-cognitive information processing is provided by the internal representation of object relations[31] or the "internal working model", which refers to the meaning of the self-foreign distinction[39]. For the sake of simplicity, we call this affective-cognitive structure "experience matrix"[32] (Figure 2). Its essential structural properties converge into a growing dynamic balance of emotionally valued diversity and integrity of relationships between the elements. In our systemic transformation of object relations theory[17], the value of the respective cognitions (plus, minus) indicates the emotional evaluations that are the result of interactions of cognitions. If there is an inconsistent relationship, orientation needs and control needs arise and stabilization processes to reduce cognitive dissonance take place[25,30].

It can now be hypothesized that obstacles to adequate affective-cognitive development arise from the fear of losing the self, coherence, orientation in life, and even existence, when circumstances challenge people's current configuration of the self. In light of the megatrends in modern societies mentioned at the beginning, and in light of the narratives of the pandemic, it seems important to note that the modulating function of language in accordance with affect regulations (and the self-regulation) depends on the quality of the social relationship as learned in past and current interactions[40,41]. Empirical evidence for the latter has been proven over decades in psychotherapeutic process and outcome research[42].

Applied to the experience of the 3 years of the pandemic, it should be emphasized, for example, that with the fluctuating need to reduce social contacts, the need for social belonging was antagonized, resulting in a persistent mixture of fear of contagion and an aggressive-depressive mood state to limit social contacts. In our model, these emotional conflicts are also interrelated, similar to how they are conceptualized in the phenomenology of emotions and in neurobiology[43,44].

Interplay of suppressed needs and emotions: The model of the affective-cognitive subsystem of the mental must be supplemented with regard to the persistent situation of need suppression in order to explain a comprehensive but diffuse aggregation of negative emotions[17]. Here are some simple examples that can be localized on the need-emotion axis: Physical displeasure follows the suppression of the need for space and movement: (1) Anxiety is a reaction to the suppressed need for physical safety and protection (*e.g.*, before the virus), followed by the aforementioned lack of orientation and control, as a correlate of two needs that are of psychopathological relevance[17,22,27]; (2) Aggression can occur in response to the suppression of the need for self-determination; and (3) Depression follows the ongoing suppression of positive social relationships.

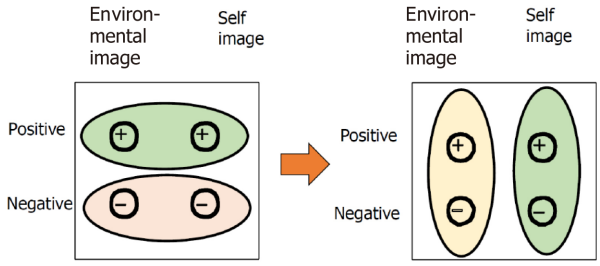

Figure 2 The core concept of object relations theory visualized as a quadripolar "experience matrix": The low-developed polarized configuration of the representations of the self and the environment with poles of positive and negative experiences (left) and the adult configuration with strong distinction of the images of the environment and the self (right)[31]. For simplification, the term "object representation" is translated here as "environmental image"; "Self-representation" is also translated as "self-image."

These systemic affective-motivational relations can be partially compensated as a coping strategy by a cognitive restructuring of the respective experiences. In view of the corona pandemic, therefore, a future option for collective psychological stabilization could be a simplified and scientifically sound but generally consistent descriptive and explanatory "theoretical model of the pandemic" (*e.g.*, infection epidemiological triade model) that allows for higher cognitive consistency. This model should integrate the diverse and sometimes contradictory information of the pandemic in a simple way, facilitating a mental order in relation to the external situation.

Basic need for space and its regulations - a new experience: In the context of emotional responses to the ongoing suppression of needs, in view of the long-lasting behavioral restrictions during the pandemic, it is worth mentioning the suppression of the need for space and freedom of movement, an aspect elaborated by ecological psychology (Supplementary material). The need for space is - albeit culturally different-a fundamental need of the "situated subject", but underscored by research. In particular, ecological psychology and behavioral biology have emphasized that it is not so much a high or low social density that is affectively important, but above all the autonomy of the regulation of physical distance and proximity is relevant[45-48]: In its importance for territoriality, it is a source of serious conflicts, and therefore it is a basic need[46-50] for living beings to be able to self-regulate distance. It should also be mentioned here that this need for self-determination in the field of mobility is an independent need, although it is only a form of the basic need for self-determination in all areas of life. As a basic biological need, its suppression can contribute to the psychodynamics of pathogenic symptom and syndrome formation[51].

The psychological significance of the need for space was highlighted in the context of the pandemic through public health measures such as distancing and isolation and through lockdowns. These restrictions on "mobility," imposed in most countries of the world and applied for several weeks to suppress the dynamics of transmission of severe acute respiratory syndrome coronavirus 2, led to the suppression of freedom of movement and produced a complex of negative emotions, mainly aggression and depression, as mentioned above. This basic form of restriction of personal freedom persisted, and the suffering under these circumstances also varies from culture to culture and also within cultures, for example in relation to social class. However, everyday experience already shows that a high density of space (*e.g.*, in the family's apartment during lockdown) can cause stress, but can also lead to the experience of security. The observation of the external emptiness can also lead to an individual and situational condition (*e.g.*, in the apartment as a single) to the experience of freedom and relaxation, but this situation can also soon cause discomfort and anxiety (horror vacui). All of these conflicting experiences were reported by patients during the corona crisis.

After discussing different levels of mental processing (cognition, affects, needs), this psychological perspective needs to be expanded to increase the ecological validity of the model and to better understand the dynamics of internal and external inconsistencies. We therefore "zoom" out of the focus model and look at the entire system of the mental and its connections to the environment.

Mental and action as a control loop - the structural model of psychoanalysis combined with action theory: A more holi -stic view of the mental system is provided above all by the fundamental structural model of psychoanalysis, which has been formulated for about 100 years[20]. In this conceptual framework, the ego has to manage the immediate external reality and coordinate it with the inner needs, which, through the drives of the id and the imperatives of the superego, form a force field that can lead to intrapsychic conflicts. The id can be understood as the affective-motivational level of the mental in relation to the foregoing, while the superego can be seen as a set of internalized reference values (setpoints) such as norms and rules that enable a low-conflict social life[20,51]. The functions of the superego thus include the capacity for self-criticism, guilt and remorse - dispositions that are necessary for interaction with the world, the perception, processing and evaluation of new and past events or stimuli. Thus, the superego is particularly relevant for the imprinting of affectively charged content. The superego can also be understood as the relevant system of connections with the social micro-environment that embeds the person in relation to the formation of opinions, a phenomenon that is group-related (family, peer group) and that was discussed at the beginning of the article. Thus, the social environment influences the individual and, conversely, the behavior of the individual (also as uniform collective behavior) influences the social environment.

The concept that behavior towards the environment in turn determines new perceptions results in a comprehensive and fundamental feedback loop that can be fundamentally captured in a control loop model of the "situated person." This model also corresponds to the basic conceptual structure of psychological and sociological action theory, which emphasizes the relevance of the (social) environment[52-54]. Now, in the sense of a human-ecological perspective, it is especially the social information environment of the person that matters.

Social environment - group phenomena and trust

The most important level of information about the social environment for the individual is the microsocial level of the group (family, peer group) with which relevant communications take place. As mentioned at the beginning, social security, social belonging and acceptance and similar social needs are first satisfied by the immediate social environment (*e.g.*, the mother). Trust in others depends on these experiences, which - pychoanalytically speaking - leads to a supportive superego. But not only the immediate microsocial environment, but also the macrosocial level with its subsystems media, politics, science, *etc* determines the important feeling of social trust. Currently, however, social trust is declining in some countries, which can be partly attributed to the non-acceptance of limits and limitations of the competences of the respective social institutions[55,56]. Thus, the acceptance of the limits of the epistemological options of science is crucial for a knowledge society: Science can only approach the truth, be it through empirical methods or (social) constructivist theoretical concepts, and it must be accepted (and publicly communicated) that science must always deal with the "known unknown." If these limitations are not communicated publicly, and if empirical relativizations of the state of science occur in the medium term, public trust in science can decline. Such (intertemporal) inconsistencies exacerbate the already fragmented (or "psychotic") social situation and favor the formation of science-skeptical groups, reinforced above all by social media. A psychoanalytic view helps us to shed light on these processes on the social level: On the one hand, the fear of the overwhelming power of institutions feeds the need to restore a (fantasized) unbridled omnipotence (Narcissism), derived from the longing for paternal protection due to infantile helplessness. On the other hand, fears can lead to further regressive phenomena. At the macro- and micro-social level, the pandemic situation revealed well-known group phenomena in crisis, such as fragmentation and splitting, which are basically regression to familiar previous defense functions, when normal adaptive affective-cognitive processing is overwhelmed. Sublimation, for example, as a defense fails when one's own body becomes the source of suffering.

Back to the corona crisis: In pandemic situations, restrictive macrosocial conditions hinder the microsocial processing of narratives with the personal social environment and disrupt people's psychosocial climate, relationships with the real world and the information world. Over the course of the three Corona years, the distal macrosocial and proximal microsocial worlds lost their consensual foundations, which can lead to cognitive stress in every single social interaction, thus becoming chronic. Proponents and supporters of the respective Corona policy, but also many ambivalent and even skeptical, resistant and opposing individuals emerged. Some of them are associated with so-called conspiracy theories, and some even show an aggressive-oppositional attitude. The general negative affective consequences of the corona regulations can now be seen, for example, in hospitalization rates or (adolescent) psychiatric departments due to chronic anxiety, aggression and depression[57]. Therefore, individual interaction with a dynamically fragmented world in the event of a crisis is obviously a risk factor for extreme psychosocial reactions.

As a consequence and to return to the initial question of this text - the basic hypothesis can be put forward that differentiated but consistent conceptual frameworks of narratives, such as an understandable pandemic theory generated in the context of science as a knowledge producer, are useful for this, since theories and models generally help to bring observations into a consistent order, thereby reducing cognitive dissonances. The multi-level system-theoretical framework presented here for a graded but more comprehensive understanding of affect-relevant cognitive disorders could also contribute to this.

Benefits of a systemic understanding of the psychosocial climate on a nested collective and individual level: Theories make it possible to integrate heterogeneous information. This can also be achieved by multi-level system-theoretical models of the psychosocial situation of humans, as a variant of which was explained here on the basis of the Corona pandemic. In context of the field of theoretical public health such "(socio) ecological models" have a long tradition[58-61]. Such models, however, must also be rooted in the anthropological perspective of the "situated experiencing person" conceived as a bio-psycho-social being[62]. This view is therefore characteristic of a human-ecological theory[17,36,62-64]. As already mentioned at the beginning, human ecology aims at such nested multi-level, multifunctional and multi-sector models, which basically strive for a differentiated concept of the environmental relations of the person and also a differentiated concept of the mental. These models thus capture the external relations of men to the environment and at the same time the internal model of the internalized environment (Supplementary material, ecological psychology), which also refers to the self-image (cf. object relations theory)[31]. In this view, on one level the person must relate environmental offers and personal needs, but also on another level she must weigh up the requirements of the environment with regard to the person's competences to meet these requirements. However, this ultimately four-pole basic constellation of the human-environment relationship system very often leads to chronic conflicts. In the case of the Corona pandemic, for example, people had to reduce exposure behavior to other people (avoiding contact, distancing, wearing masks), but at the same time maintaining contact with important people, which led to conflict.

In this way, the macro version of this integrative model thus fundamentally captures that events in the natural environment (*e.g.*, the coronavirus or climate change) affect the health of the population (ecosystem health), which is dealt with by institutions of society (*e.g.*, science as a specialized social system), for example insofar as this knowledge and corresponding plans for problem management may be passed on *via* mass media and under political control. The model also captures that in the next phase people change their attitudes and behavior (*e.g.*, wear masks or reduce the consumption of non-renewable energy), and finally there is a better situation in the population and so the measures as in the

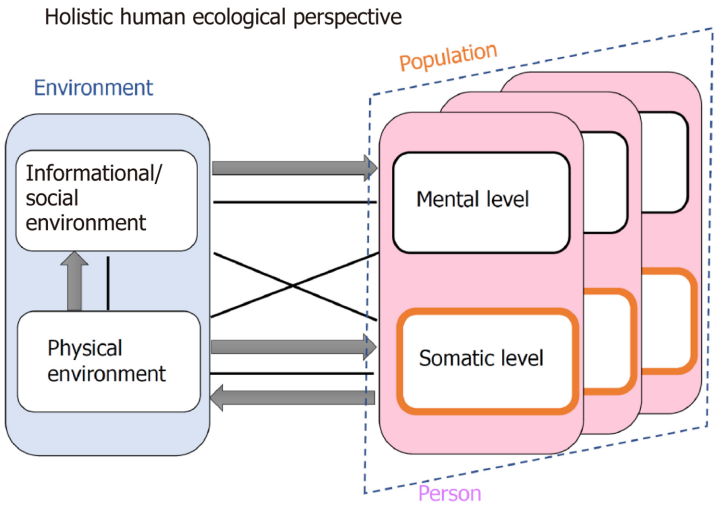

Figure 3 A socioecological framework of health with interlinked conceptual building blocks (see text): In relation to pandemics, the virus acts as part of the physical environment at the somatic level of the person/population (horizontal grey arrow, bottom). This process is captured by science as a subsystem of society (vertical grey arrow), and this information is communicated to the population *via* media (horizontal grey arrow, top), which changes the exposure behavior of the population (horizontal grey arrow).

transition from pandemic to endemic can be relaxed (Figure 3).

It is helpful in this basic modeling to distinguish two levels of interactions – an informational level and a material level: the virus affects humans directly and materially, but invisibly, and in some cases causes severe COVID-19 diseases. This can be observed by science and this information can be passed on to the entire population (Figure 3). Such a model type could therefore expand the theoretical field of public health as a form of "social health ecology" devoted to health-related nature-society-human interactions (eco-socio-psycho-somatics) and could also be incorporated in a simplified form into narratives of health promotion and prevention.

In this model, language, as used in society, plays a crucial role in describing, evaluating and effectively communicating scientific observations to the public. And this brings us back to our initial question: The communicated texts should make sense through their conceptual framework and thus be able to calm emotions. In this respect, they are also "narratives" in the strict sense of the word.

CONCLUSION

With the emergence of an increasingly fragmented and crisis-ridden world, the effects on already fragile personalities are becoming increasingly intense on the cognitive and affective level. Children, in particular, are currently confronted with dissociated images of a dangerous world and parents as role models for them are also under persistent cognitive stress. This chronic tension causes individually and also collectively different adaptation mechanisms such as denial, projection or splitting. This is also evident in the management of the Corona pandemic on several levels, insofar narratives for everyday behavior were contradictory and thus polarized public opinion.

Because of this relevance to public mental health, we suggest that scientific and political authorities build a more consistent, but not oversimplified, picture of societal health problems that can bridge sometimes inevitable narrative inconsistencies. Due to the multidimensionality of this problem, we argue for integrative models that are developed through an integrated interdisciplinary discourse. This discourse should be implemented in the disciplinary, media, political and popular culture debates on health, health care, research and well-being. The need to develop a new way and organization of truth production in knowledge societies has been shown to us by the pandemic situation, which like an "uneasiness in the culture" reminded us of the overwhelming power of nature, the fragility of one's own body and the weaknesses of social institutions that regulate the relationships between people in the family, society and the state[65].

ACKNOWLEDGEMENTS

The authors thank Gavin Lord, native English speaker, for his correction of grammar and style.

FOOTNOTES

Author contributions: Tretter F and Löffler-Stastka H contributed to writing, editing, and revising of this paper.

Conflict-of-interest statement: The authors have no conflicts of interest to declare.

Country/Territory of origin: Austria

ORCID number: Felix Tretter 0000-0002-1076-1220; Henriette Löffler-Stastka 0000-0001-8785-0435.

S-Editor: Qu XL
L-Editor: Filipodia
P-Editor: Zhang YL

REFERENCES

1 **Brand U**, Wissen M. The Imperial Mode of Living: Everyday Life and the Ecological Crisis of Capitalism. [cited 13 December 2023]. Available from: https://www.buecher.de/shop/alltag/the-imperial-mode-of-living/brand-ulrichwissen-markus/products_products/detail/prod_id/59409248/
2 **Currie G**. Narrative. Routledge Encyclopedia of Philosophy. 2023; [DOI: 10.4324/9780415249126-M031-1]
3 **World Health Organization**. Infodemic. [cited 18 August 2023]. Available from: https://www.who.int/health-topics/infodemic#tab=tab_1
4 **Lyotard F**. The Postmodern Condition. Manchester Univ. Press, Manchester. 1984. [cited 13 December 2023]. Available from: https://manchesteruniversitypress.co.uk/9780719014505/
5 **Eber JM**, Partheymueller J, Paul KT. Impfbereitschaft und Impfpflicht: Ein Update. [cited 25 January 2022]. Available from: https://viecer.univie.ac.at/corona-blog/corona-blog-beitraege/corona-dynamiken36/
6 **Schwab K**, Malleret T. COVID-19: The Great Reset. 2020. [cited 13 December 2023]. Available from: https://www.google.com/url?sa=t&rct=j&q=&esrc=s&source=web&cd=&ved=2ahUKEwiX18LNj4yDAxVF0gIHHemyCF4QFnoECA4QAQ&url=http%3A%2F%2Freparti.free.fr%2Fschwab2020.pdf&usg=AOvVaw15d_poATgVtUvi3ZaWpk3W&opi=89978449
7 **Ng E**. Cancel Culture. A Critical Analysis. Palgrave Macmillan. 2022. [cited 13 December 2023]. Available from: https://newbooksnetwork.com/cancel-culture
8 **Noelle-Nauman E**. Spiral of Silence. Univ Chicago Press. 1993. [cited 13 December 2023]. Available from: https://press.uchicago.edu/ucp/books/book/chicago/S/bo3684069.html
9 **Mischel W**, Shoda Y. The mind in context. The Guilford Press. Jan 29, 2010. [cited 13 December 2023]. Available from: https://www.guilford.com/books/The-Mind-in-Context/Mesquita-Barrett-Smith/9781606235539
10 **Rosa H**. Social Acceleration: A New Theory of Modernity. Columbia Press. Jun, 2015. [cited 13 December 2023]. Available from: https://cup.columbia.edu/book/social-acceleration/9780231148344
11 **Rosa H**. Resonance: A Sociology of Our Relationship to the World. Polity Publisher. 2021.
12 **Brüntrup G**, Reder M, Gierstl L. Authenticity: Interdisciplinary Perspectives from Philosophy, Psychology, and Psychiatry. Springer. 2020. [cited 13 December 2023]. Available from: https://dokumen.pub/authenticity-interdisciplinary-perspectives-from-philosophy-psychology-and-psychiatry-1st-ed-9783658296605-9783658296612.html
13 **Tretter F**. Authenticity-Psychiatric Perspectives. Authenticity. Studien zur Interdisziplinären Anthropologie. Springer. 2020. [cited 13 December 2023]. Available from: https://dokumen.pub/authenticity-interdisciplinary-perspectives-from-philosophy-psychology-and-psychiatry-1st-ed-9783658296605-9783658296612.html
14 **Brüntrup G**. Personal identity-a process account. 2021. [cited 13 December 2023]. Available from: https://www.taylorfrancis.com/chapters/edit/10.4324/9781003154198-6/personal-identity-process-account-godehard-br%C3%BCntrup
15 **Kernberg O**. Internal world and external reality. Object relations theory applied. Aronson. 1980. [cited 13 December 2023]. Available from: https://archive.org/details/internalworldext0000kern
16 **Ciompi L**. The concept of affect logic: an integrative psycho-socio-biological approach to understanding and treatment of schizophrenia. *Psychiatry* 1997; **60**: 158-170 [PMID: 9257355 DOI: 10.1080/00332747.1997.11024795]
17 **Tretter F**, Löffler-Stastka H. Steps Toward an Integrative Clinical Systems Psychology. *Front Psychol* 2018; **9**: 1616 [PMID: 30283371 DOI: 10.3389/fpsyg.2018.01616]
18 **Caspar F**. Plan analysis. Handbook of psychotherapy case formulation. Guilford. 2007. [cited 13 December 2023]. Available from: https://www.guilford.com/books/Handbook-of-Psychotherapy-Case-Formulation/Tracy-Eells/9781462548996
19 **Festinger L**. A Theory of Cognitive Dissonance. Row, Peterson. 1957. [cited 13 December 2023]. Available from: https://www.sup.org/books/title/?id=3850
20 **Freud S**. Das Ich und das Es. Internationaler Psychoanalytischer Verlag. 1923. [cited 13 December 2023]. Available from: https://archive.org/details/Freud_1923_Das_Ich_und_das_Es_k
21 **Kirshner LA**. The concept of the self in psychoanalytic theory and its philosophical foundations. *J Am Psychoanal Assoc* 1991; **39**: 157-182 [PMID: 1844123 DOI: 10.1177/000306519103900108]
22 **Grawe K**. Psychologische Therapie. Hogrefe. 1998. [cited 13 December 2023]. Available from: https://www.hogrefe.com/at/shop/psychologische-therapie-65048.html
23 **Heider F**. Attitudes and cognitive organization. *J Psychol* 1946; **21**: 107-112 [PMID: 21010780 DOI: 10.1080/00223980.1946.9917275]
24 **Cartwright D**, HARARY F. Structural balance: a generalization of Heider's theory. *Psychol Rev* 1956; **63**: 277-293 [PMID: 13359597 DOI: 10.1037/h0046049]

25 **Tretter F**. Systemtheorie des Wahns-graphentheoretische Perspektiven. Wahnanalysen. 2012. [cited 13 December 2023]. Available from: https://www.mwv-berlin.de/produkte/!/title/wahnanalysen/id/137

26 **Borsboom D**. A network theory of mental disorders. *World Psychiatry* 2017; **16**: 5-13 [PMID: 28127906 DOI: 10.1002/wps.20375]

27 **Grawe K**. Neuropsychotherapie. Hogrefe. 2004. [cited 13 December 2023]. Available from: https://www.hogrefe.com/at/shop/neuropsychotherapie-65496.html

28 **West R**. Theory of Addiction. 2006. [cited 13 December 2023]. Available from: https://academic.oup.com/alcalc/article/42/2/161/123186

29 **Vaghefi I**, Saremi HQ. From IT Addiction to Discontinued Use: A Cognitive Dissonance Perspective. *Sch* 2017; 5650-5659 [DOI: 10.24251/HICSS.2017.681]

30 **West R**. The PRIME Theory of motivation as a possible foundation for addiction treatment. Drug Addiction Treatment in the 21st Century: Science and Policy Issues. Theory of Addiction. 2007. [cited 13 December 2023]. Available from: http://www.primetheory.com/motivation-theory-publications.php

31 **Kernberg O**. Object-relations theory and clinical psychoanalysis. Aronson. 1976. [cited 13 December 2023]. Available from: https://books.google.at/books?id=D-2UHatqAUEC&printsec=frontcover&hl=de&source=gbs_ge_summary_r&cad=0#v=onepage&q&f=false

32 **Fontano A**. Quadripolar Relational Model: a framework for the description of borderline and narcissistic personality disorders. Neurons and Cognition. Oct 25, 2016. [cited 13 December 2023]. Available from: https://arxiv.org/abs/1512.05875v4

33 **Werbart A**, Bergstedt A, Levander S. Love, Work, and Striving for the Self in Balance: Anaclitic and Introjective Patients' Experiences of Change in Psychoanalysis. *Front Psychol* 2020; **11**: 144 [PMID: 32116945 DOI: 10.3389/fpsyg.2020.00144]

34 **Blatt SJ**. Polarities of Experience: Relatedness and Self-Definition in Personality Development. Psychopathology, and the Therapeutic Process. American Psychological Association. 2008. [cited 29 December 2023]. Available from: https://psycnet.apa.org/record/2008-01813-000 [DOI: 10.1037/11749-000]

35 **Spiegel L**. The self, the sense of self, and perception. *Psychoanal Child* 1959; **14**: 81-109 [DOI: 10.1080/00797308.1959.11822823]

36 **Tretter F**, Loeffler-Stastka H. How does the 'environment' come to the person? The 'ecology of the person' and addiction. *World J Psychiatry* 2021; **11**: 915-936 [PMID: 34888165 DOI: 10.5498/wjp.v11.i11.915]

37 **Steinmair D**, Zervos K, Wong G, Löffler-Stastka H. Importance of communication in medical practice and medical education: An emphasis on empathy and attitudes and their possible influences. *World J Psychiatry* 2022; **12**: 323-337 [PMID: 35317334 DOI: 10.5498/wjp.v12.i2.323]

38 **Leblanc H**, Ramirez S. Linking Social Cognition to Learning and Memory. *J Neurosci* 2020; **40**: 8782-8798 [PMID: 33177112 DOI: 10.1523/JNEUROSCI.1280-20.2020]

39 **Bott NT**, Radke A, Stephens ML, Kramer JH. Frontotemporal dementia: diagnosis, deficits and management. *Neurodegener Dis Manag* 2014; **4**: 439-454 [PMID: 25531687 DOI: 10.2217/nmt.14.34]

40 **Steinmair D**, Löffler-Stastka H. Personalized treatment - which interaction ingredients should be focused to capture the unconscious. *World J Clin Cases* 2022; **10**: 2053-2062 [PMID: 35321177 DOI: 10.12998/wjcc.v10.i7.2053]

41 **Fonagy P**. The Internal Working Model or the Interpersonal Interpretive Function. *J Infant, Child, Adol Psychother* 2002; **2**: 27-38 [DOI: 10.1080/15289168.2002.10486417]

42 **Barkham M**, Lutz W, Castonguay LG. Bergin and Garfield's Handbook of Psychotherapy and Behavior Change 7th Edition. John Wiley and Sons Inc. 2021. [cited 29 December 2023]. Available from: https://psycnet.apa.org/record/2021-81510-000

43 **Damasio A**. Looking for Spinoza: Joy, sorrow, and the feeling brain . Harcourt. 2003. [cited 18 December 2023]. Available from: https://books.google.at/books/about/Looking_for_Spinoza.html?id=iZzPyJID9RUC&redir_esc=y

44 **Panksepp J**. At the interface of the affective, behavioral, and cognitive neurosciences: decoding the emotional feelings of the brain. *Brain Cogn* 2003; **52**: 4-14 [PMID: 12812799 DOI: 10.1016/s0278-2626(03)00003-4]

45 **Bischof N**. Das Rätsel Ödipus. Die biologischen Wurzeln des Urkonfliktes von Intimität und Autonomie. Piper München. 1985. [cited 13 December 2023]. Available from: https://www.google.com/url?sa=t&rct=j&q=&esrc=s&source=web&cd=&ved=2ahUKEwjl8qHVi4yDAxWCwAIHHYbRBmMQFnoECA8QAQ&url=https%3A%2F%2Fepub.ub.unimuenchen.de%2F2850%2F1%2F2850.pdf&usg=AOvVaw38BqxFedevhQRr3LNNxaiN&opi=89978449

46 **Heidegger M**. "Sein und Zeit"-Räumlichkeit ist eine Wesensbestimmung des menschlichen Daseins. 1927. [cited 13 December 2023]. Available from: https://www.google.com/search?client=firefox-b-e&q=Heidegger+M.+%E2%80%9CSein+und+Zeit%E2%80%9D+Ra%CC%88umlichkeit+ist+eine+Wesensbestimmung+des+menschlichen+Daseins%2C+1927

47 **Eibl-Eibesfeldt I**. Ethology: The Biology of Behavior. Holt. 1970. [cited 13 December 2023]. Available from: https://archive.org/details/ethologybiologyo00eiblrich/page/n9/mode/2up

48 **Lewin K**. Principles of Topological Psychology. McGraw-Hill. 1936. [cited 13 December 2023]. Available from: https://books.google.at/books/about/Principles_of_Topological_Psychology.html?id=_uicVLqOqoAC&redir_esc=y

49 **Poppelreuter T**. 'Sensation of Space and Modern Architecture': a psychology of architecture by Franz Löwitsch. *J Archit* 2012; **17**: 251-72 [DOI: 10.1080/13602365.2012.678645]

50 **Barker R**. Ecological Psychology, 242. Stanford Univ Press. 1968. [cited 29 December 2023]. Available from: https://Lib.ugent.be/catalog/rug01:000026064

51 **Freud S**. An Outline of psychoanalysis. Penguin. 2003. [cited 13 December 2023]. Available from: https://www.penguin.co.uk/books/57161/an-outline-of-psychoanalysis-by-sigmund-freud-intromalcolm-bowie-transhelena-ragg-kirkby/9780141184043

52 **Miller GA**, Galanter E, Pribram KA. Plans and the structure of behavior, Holt, Rhinehart and Winston. 1960. [cited 13 December 2023]. Available from: https://archive.org/stream/plansstructureof00mill/plansstructureof00mill_djvu.txt

53 **Heckhausen J**, Heckhausen H. Motivation and Action. Springer. 1980. [cited 13 December 2023]. Available from: https://Link.springer.com/book/10.1007/978-3-642-75961-1

54 **Parsons T**. Action Theory and the Human Condition. Free Press. 1978. [cited 13 December 2023]. Available from: https://books.google.at/books/about/Action_Theory_and_the_Human_Condition.html?id=WuroAAAAIAAJ&redir_esc=y

55 **Löffler-Stastka H**. Zur Akzeptanz der Begrenzung. *Psychopraxis. neuropraxis* 2022; **25**: 332-335 [DOI: 10.1007/s00739-022-00858-w]

56 **Brady HE**, Lehman Schlozman K. Institutions, Experts and the Loss of Trust. *J Am Acad Arts Sci* 2022; 4

57 **Pietrabissa G**, Volpi C, Bottacchi M, Bertuzzi V, Guerrini Usubini A, Löffler-Stastka H, Prevendar T, Rapelli G, Cattivelli R, Castelnuovo G, Molinari E, Sartorio A. The Impact of Social Isolation during the COVID-19 Pandemic on Physical and Mental Health: The Lived Experience of Adolescents with Obesity and Their Caregivers. *Int J Environ Res Public Health* 2021; **18** [PMID: 33804231 DOI: 10.3390/ijerph18063026]

58 **Bronfenbrenner U**. The Ecology of Human Development: Experiments by Nature and Design. Harvard University Press. 1979. [cited 13

December 2023]. Available from: https://www.hup.harvard.edu/books/9780674224575

59 **Stokols D**. Translating social ecological theory into guidelines for community health promotion. *Am J Health Promot* 1996; **10**: 282-298 [PMID: 10159709 DOI: 10.4278/0890-1171-10.4.282]

60 **Krieger N**. Living and Dying at the Crossroads: Racism, Embodiment, and Why Theory Is Essential for a Public Health of Consequence. *Am J Public Health* 2016; **106**: 832-833 [PMID: 27049420 DOI: 10.2105/AJPH.2016.303100]

61 **King AC**, Odunitan-Wayas FA, Chaudhury M, Rubio MA, Baiocchi M, Kolbe-Alexander T, Montes F, Banchoff A, Sarmiento OL, Bälter K, Hinckson E, Chastin S, Lambert EV, González SA, Guerra AM, Gelius P, Zha C, Sarabu C, Kakar PA, Fernes P, Rosas LG, Winter SJ, McClain E, Gardiner PA, On Behalf Of The Our Voice Global Citizen Science Research Network. Community-Based Approaches to Reducing Health Inequities and Fostering Environmental Justice through Global Youth-Engaged Citizen Science. *Int J Environ Res Public Health* 2021; **18** [PMID: 33494135 DOI: 10.3390/ijerph18030892]

62 **Engel GL**. The need for a new medical model: a challenge for biomedicine. *Science* 1977; **196**: 129-136 [PMID: 847460 DOI: 10.1126/science.847460]

63 **Eisenberg L**, Sartorius N. Human ecology in the repertoire of health development. *World Health Forum* 1988; **9**: 564-568 [PMID: 3252857]

64 **Kirmayer LJ**, Crafa D. What kind of science for psychiatry? *Front Hum Neurosci* 2014; **8**: 435 [PMID: 25071499 DOI: 10.3389/fnhum.2014.00435]

65 **Freud S**. Das Unbehagen in der Kultur: Gesammelte Werke. Imago. 1948. [cited 13 December 2023]. Available from: https://www.google.com/url?sa=t&rct=j&q=&esrc=s&source=web&cd=&ved=2ahUKEwjUl6yBj4yDAxUv2AIHHcDyATgQFnoECBIQAQ&url=https%3A%2F%2Fwww.sas.upenn.edu%2F~cavitch%2Fpdf-library%2FFreud_SE_Civ_and_Dis_complete.pdf&usg=AOvVaw0gaX3DlYG1hMYbDGJB2RMd&opi=89978449

World Journal of Psychiatry

Submit a Manuscript: https://www.f6publishing.com

World J Psychiatry 2024 February 19; 14(2): 225-233

DOI: 10.5498/wjp.v14.i2.225

ISSN 2220-3206 (online)

MINIREVIEWS

Automatic recognition of depression based on audio and video: A review

Meng-Meng Han, Xing-Yun Li, Xin-Yu Yi, Yun-Shao Zheng, Wei-Li Xia, Ya-Fei Liu, Qing-Xiang Wang

Specialty type: Psychiatry

Provenance and peer review: Invited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification
Grade A (Excellent): 0
Grade B (Very good): B
Grade C (Good): 0
Grade D (Fair): 0
Grade E (Poor): 0

P-Reviewer: Horkaew P, Thailand

Received: November 25, 2023
Peer-review started: November 25, 2023
First decision: December 6, 2023
Revised: December 18, 2023
Accepted: January 24, 2024
Article in press: January 24, 2024
Published online: February 19, 2024

Meng-Meng Han, Wei-Li Xia, Ya-Fei Liu, Qing-Xiang Wang, Shandong Mental Health Center, Shandong University, Jinan 250014, Shandong Province, China

Meng-Meng Han, Xing-Yun Li, Xin-Yu Yi, Key Laboratory of Computing Power Network and Information Security, Ministry of Education, Shandong Computer Science Center (National Supercomputer Center in Jinan), Qilu University of Technology (Shandong Academy of Sciences), Jinan 250353, Shandong Province, China

Xing-Yun Li, Xin-Yu Yi, Shandong Engineering Research Center of Big Data Applied Technology, Faculty of Computer Science and Technology, Qilu University of Technology (Shandong Academy of Sciences), Jinan 250353, Shandong Province, China

Xing-Yun Li, Xin-Yu Yi, Shandong Provincial Key Laboratory of Computer Networks, Shandong Fundamental Research Center for Computer Science, Jinan 250353, Shandong Province, China

Yun-Shao Zheng, Department of Ward Two, Shandong Mental Health Center, Shandong University, Jinan 250014, Shandong Province, China

Corresponding author: Qing-Xiang Wang, PhD, Associate Professor, Shandong Mental Health Center, Shandong University, No. 49 Wenhua East Road, Jinan 250014, Shandong Province, China. wangqx@qlu.edu.cn

Abstract

Depression is a common mental health disorder. With current depression detection methods, specialized physicians often engage in conversations and physiological examinations based on standardized scales as auxiliary measures for depression assessment. Non-biological markers-typically classified as verbal or non-verbal and deemed crucial evaluation criteria for depression-have not been effectively utilized. Specialized physicians usually require extensive training and experience to capture changes in these features. Advancements in deep learning technology have provided technical support for capturing non-biological markers. Several researchers have proposed automatic depression estimation (ADE) systems based on sounds and videos to assist physicians in capturing these features and conducting depression screening. This article summarizes commonly used public datasets and recent research on audio- and video-based ADE based on three perspectives: Datasets, deficiencies in existing research, and future development directions.

Key Words: Depression recognition; Deep learning; Automatic depression estimation System; Audio processing; Image processing; Feature fusion; Future development

Core Tip: The automatic recognition of depression based on deep learning has gradually become a research hotspot. Researchers have proposed automatic depression estimation (ADE) systems utilizing sound and video data to assist physicians in screening for depression. This article provides an overview of the latest research on ADE systems, focusing on sound and video datasets, current research challenges, and future directions.

Citation: Han MM, Li XY, Yi XY, Zheng YS, Xia WL, Liu YF, Wang QX. Automatic recognition of depression based on audio and video: A review. *World J Psychiatry* 2024; 14(2): 225-233
URL: https://www.wjgnet.com/2220-3206/full/v14/i2/225.htm
DOI: https://dx.doi.org/10.5498/wjp.v14.i2.225

INTRODUCTION

With societal developments, the diagnosis and treatment of depression have become increasingly crucial. Depression is a prevalent psychological disorder characterized by symptoms such as low mood, diminished appetite, and insomnia in affected individuals[1]. Patients with severe depression may also exhibit a tendency towards suicide. In the field of medicine, researchers aspire to conduct comprehensive investigations of depression from both biological and non-biological perspectives. Li *et al*[2] summarized biological markers, revealing associations between depression and indicators, such as gamma-glutamyl transferase, glucose, triglycerides, albumin, and total bilirubin. Non-biological markers can be broadly categorized into verbal and non-verbal features. Verbal features typically pertain to a subject's intonation, speech rate, and emotional expressions in speech extracted from audio recordings. Early studies by Cannizzaro *et al*[3] and Leff *et al*[4] identified differences in the speech of individuals with psychiatric disorders compared to the general population. Non-verbal features typically refer to the facial expressions and body movements commonly embedded in video files. The Facial Action Coding System[5], a frequently employed tool for facial expression analysis, decomposes facial muscles into multiple action units (AUs) with corresponding numerical identifiers. For instance, AU1 and AU2 represent inner brow raise and outer brow raise, respectively. A graphical representation of the AU can be accessed through the link indicated in the footnote (https://imotions.com/blog/learning/research-fundamentals/facial-action-coding-system/)[1]. While Girard *et al*[6] found differences in AU 10, 12, 14, and 15 between individuals with depression and the general population, a unified research framework for bodily changes is yet to be established, with the core challenge lying in quantifying alterations in body movements. Joshi *et al*[7] demonstrated the potential of studying body movements for ADE using a method based on space-time interest points and a bag of words to analyze patients'upper-body movements.

During clinical assessments, specialized physicians detect and treat depression based on diagnostic criteria manuals issued by the relevant organizations. For instance, the World Health Organization released the 11th revision of the International Classification of Diseases in 2022, providing detailed classifications of various mental disorders. The American Psychiatric Association published the Diagnostic and Statistical Manual of Mental Disorders (DSM)-4[8], in 1994, and its updated version, DSM-5[9], in 2013. In 2001, China released the Chinese Classification and Diagnostic Criteria of Mental Disorders, Third Edition. Guided by diagnostic manuals, specialized physicians assessed the severity of depression in the participants based on the scores obtained from these scales. Rating scales are typically categorized into self-report and observer-report scales. The patient health questionnaire[10] is a lightweight self-report scale, whereas the Hamilton depression rating scale (HAMD)[11] is a common observer-report scale. Observer-report scales require specialized physicians to interview patients and score the details based on the scale. Completing an interview based on the HAMD scale typically takes 15-20 min.

In addition to detecting clinical depression based on rating scales, biological markers have been employed to assist with the assessment. Physicians use biochemical indicators extracted through techniques, such as blood tests, to aid their judgment. With the advancements in detection technologies, biological markers can be quantitatively measured, allowing specialized physicians to directly refer to numerical values to determine the clinical significance of a test. However, non-biological markers, which are crucial features of depression, have not been extensively utilized, attributed to several factors. First, changes in non-biological markers, such as facial expressions and intonation, are often subtle. Specialized physicians require extensive training and accumulated experience to capture these changes; such training is typically time-consuming and inefficient. Second, unlike biological markers, systematic patterns of change in non-biological markers depend on their ability to capture spatial and temporal information, a challenging task for early computer technologies. The development of deep-learning technology and the computational capabilities of computers provide an opportunity to address these challenges. Deep-learning, with its robust capability of capturing temporal and spatial information, offers new avenues for constructing assistive systems. Automatic depression estimation (ADE) has become a significant research direction in the field of computational medicine, resulting in several ADE methods being proposed.

A complete ADE study typically comprises three steps. The first step involves data collection, categorized based on the free or need for specific emotional stimulus experiments. The former typically utilizes devices such as cameras and microphones to capture audio-visual information of subjects during medical consultations or in natural states. The latter requires the design of specific emotional paradigms, followed by recording subjects' audio-visual information under emotional stimuli. The second step involves constructing deep-learning models for ADE. In this phase, researchers designed different deep-learning architectures based on data characteristics to capture information for ADE. Finally, the model undergoes training and testing for ADE to essentially perform two tasks: classification, i.e., distinguishing whether the individual is a patient with depression or further categorizing the severity (non-depressed, mild, moderate, and severe), and scoring tasks, *i.e.*, predicting the assessment scale scores of the subjects. Depending on the task, researchers choose different evaluation metrics to train and test the effectiveness of the model.

The initial ADE typically requires manual feature extraction and the application of machine learning methods such as decision trees and support vector machines for feature classification. Peng *et al*[12] initially constructed a sentiment lexicon, counted word frequencies, and then input these features into a support vector machine for ADE. Alghowinem *et al*[13] first used the openSMILE tool to extract audio features and then employed machine learning methods for ADE. Wen *et al*[14] extracted dynamic feature descriptors from facial region sub-volumes and used sparse coding to implicitly organize the extracted feature descriptors for depression diagnosis. With the development of deep learning and computational capabilities, deep models can perform feature extraction from complex data, eliminating manual feature extraction. Notably, owing to the specificity of audio information, certain manual feature extraction steps still exist. Therefore, a series of deep learning-based ADE methods, such as, have been proposed. In this review, we focus primarily on recent ADE methods based on deep learning approaches. We first introduce commonly used publicly available ADE datasets and then provide an overview and summary of recent outstanding audio-visual ADE models. All articles are summarized in Table 1. Finally, we summarize the existing challenges and future directions of ADE.

DATASETS

While data form the foundation of ADE research, owing to the inherent challenges in collecting depression data, such as strong privacy concerns, lengthy collection periods, and limited data volumes, obtaining subject authorization for public sharing is difficult, resulting in a scarcity of publicly available audio-visual datasets. Commonly utilized public datasets primarily originate from audio-visual emotion recognition challenges (AVEC), specifically the AVEC2013[15], AVEC2014 [16], and Distress Analysis Interview Corpus/Wizard-of-Oz set (DAIC-WOZ)[17] datasets.

AVEC2013

The AVEC2013 dataset was released as part of the third AVEC Challenge. This dataset comprises 340 video segments collected from 292 participants. AVEC2013 required participants to perform tasks such as vowel phonation, reading, recounting memories, and narrating a story based on a picture with their audio-visual information recorded. The Beck Depression Inventory (BDI) scores served as labels for AVEC2013.

AVEC2014

The AVEC2014 dataset was released as part of the fourth AVEC. This dataset comprises 150 audio-video data segments involving a total of 84 subjects. As a subset of AVEC2013, AVEC2014 required each participant to complete two tasks, Northwind and Freeform, which involved reading excerpts from articles and answering specific questions. Similar to AVEC2013, AVEC2014 also utilizes BDI scores as data labels.

DAIC-WOZ

This dataset encompasses the audio-visual information of subjects collected through various interview formats, with each data type being independent. The video information, which included a maximum of 263 audio-visual data points, was based on facial features (*e.g.*, annotated directions, facial key points, and AUs features) after conversion.

AUDIO-BASED DEPRESSION ESTIMATION

Audio-based methods are crucial for ADE. In this process, participants often combine manual features with deep features for ADE. Manual features typically include time- and frequency-domains. Deep features are typically obtained from spectrograms using deep-learning models. These spectrograms often represent the waveform, spectrogram, Mel spectrogram, or processed data of raw audio graphically.

He and Cao[18] combined manually extracted audio features with deep-learning features for ADE. They divided the model into two parts. The first part employed a deep network to extract deep features from spectrograms and raw speech waveforms. The other part extracts median robust extended local binary patterns from spectrograms and low-level descriptors from raw speech. Finally, these features were fused using a fusion model to make the final decision. This approach achieved root mean squared error (RMSE) and mean absolute error (MAE) values of 10.001 and 8.201 on the AVEC2013 dataset and 9.999 and 8.191 on the AVEC2014 dataset. Zuo and Mak[19] recognized the potential performance decline associated with limited audio data. With a smaller dataset, capturing the patterns of depressive expressions becomes challenging, and deep models tend to learn audio features specific to individual subjects, leading to overfitting.

Table 1 Summary of advanced automatic depression estimation methods

Method	Year	Framework	Dataset	Modal	Evaluation Criterion			
					MAE	RMSE	Accuracy	F1-score
He and Cao[18]	2018	2DCNN	AVEC2013	A	8.201	10.001	-	-
			AVEC2014	A	8.191	9.999	-	-
SIDD	2023	-	DAIC-WOZ	A	-	-	-	0.601
MSCDR	2022	1DCNN/ RNN	DAIC-WOZ	A	-	-	0.771	0.746
DALF	2023	2DCNN	DAIC-WOZ	A	-	-	-	0.784
STFN	2023	1DCNN	DAIC-WOZ	A	5.38	6.36	0.780	-
Speech Former++	2023	Transformer	DAIC-WOZ	A	-	-	0.733	-
Mao *et al*[24]	2022	CNN RNN	DAIC-WOZ (5)	A	-	-	-	0.958
LGA-CNN	2020	2DCNN	AVEC2013	V-F	6.59	8.39	-	-
			AVEC2014	V-F	6.51	8.30	-	-
SAN	2022	2DCNN	AVEC2013	V-F	7.02	9.37	-	-
			AVEC2014	V-F	6.59	9.24	-	-
Zhao *et al*[27]	2023	2DCNN	AVEC2013	V-F	5.97	7.36		
			AVEC2014	V-F	5.85	7.23		
PRA-Net	2023	2DCNN	AVEC2013	V-F	6.08	7.59	-	-
			AVEC2014	V-F	6.04	7.98	-	-
Yuan and Wang [32]	2019	MLP	Private	V-E	-	-	0.831	-
EnSA	2022	Transformer	Private	V-E	-	-	0.955	-
SATCN	2022	1DCNN	Private	V-B	-	-	0.758	-
Zhao and Wang [35]	2022	Transformer	Private	V-B	-	-	0.729	-
ULCDL	2023	RNN	DAIC-WOZ	A + V	-	-	0.830	0.900
Niu *et al*[37]	2020	2D/3DCNN	AVEC2013	A + V	6.14	8.16	-	-
			AVEC2014	A + V	5.21	7.03	-	-
Shao *et al*[38]	2021	RNN/CNN	Private	V + V	-	-	0.854	-
TAMFN	2022	2DCNN	D-Vlog	A + V	-	-	-	0.750
Uddin *et al*[41]	2022	2DCNN	AVEC2013	A + V	5.38	6.83	-	-
			AVEC2014	A + V	5.03	6.16	-	-

V: Video data; A: Audio data; F: Facial information; B: Body information; MAE: Mean absolute error; RMSE: Root mean squared error; MSCDR: Machine speech chain model for depression recognition; SIDD: Speaker-invariant depression detector; DALF: Depression classification; STFN: Spatial-temporal feature network; LGA-CNN: Local global attention convolutional neural network; SAN: Self-adaptation network; PRA-Net: Part-and-Relation Attention Network; SATCN: Spatial attention-dilated temporal convolutional network; ULCDL: Uncertainty-aware label contrastive and distribution learning; TAMFN: Tme-aware attention-based multi-modal fusion depression detection network; DAIC-WOZ: Distress Analysis Interview Corpus/Wizard-of-Oz set; AVEC: Audio-visual emotion recognition challenges; DCNN: Dilated Convolutional Neural Network; CNN: Convolutional neural network; RNN: Recurrent neural networks.

To address this issue, they proposed a speaker-invariant depression detector, which achieved an F1 score of 0.601 on the DAIC-WOZ dataset. Du *et al*[20] incorporated patients' vocal tract changes into conventional speech perceptual features and developed a machine speech chain model for depression recognition (MSCDR) for ADE. The MSCDR extracts speech features from both generation and perception aspects and uses recurrent neural networks (RNN) to extract time-domain features for depression detection. The MSCDR achieved accuracy and F1 scores of 0.771 and 0.746, respectively, on the DAIC-WOZ dataset.

Yang *et al*[21] observed that many ADE models based on manually designed features lack good interpretability, with features not fully utilized. Therefore, the depression classification (DALF) was proposed. Learnable filters in DALF can more effectively decompose audio signals and retain effective features. Analyzing the automatically learned filters allows for a deeper understanding of the focus areas of the model. This method achieved an F1 score of 0.784 on the DAIC-WOZ dataset. Han *et al*[22] introduced a spatial-temporal feature network (STFN) to capture audio features. The STFN initially captured the deep features of audio information and then used a novel mechanism called hierarchical contrastive predictive coding loss, replacing the commonly used RNN to capture temporal information. This approach reduces the parameter count of the model, making it more trainable. As such, the STFN achieved accuracy, RMSE, and MAE values of 0.780, 6.36, and 5.38, respectively, on the DAIC-WOZ dataset. Chen *et al*[23] focused on integrating the Transformer architecture with audio features. Their proposed model, SpeechFormer++, utilized prior knowledge to guide feature extraction, achieving an accuracy of 0.733% on the DAIC-WOZ dataset. Mao *et al*[24] recognized that text features in audio are also important for capturing the patterns of depressive expressions. Consequently, they proposed an attention-based fused representation of text and speech features. This approach initially inputs text information and low-level features of raw speech into an encoder for encoding and subsequently employs the encoded features for depression detection, achieving an F1 score of 0.958 in a five-class classification task using the DAIC-WOZ dataset.

Overall, the design of ADE models based on audio relies on the initial feature selection. Because audio information cannot be utilized directly by deep models, it is typically transformed before being extracted by deep models. These transformations are diverse, including directly using the raw waveform, applying Fourier transform or Fast Fourier Transform to transform the time-frequency domain information, converting audio into Mel spectrograms, and directly extracting audio features such as frame intensity, frame energy, and fundamental frequency. Diverse feature selection methods provide various possibilities for ADE, leading to discussions regarding which audio representation is more beneficial for ADE. The construction of the model must be aligned with the selected features for an effective feature extraction. Given that depression datasets are often small, methods to limit the learning of individual features by the model, as demonstrated by Zuo and Mak[19], should be carefully considered.

VIDEO-BASED DEPRESSION ESTIMATION

Video information often preserves changes in participants' facial expressions during exposure to stimulus paradigms. Facial expressions include both facial and bodily expressions. In medical research, video-based ADE models typically incorporate various attention mechanisms to enhance local facial features. He *et al*[25] proposed an ADE framework called the deep local global attention convolutional neural network (DLGA-CNN). In the DLGA-CNN, multiple attention mechanisms are introduced and utilized for extracting multiscale local and global features. Finally, these multiscale features are fused and employed for depression detection. The DLGA-CNN achieved RMSE and MAE values of 8.39 and 6.59 on AVEC2013 and 8.30 and 6.51 on AVEC2014. He *et al*[26] also recognized the presence of annotation noise in depression datasets, which could negatively affect feature extraction and result in suboptimal ADE performance. Therefore, they proposed a self-adaptation network (SAN) to relabel erroneous annotations in the datasets. SAN achieved RMSE and MAE values of 9.37 and 7.02 on AVEC2013 and 9.24 and 6.95 on AVEC2014.

Zhao *et al*[27] acknowledged the significance of local and global information and proposed an ADE architecture based on facial images. To enhance the quality of facial images, the architecture initially utilizes the Gamma Correction[28] and DeblurGAN-v2[29] algorithms to balance brightness and contrast and improve image clarity. The architecture employs ConvFFN[30] as the main framework and designs the Hi-Lo attention module to enhance the features in different facial regions. Ultimately, this method achieved RMSE and MAE values of 7.36 and 5.97 on the AVEC2013 dataset and 7.23 and 5.85 on the AVEC2014 dataset. Liu *et al*[31] introduced another approach, Part-and-Relation Attention Network (PRA-Net), for feature extraction from facial regions for ADE. PRA-Net initially segments the extracted facial feature maps by region; these segmented regions are fed into a self-attention mechanism to capture interregional correlations. The classifier merges the regional feature maps with weights for the final decision. PRA-Net achieved RMSE and MAE values of 7.59 and 6.08 on the AVEC2013 dataset and 7.98 and 6.04 on the AVEC2014 dataset.

In addition to extracting features from the entire face, Yuan and Wang[32] explored the use of gaze features for ADE. They employed a fully connected network to extract gaze features from the participants and achieved an accuracy value of 0.831. Subsequently, Zhao and Wang[33] designed an attention-based architecture, EnSA, for ADE that achieved an accuracy of 0.955.

In addition to using facial expressions for ADE, utilizing body expressions is also an important approach. Yu *et al*[34] initially captured the participants' body skeleton change sequences using Kinect. Subsequently, they constructed a spatial attention-dilated temporal convolutional network (SATCN) based on an improved temporal convolutional network. SATCN achieved a maximum accuracy of 0.758 for binary classification tasks and a maximum accuracy value of 0.643 for multiclass datasets. Similarly, Zhao and Wang[35] employed body skeletal information for ADE. They observed differences in reaction times between the case and control groups for specific tasks. Consequently, they used the reaction time as prior knowledge along with skeletal information and input them into a Transformer for ADE. This approach achieved an accuracy value of 0.729. Compared to the abundance of facial-based ADE models, the number of models based on body expressions is relatively limited, warranting further research and exploration.

Unlike audio information, the advancement of convolutional networks enables the direct utilization of image information. Consequently, the construction of end-to-end ADE models has become mainstream in recent years. The inputs for these models do not require complex preprocessing and typically involve region cropping and lighting balancing. Extracting local information has become a crucial aspect of model construction and has emerged as a primary

research direction for ADE based on video information.

FUSION OF AUDIO- AND VISUAL-BASED DEPRESSION ESTIMATION

In addition to using unimodal information for depression prediction, depression-detection models that jointly utilize multiple modalities are being developed. Various methods of complementing information enhance the accuracy of multi-modal models compared to unimodal models, with the combination of audio and visual information a commonly used approach.

Yang *et al*[36] designed uncertainty-aware label contrastive and distribution learning (ULCDL) to integrate facial, audio, and text information for ADE. ULCDL introduces a contrastive learning framework into ADE to enhance a model's learning capability, achieving an accuracy value of 0.830 and F1 score of 0.900 on the DAIC-WOZ dataset. Niu *et al*[37] combined facial sequences with audio spectrograms to detect ADE. Leveraging the characteristics of both features, they proposed spatiotemporal attention and multi-modal attention feature fusion networks to enhance and obtain cross-modal attention for the two features. This architecture achieved RMSE and MAE values of 8.16 and 6.14 on AVEC2013 and 7.03 and 5.21 on AVEC2014. Shao *et al*[38] observed that different features from the same data can be complementary. They combined the participants' RGB images of the body and body skeleton images for the ADE, achieving an accuracy value of 0.854 on a dataset comprising 200 participants. Zhou *et al*[39] approached ADE from the perspective of video blogs. Their proposed time-aware attention-based multi-modal fusion depression detection network (TAMFN) extracts and fuses multi-modal information from three aspects: Global features, inter-modal correlations, and temporal changes. TAMFN obtained an F1 score of 0.75 on the D-Vlog[40] dataset. Uddin *et al*[41] initially segmented audio and video into equally sized segments before using volume local directional structural patterns and temporal attention pooling to encode facial and audio information to obtain the importance of each video and audio segment. The next step involved formatting video and audio segments. Finally, multi-modal factorized bilinear pooling was employed to fuse the features and make decisions. This method achieved RMSE and MAE values of 6.83 and 5.38 on AVEC2013 and 6.16 and 5.03 on AVEC2014.

Multimodality is a new approach to ADE. Multimodal information mimics the patterns of diagnosis and treatment from multiple perspectives in clinical examinations. The most crucial aspect of multimodal information is the exploration and integration of hidden relationships among the various types of information. Initially, feature and decision fusions were the primary methods for combining features. However, these two approaches are simple and do not consider deep feature integration. With further research, ADE will demand multiscale and deep fusion of multimodal features. Cross-modal fusion methods are no longer limited to feature and decision fusions. When constructing new fusion methods, identifying relationships between different types of information and methods to capture these relationships become crucial.

DISCUSSION

Facial information has been favored by most researchers for ADE methods based on video information. Studies such as[6] subdivided faces into multiple AUs for investigation. Inspired by these studies, researchers recognized the importance of local facial information. A series of attention mechanisms were proposed and employed to facilitate the model's focus on local information. Although researches[34,35] has explored aspects such as gait and body movements in individuals with depression, compared with the excessive attention paid to ADE methods based on facial information, methods based on body expressions for ADE appear to be relatively scarce. Notably, databases analyzing the body movements of individuals with depression are often not publicly accessible. In addition, publicly available depression databases rarely contain body information. The lack of visibility and the difficulty in data collection are significant reasons for the limited development of ADE methods based on body expressions. Despite these challenges, we believe that this is an important research direction as facial expressions. We hope to develop more ADE methods based on the proposed body changes. Research related to human motion recognition, keypoint capture, and skeleton tracking may serve as valuable references for constructing ADE models based on body expressions.

For audio-based ADE methods, current approaches primarily involve combining handcrafted features or their transformed versions with deep features. Unlike facial expressions, audio information possesses richer individual characteristics, making feature selection more difficult. Finding a unified and effective feature selection pattern, along with deep learning architectural methods, remains a crucial task for future research.

The integration of multi-modal features is crucial for future depression detection. In clinical assessments, specialized doctors evaluate the subjects from various perspectives. Similarly, ADE based on deep learning should mimic this approach by extracting and merging features from multiple perspectives and modalities. In particular, methods for feature fusion should be carefully designed by considering common tendencies, temporal synchronicity, and the dynamic nature of modalities. With ongoing enhancements in computational power, ADE methods based on large models will continue to be proposed.

However, data collection and availability remain significant limitations for the development of ADE. First, owing to privacy policies and research ethics, existing open-source datasets are scarce. Second, multi-modal data are rarely used in open-source datasets. While the DAIC-WOZ dataset provides transcripts, audio, and desensitized video information, datasets that offer other features potentially relevant to depression detection are lacking. Third, most of the current research on AI-based depression diagnosis and treatment has a relatively small sample size, making it challenging to

accurately reflect the characteristics of the overall population with depression. Fourth, data collection by the different research groups did not follow a unified standard.

In practical applications, deep learning-based ADE methods are still in the early stages of development. Nemesure *et al* [42] assessed the mental well-being of student populations by combining electronic health records with machine learning methods. Aguilera *et al*[43] developed applications and applied them to primary care. We believe that the interpretability of deep learning is a major limitation in its application. Future research should focus on two directions to enhance model credibility. The first is the construction of knowledge-guided ADE models. The research framework proposed by Hitzler and Sarker[44] is a novel research direction. The second is the incorporation of relevant analyses for model interpretability. Researchers can analyze the operating mechanism of a model using techniques such as visualization and feature capture.

In summary, researchers should focus on ADE based on bodily expressions. Additionally, unified and effective methods for audio feature extraction should continue to be explored. When constructing ADE models, special attention should be paid to the interpretability of the models. We hope that future research will introduce new perspectives and methods to address this aspect. Regarding data collection, research groups should consider publicly sharing their research paradigms, psychological effect evaluations, and desensitization data to help considerably advance the construction of large models and research progress in ADE.

CONCLUSION

In this paper, we provided an overview of prominent audio- and video-based ADE models in recent years, covering the aspects of audio, video, and fusion. An analysis of the relevant research revealed a lack of exploration of the body expressions of individuals with depression. We encourage researchers to delve further into audio feature extraction. In addition, we believe that the construction of large models is crucial for future research. We hope that researchers will develop outstanding ADE models in the future.

FOOTNOTES

Author contributions: Han MM, Li XY, Yi XY, Zheng YS and Wang QX designed the research study; Xia WL and Liu YF conducted literature retrieval; Han MM, Li XY, Yi XY, Zheng YS, and Wang QX summarized and analyzed relevant literature; Zheng YS provided medical knowledge; Han MM, Li XY, Yi XY, and Wang QX were responsible for writing and revising the manuscript; Wang QX reviewed the manuscript and approved its publication. All authors have read and approve the final manuscript.

Supported by Shandong Province Key R and D Program, No. 2021SFGC0504; Shandong Provincial Natural Science Foundation, No. ZR2021MF079; and Science and Technology Development Plan of Jinan (Clinical Medicine Science and Technology Innovation Plan), No. 202225054.

Conflict-of-interest statement: There is no conflict of interest associated with any of the senior author or other coauthors contributed their efforts in this manuscript.

Country/Territory of origin: China

ORCID number: Meng-Meng Han 0009-0003-1259-5048; Xing-Yun Li 0000-0002-5125-281X; Xin-Yu Yi 0009-0004-8734-075X; Qing-Xiang Wang 0000-0002-8159-7739.

S-Editor: Qu XL
L-Editor: A
P-Editor: Zheng XM

REFERENCES

1 **Benazzi F**. Various forms of depression. *Dialogues Clin Neurosci* 2006; **8**: 151-161 [PMID: 16889102 DOI: 10.31887/DCNS.2006.8.2/fbenazzi]
2 **Li X**, Mao Y, Zhu S, Ma J, Gao S, Jin X, Wei Z, Geng Y. Relationship between depressive disorders and biochemical indicators in adult men and women. *BMC Psychiatry* 2023; **23**: 49 [PMID: 36653784 DOI: 10.1186/s12888-023-04536-y]
3 **Cannizzaro M**, Harel B, Reilly N, Chappell P, Snyder PJ. Voice acoustical measurement of the severity of major depression. *Brain Cogn* 2004; **56**: 30-35 [PMID: 15380873 DOI: 10.1016/j.bandc.2004.05.003]
4 **Leff J**, Abberton E. Voice pitch measurements in schizophrenia and depression. *Psychol Med* 1981; **11**: 849-852 [PMID: 7323240 DOI:

10.1017/s0033291700041349]
5 **Ekman P**. What the face reveals: Basic and applied studies of spontaneous expression using the facial action coding system (facs). 2nd ed. Rosenberg E, editor. Cary, NC: Oxford University Press, 2005
6 **Girard JM**, Cohn JF, Mahoor MH, Mavadati S, Rosenwald DP. Social Risk and Depression: Evidence from Manual and Automatic Facial Expression Analysis. *Proc Int Conf Autom Face Gesture Recognit* 2013; 1-8 [PMID: 24598859 DOI: 10.1109/FG.2013.6553748]
7 **Joshi J**, Goecke R, Parker G, Breakspear M. Can body expressions contribute to automatic depression analysis? *IEEE Xplore*
8 **American Psychiatric Association**. Dsm-iv-tr: Diagnostic and statistical manual of mental disorders. 4th ed. Arlington, TX: American Psychiatric Press; 2000
9 **First MB**. Diagnostic and statistical manual of mental disorders, 5th edition, and clinical utility. *J Nerv Ment Dis* 2013; **201**: 727-729 [PMID: 23995026 DOI: 10.1097/NMD.0b013e3182a2168a]
10 **Kroenke K**, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. *J Gen Intern Med* 2001; **16**: 606-613 [PMID: 11556941 DOI: 10.1046/j.1525-1497.2001.016009606.x]
11 **HAMILTON M**. A rating scale for depression. *J Neurol Neurosurg Psychiatry* 1960; **23**: 56-62 [PMID: 14399272 DOI: 10.1136/jnnp.23.1.56]
12 **Peng Z**, Hu Q, Dang J. Multi-kernel SVM based depression recognition using social media data. *Int J Mach Learn Cybern* 2019; **10**: 43-57 [DOI: 10.1007/s13042-017-0697-1]
13 Alghowinem S, Goecke R, Wagner M, Epps J, Gedeon T, Breakspear M, Parker G. A comparative study of different classifiers for detecting depression from spontaneous speech. *IEEE Xplore* 2013 [DOI: 10.1109/ICASSP.2013.6639227]
14 **Wen L**, Li X, Guo G, Zhu Y. Automated depression diagnosis based on facial dynamic analysis and sparse coding. *IEEE Trans Inf Forensics Secur* 2015; **10**: 1432-1441 [DOI: 10.1109/tifs.2015.2414392]
15 **Valstar M**, Schuller B, Smith K, Eyben F, Jiang B, Bilakhia S, Schnieder S, Cowie R, Pantic M. AVEC 2013: The continuous audio/visual emotion and depression recognition challenge. Proceedings of the 3rd ACM international workshop on Audio/visual emotion challenge. *ACM* 2013 [DOI: 10.1145/2512530.2512533]
16 **Valstar M**, Schuller B, Smith K, Almaev T, Eyben F, Krajewski J, Cowie R, Pantic M. AVEC 2014: 3D Dimensional Affect and Depression Recognition Challenge. Proceedings of the 4th International Workshop on Audio/Visual Emotion Challenge. *ACM* 2014 [DOI: 10.1145/2661806.2661807]
17 **Gratch J**, Artstein R, Lucas GM, Stratou G, Scherer S, Nazarian A, Wood R, Boberg J, Devault D, Marsella S, Traum DR. The Distress Analysis Interview Corpus of Human and Computer Interviews. *Proc of LREC* 2014; 3123-3128
18 **He L**, Cao C. Automated depression analysis using convolutional neural networks from speech. *J Biomed Inform* 2018; **83**: 103-111 [PMID: 29852317 DOI: 10.1016/j.jbi.2018.05.007]
19 **Zuo L**, Mak MW. Avoiding dominance of speaker features in speech-based Depression detection. *Pattern Recognit Lett* 2023; 50-56 [DOI: 10.1016/j.patrec.2023.07.016]
20 **Du M**, Liu S, Wang T, Zhang W, Ke Y, Chen L, Ming D. Depression recognition using a proposed speech chain model fusing speech production and perception features. *J Affect Disord* 2023; **323**: 299-308 [PMID: 36462607 DOI: 10.1016/j.jad.2022.11.060]
21 **Yang W**, Liu J, Cao P, Zhu R, Wang Y, Liu JK, Wang F, Zhang X. Attention guided learnable time-domain filterbanks for speech depression detection. *Neural Netw* 2023; **165**: 135-149 [PMID: 37285730 DOI: 10.1016/j.neunet.2023.05.041]
22 **Han ZJ**, Shang YY, Shao ZH, Liu JY, Guo GD, Liu T, Ding H, Hu Q. Spatial-Temporal Feature Network for Speech-Based Depression Recognition. *IEEE Trans Cogn Dev Syst* 2023 [DOI: 10.1109/TCDS.2023.3273614]
23 **Chen W**, Xing X, Xu X, Pang J, Du L. SpeechFormer++: A hierarchical efficient framework for paralinguistic speech processing. *IEEE ACM Trans Audio Speech Lang Process* 2023; **31**: 775-788 [DOI: 10.1109/taslp.2023.3235194]
24 **Mao K**, Zhang W, Wang DB, Li A, Jiao R, Zhu Y, Wu B, Zheng T, Qian L, Lyu W, Ye M, Chen J. Prediction of depression severity based on the prosodic and semantic features with bidirectional LSTM and time distributed CNN. *IEEE Trans Affect Comput*1-1 [DOI: 10.1109/taffc.2022.3154332]
25 **He L**, Chan JCW, Wang Z. Automatic depression recognition using CNN with attention mechanism from videos. *Neurocomputing* 2021; **422**: 165-175 [DOI: 10.1016/j.neucom.2020.10.015]
26 **He L**, Tiwari P, Lv C, Wu W, Guo L. Reducing noisy annotations for depression estimation from facial images. *Neural Netw* 2022; **153**: 120-129 [PMID: 35717754 DOI: 10.1016/j.neunet.2022.05.025]
27 **Zhao J**, Zhang L, Cui Y, Shi J, He L. A novel Image-Data-Driven and Frequency-Based method for depression detection. *Biomed Signal Process Control* 2023; **86**: 105248 [DOI: 10.1016/j.bspc.2023.105248]
28 **Huang SC**, Cheng FC, Chiu YS. Efficient contrast enhancement using adaptive gamma correction with weighting distribution. *IEEE Trans Image Process* 2013; **22**: 1032-1041 [PMID: 23144035 DOI: 10.1109/TIP.2012.2226047]
29 **Kupyn O**, Martyniuk T, Wu J, Wang Z. DeblurGAN-v2: Deblurring (orders-of-magnitude) faster and better. *Proc IEEE Int Conf Comput Vis* 2019 [DOI: 10.1109/ICCV.2019.00897]
30 **Ding X**, Zhang X, Zhou Y, Han J, Ding G, Sun J. Scaling up your kernels to 31x31: Revisiting large kernel design in CNNs. *Proc IEEE Comput Soc Conf Comput Vis Pattern Recognit* 2022 [DOI: 10.1109/CVPR52688.2022.01166]
31 **Liu Z**, Yuan X, Li Y, Shangguan Z, Zhou L, Hu B. PRA-Net: Part-and-Relation Attention Network for depression recognition from facial expression. *Comput Biol Med* 2023; **157**: 106589 [PMID: 36934531 DOI: 10.1016/j.compbiomed.2023.106589]
32 **Yuan Y**, Wang Q. Detection model of depression based on eye movement trajectory. *IEEE Proc Int Conf Data Sci Adv Anal* 2019 [DOI: 10.1109/DSAA.2019.00082]
33 **Zhao J**, Wang Q. Eye movement attention based depression detection model. *IEEE Proc Int Conf Data Sci Adv Anal* 2022 [DOI: 10.1109/DSAA54385.2022.10032433]
34 **Yu Y**, Li W, Zhao Y, Ye J, Zheng Y, Liu X, Wang Q. Depression and Severity Detection Based on Body Kinematic Features: Using Kinect Recorded Skeleton Data of Simple Action. *Front Neurol* 2022; **13**: 905917 [PMID: 35847201 DOI: 10.3389/fneur.2022.905917]
35 **Zhao X**, Wang Q. Depression detection based on human simple kinematic skeletal data. *IEEE Proc Int Conf Data Sci Adv Anal* 2022 [DOI: 10.1109/DSAA54385.2022.10032376]
36 **Yang B**, Wang P, Cao M, Zhu X, Wang S, Ni R, Yang C. Uncertainty-Aware Label Contrastive Distribution Learning for Automatic Depression Detection. *IEEE Trans Comput Soc Syst* 2023 [DOI: 10.1109/TCSS.2023.3311013]
37 **Niu M**, Tao J, Liu B, Huang J, Lian Z. Multimodal spatiotemporal representation for automatic depression level detection. *IEEE Trans Affect Comput* 2023; **14**: 294-307 [DOI: 10.1109/taffc.2020.3031345]

38 **Shao W**, You Z, Liang L, Hu X, Li C, Wang W, Hu B. A Multi-Modal Gait Analysis-Based Detection System of the Risk of Depression. *IEEE J Biomed Health Inform* 2022; **26**: 4859-4868 [PMID: 34699374 DOI: 10.1109/JBHI.2021.3122299]

39 **Zhou L**, Liu Z, Shangguan Z, Yuan X, Li Y, Hu B. TAMFN: Time-Aware Attention Multimodal Fusion Network for Depression Detection. *IEEE Trans Neural Syst Rehabil Eng* 2023; **31**: 669-679 [PMID: 36417750 DOI: 10.1109/TNSRE.2022.3224135]

40 **Yoon J**, Kang C, Kim S, Han J. D-vlog: Multimodal Vlog Dataset for Depression Detection. *Proc Conf AAAI Artif Intell* 2022; **36**: 12226-12234 [DOI: 10.1609/aaai.v36i11.21483]

41 **Uddin MA**, Joolee JB, Sohn KA. Deep multi-modal network based automated depression severity estimation. *IEEE Trans Affect Comput* 2022; 1-1 [DOI: 10.1109/taffc.2022.3179478]

42 **Nemesure MD**, Heinz MV, Huang R, Jacobson NC. Predictive modeling of depression and anxiety using electronic health records and a novel machine learning approach with artificial intelligence. *Sci Rep* 2021; **11**: 1980 [PMID: 33479383 DOI: 10.1038/s41598-021-81368-4]

43 **Aguilera A**, Figueroa CA, Hernandez-Ramos R, Sarkar U, Cemballi A, Gomez-Pathak L, Miramontes J, Yom-Tov E, Chakraborty B, Yan X, Xu J, Modiri A, Aggarwal J, Jay Williams J, Lyles CR. mHealth app using machine learning to increase physical activity in diabetes and depression: clinical trial protocol for the DIAMANTE Study. *BMJ Open* 2020; **10**: e034723 [PMID: 32819981 DOI: 10.1136/bmjopen-2019-034723]

44 **Hitzler P**, Sarker MK. Neuro-Symbolic Artificial Intelligence: The State of the Art. IOS Press. 2021. Available from: https://ebooks.iospress.nl/volume/neuro-symbolic-artificial-intelligence-the-state-of-the-art

World Journal of Psychiatry

Submit a Manuscript: https://www.f6publishing.com

World J Psychiatry 2024 February 19; 14(2): 234-244

DOI: 10.5498/wjp.v14.i2.234

ISSN 2220-3206 (online)

ORIGINAL ARTICLE

Case Control Study

Impaired implicit emotion regulation in patients with panic disorder: An event-related potential study on affect labeling

Hai-Yang Wang, Li-Zhu Li, Yi Chang, Xiao-Mei Pang, Bing-Wei Zhang

Specialty type: Psychiatry

Provenance and peer review: Unsolicited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

Grade A (Excellent): A
Grade B (Very good): 0
Grade C (Good): C
Grade D (Fair): 0
Grade E (Poor): 0

P-Reviewer: Garcia-Campayo J, Spain Kar SK, India

Received: September 30, 2023
Peer-review started: September 30, 2023
First decision: December 6, 2023
Revised: December 12, 2023
Accepted: December 29, 2023
Article in press: December 29, 2023
Published online: February 19, 2024

Hai-Yang Wang, Department of Neurology, Jining No. 1 People's Hospital, Shandong First Medical University, Jining 272000, Shandong Province, China

Hai-Yang Wang, Li-Zhu Li, Yi Chang, Xiao-Mei Pang, Bing-Wei Zhang, Department of Neurology and Psychiatry, First Affiliated Hospital of Dalian Medical University, Dalian 116011, Liaoning Province, China

Li-Zhu Li, Department of Neurology, Sixth Peoples' Hospital of Shenyang, Shenyang 110003, Liaoning Province, China

Corresponding author: Bing-Wei Zhang, MD, PhD, Professor, Researcher, Department of Neurology and Psychiatry, First Affiliated Hospital of Dalian Medical University, No. 222 Zhongshan Road, Dalian 116011, Liaoning Province, China. zhangbingweidoc@163.com

Abstract

BACKGROUND

Panic disorder (PD) involves emotion dysregulation, but its underlying mechanisms remain poorly understood. Previous research suggests that implicit emotion regulation may play a central role in PD-related emotion dysregulation and symptom maintenance. However, there is a lack of studies exploring the neural mechanisms of implicit emotion regulation in PD using neurophysiological indicators.

AIM

To study the neural mechanisms of implicit emotion regulation in PD with event-related potentials (ERP).

METHODS

A total of 25 PD patients and 20 healthy controls (HC) underwent clinical evaluations. The study utilized a case-control design with random sampling, selecting participants for the case group from March to December 2018. Participants performed an affect labeling task, using affect labeling as the experimental condition and gender labeling as the control condition. ERP and behavioral data were recorded to compare the late positive potential (LPP) within and between the groups.

RESULTS

Both PD and HC groups showed longer reaction times and decreased accuracy

under the affect labeling. In the HC group, late LPP amplitudes exhibited a dynamic pattern of initial increase followed by decrease. Importantly, a significant group × condition interaction effect was observed. Simple effect analysis revealed a reduction in the differences of late LPP amplitudes between the affect labeling and gender labeling conditions in the PD group compared to the HC group. Furthermore, among PD patients under the affect labeling, the late LPP was negatively correlated with disease severity, symptom frequency, and intensity.

CONCLUSION

PD patients demonstrate abnormalities in implicit emotion regulation, hampering their ability to mobilize cognitive resources for downregulating negative emotions. The late LPP amplitude in response to affect labeling may serve as a potentially valuable clinical indicator of PD severity.

Key Words: Panic disorder; Implicit; Emotion regulation; Affect labeling; Late positive potential

Core Tip: This study investigates neural mechanisms of implicit emotion regulation in panic disorder (PD) using event-related potentials. PD patients exhibit anomalies during an affect labeling task, including prolonged reaction times and reduced accuracy. Neurophysiological data indicate diminished differences in late positive potential (LPP) amplitude between affect labeling and gender labeling in PD, negatively correlating with disease severity, symptom frequency, and intensity. Resultantly, PD patients demonstrate impaired implicit emotion regulation, hindering cognitive resource mobilization for negative emotion downregulation. The late LPP amplitude in response to affect labeling may serve as a valuable clinical indicator of PD severity.

Citation: Wang HY, Li LZ, Chang Y, Pang XM, Zhang BW. Impaired implicit emotion regulation in patients with panic disorder: An event-related potential study on affect labeling. *World J Psychiatry* 2024; 14(2): 234-244
URL: https://www.wjgnet.com/2220-3206/full/v14/i2/234.htm
DOI: https://dx.doi.org/10.5498/wjp.v14.i2.234

INTRODUCTION

Panic disorder (PD) is a severe anxiety disorder characterized by spontaneous and recurring panic attacks and a constant fear of experiencing panic symptoms[1]. Epidemiological studies have reported a lifetime prevalence of PD at 4.7%[2]. Despite advancements in understanding PD, the neural mechanisms underlying its onset remain incompletely understood. Clinical observations and experimental evidence suggest that deficiencies in emotion regulation play a crucial role in the development of PD[3] because they contribute to heightened fear responses.

Emotion regulation involves individuals modifying their emotional responses in response to environmental demands, exerting control over the duration, intensity, and underlying characteristics of emotions[4]. Previous studies on emotion regulation have primarily focused on explicit strategies. In the context of PD, research on the neural mechanisms of emotion regulation has predominantly examined conscious strategies, revealing abnormal activation in the dorsolateral prefrontal cortex (DLPFC) and the ventromedial prefrontal cortex in individuals with PD during emotional regulation processes[3]. However, meta-analyses on repetitive transcranial magnetic stimulation (rTMS) targeting brain regions associated with conscious emotion regulation, such as the DLPFC, have not provided conclusive evidence regarding the efficacy of rTMS in treating PD[5,6].

According to Gross's model[7], emotion regulation strategies can be explicit (conscious) or implicit (unconscious). In clinical settings, it is observed that panic attacks in PD patients often occur suddenly and cease abruptly, with some patients even experiencing attacks during sleep[1,8]. There is no conscious emotion regulation process before or during panic attacks in patients. The catastrophic cognitive theory suggests that in PD, patients automatically evaluate both internal and external stimuli that are insufficient to elicit intense reactions as threat signals, leading to the initiation and maintenance of their anxiety[8]. Additionally, our previous findings indicate that PD patients exhibit anomalous mismatch negativity responses to acoustic and visual stimuli (both emotional and non-emotional), indicating abnormal automatic information processing in these individuals[9]. Therefore, we speculate that the core mechanism underlying emotion regulation dysfunction in PD patients may not originate from explicit abnormalities in emotion regulation but instead from implicit abnormalities in emotion regulation.

While the reported evidence suggests a significant role of implicit emotion dysregulation in the pathogenesis of PD [10], the specific mechanisms underlying these regulatory effects remain unclear. Affect labeling is an effective way to reduce unwanted emotions and the distress associated with negative events through putting feelings into words[11]. As the intent to reduce distress is not explicit, affect labeling has been conceptualized as a form of implicit emotion regulation that typically involves verbally labeling the emotional content of a facial stimulus, such as labeling an angry facial expression as "angry" or a fearful facial expression as "fearful"[11,12]. Although the regulatory effects of affect labeling on emotions have been established[11,13], the precise mechanism by which it reduces emotions, whether through

direct weakening or a dynamic process of initial enhancement followed by attenuation, remains unclear, especially in PD patients. Therefore, employing high-temporal-resolution event-related potentials (ERP) can help elucidate these questions.

The late positive potential (LPP) is a prominent component of ERP, typically occurring around 300 ms after stimulus onset. It is widely utilized in the study of emotion regulation[14], and its amplitude is known to increase with the subjective intensity of emotional experience, serving as an indicator of emotional regulation effectiveness. While previous LPP research suggests that affect labeling can reduce emotional experience[11,13], these findings are based on measuring the overall effect after labeling. Affect labeling tasks involve cognitive and motivation-related processing, and the LPP reflects changes in cognitive resources and motivation-related stimulus processing[15]. As a result, the amplitude of the LPP may dynamically vary instead of simply weakening.

To date, no studies have investigated the neural correlates of affect labeling in PD using ERP. In our current investigation, we recorded LPP data during affect labeling tasks performed by both PD patients and healthy individuals. We used emotional faces (negative and positive) as stimuli, building upon findings from research on implicit emotion dysregulation in anxiety disorders[16]. Building on clinical observations and previous studies, we developed two hypotheses: (1) In healthy individuals, the amplitude of the LPP is expected to dynamically fluctuate rather than simply decrease when using affect labeling to downregulate emotions; and (2) Compared to healthy controls (HC), individuals with PD are anticipated to show a deficit in the regulatory effect of affect labeling, potentially attributed to impaired cognitive processing.

MATERIALS AND METHODS

Participants

Twenty-five individuals (7 males, 18 females) diagnosed with clinically predominant PD according to the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (DSM-IV)[17], and 20 HC (9 males, 11 females) without a history of DSM-IV Axis I disorders were recruited from the outpatient and emergency departments of the First Affiliated Hospital of Dalian Medical University and the surrounding communities. The sample size was determined based on previously published ERP studies related to PD[9]. The PD group scored 14 or higher on the Hamilton Anxiety Rating Scale (HAMA) and 7 or lower on the Hamilton Depression Rating Scale (HAMD). Benzodiazepine medication was discontinued for at least one week, and a standardized Structured Clinical Interview for DSM-IV was conducted by a qualified physician to screen for other Axis I diagnoses. The HC group was recruited during the same period and matched the demographic characteristics of the PD group. The HC group scored 7 or lower on the HAMA and HAMD. PD patients completed the PD Severity Scale (PDSS)[18] and the Panic-Associated Symptom Scale (PASS)[19] to assess the severity of PD and associated symptoms. All participants scored ≥ 24 on the Mini-Mental State Examination and abstained from using psychoactive substances in the 24 h preceding the examination. Participants with other psychiatric disorders, severe physical illnesses, brain disorders, or substance dependence were excluded. Informed consent was obtained from all participants prior to their participation, following the principles of the Declaration of Helsinki. This study was approved by the Ethics Committee of the First Hospital of Dalian Medical University.

Stimulus materials

From the Chinese Facial Affective Picture System[20], a set of 60 negative emotional face pictures (including anger, fear, and sadness) and 60 positive emotional face pictures were selected. The distribution of male and female pictures was equal in both categories. Statistical analysis revealed no significant differences in valence and arousal ratings between male and female pictures (t = -1.54, P > 0.05; t = 0.19, P > 0.05). The mean valence ratings for positive male and female pictures were 5.6 (SD = 0.6) and 6.3 (SD = 0.7), respectively, while negative male and female pictures received valence ratings of 2.8 (SD = 0.3) and 3.0 (SD = 0.5), respectively. Arousal ratings showed that positive male and female pictures had mean scores of 4.6 (SD = 1.1) and 4.8 (SD = 1.0), respectively, whereas negative male and female pictures had mean scores of 6.1 (SD = 1.2) and 5.8 (SD = 1.2), respectively.

Experiment design and procedure

The experiment followed a classic paradigm[21] that involved two tasks: Affect labeling (experimental group) and gender labeling (control group). Participants first fixated on a "+" in the center of the screen for 1000 ms. Then, for 3500 ms, they viewed randomly presented label words and targeted emotional facial expressions. In the gender labeling task, participants determined the gender of the facial image and pressed the left or right key accordingly. The gender labels used were "male" and "female." The affect labeling task followed the same procedure, with participants selecting the label word that best described the emotion. Each trial followed the procedure depicted in Figure 1, with the next trial commencing after the image disappeared. The experiment comprised a practice phase and a formal experiment phase, with the practice images excluded from the formal phase. The practice phase continued until participants demonstrated comprehension of the experimental procedure and achieved an accuracy rate of 80% or higher. The formal experiment phase consisted of 240 trials, with 120 trials allocated to affect labeling (randomly divided into E1 and E2 groups) and 120 trials to gender labeling (randomly divided into S1 and S2 groups). Each set of trials constituted a block. To ensure balance between participant groups, the experiment was conducted in two versions: E1-S1-E2-S2 and S2-E2-S1-E1.

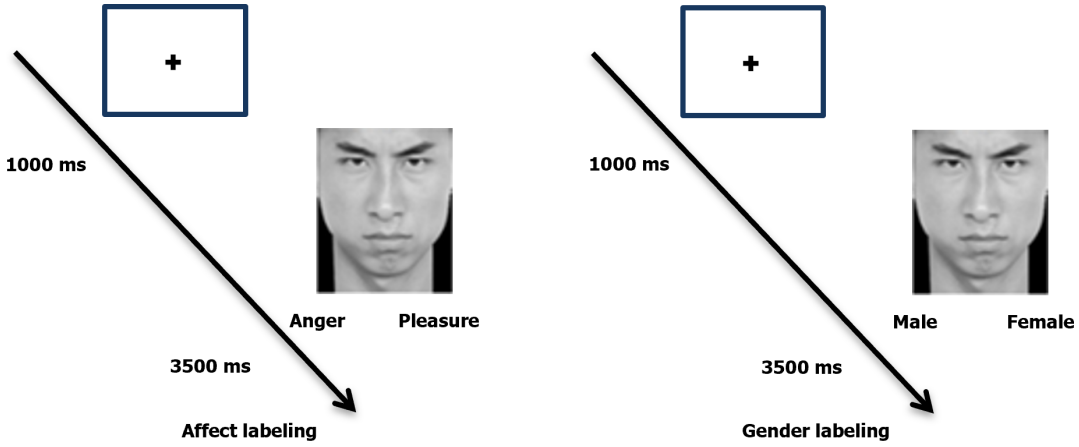

Figure 1 Task design. In the left panel, participants engage in affect labeling trials by selecting the suitable affect label that best describes the facial expression of the target face. In contrast, the right panel demonstrates gender labeling (control) trials, where participants are tasked with selecting the name corresponding to the gender-appropriate category of the target face.

Electroencephalogram recording

Stimulus presentation and behavioral response data (reaction time, accuracy) were controlled and recorded using E-prime 2.0 software. Electroencephalogram (EEG) data were collected using a Neuroscan SynAmps2 amplifier with a 64-channel Ag/AgCl electrode cap following the standardized 10-20 system. Continuous EEG signals were recorded and analyzed offline using NeuroScan 4.5 software. During EEG recording, an average reference was applied, and bipolar electrodes were used to capture horizontal eye movements and vertical eye movements. The data were sampled at a rate of 500 Hz in direct current mode and filtered with a bandpass of 0.05 to 100 Hz. Electrode impedance was maintained below 5 kΩ throughout the data collection process.

Data analysis

The participants' EEG waveforms were analyzed offline using NeuroScan 4.5 software. Bilateral mastoids served as the average reference electrodes. Manual removal of eye movements and artifacts was performed. The EEG data were filtered with a low-pass filter at 30 Hz and a high-pass filter at 0.5 Hz. Segmentation of the EEG data yielded two time windows: Early LPP and late LPP. The early LPP time window extended from 200 ms before stimulus onset to 1000 ms after stimulus onset, while the late LPP was defined as the time window spanning from 200 ms before response onset to 1000 ms after response onset. Artifacts were rejected, and the data were averaged to obtain the grand average waveform. The measured ERP components, based on prior literature, comprised the early LPP (300-800 ms after stimulus onset, reflecting emotional experience following stimulus presentation) and the late LPP (300-1000 ms after task response, reflecting emotional processing and experience during task performance). To investigate the dynamic changes of the late LPP, the late LPP was further divided into two time windows (350-630 ms, 630-1000 ms) based on the grand average waveform from this experiment. Five electrode sites along the midline of the frontal-parietal region were recorded: Frontal midline (Fz), frontocentral midline (FCz), central midline (Cz), centroparietal midline (CPz), and parietal midline (Pz).

The behavioral data (reaction time, accuracy) and EEG components were analyzed using SPSS 22.0. A 2 × 2 repeated measures analysis of variance (RMANOVA) was conducted on the behavioral data, with group (PD, HC) as the between-subjects factor and task type (affect labeling, gender labeling) as the within-subjects factor. The LPP amplitude data were analyzed using a 2 × 2 × 5 RMANOVA, considering group, task type, and electrode location (Fz, FCz, Cz, CPz, Pz). Separate within-group RMANOVAs (2 × 5) were performed for the HC and PD groups, with task type and electrode location as the within-subjects' factors. Covariance analysis was applied, taking into account covariates based on the behavioral results. Effect sizes were measured with partial eta-squared (η_p^2). Greenhouse-Geisser correction was applied, when necessary, to adjust degrees of freedom and *P*-values for main effects and interaction effects. Pearson correlation analysis was used to examine the relationships between electrophysiological data, clinical data, and behavioral data in the PD group. Two-tailed tests were conducted, and statistical significance was set at $P < 0.05$.

RESULTS

Demographic and clinical data

Demographic and clinical characteristics of the HC and PD groups are presented in Table 1. There were no significant differences among the three groups in terms of gender, age, body mass index, and education. However, significant differences were observed in HAMA and HAMD scores ($P < 0.001$), with the PD group exhibiting the highest scores for both HAMA and HAMD.

Table 1 Demographics and clinical characteristics of the participants

	PD (n = 25)	HC (n = 20)	t/χ^2	P value
Age (yr)	47.20 ± 10.928	49.65 ± 12.766	0.681	0.500
Gender (male/female)	7/18	9/11	1.401	0.236
Education in years	13.52 ± 10.689	14.05 ± 12.037	0.156	0.877
BMI	24.89 ± 3.612	24.77 ± 3.222	0.120	0.905
HAMA	19.40 ± 4.830	2.95 ± 3.000	13.299	< 0.001[a]
HAMD	12.76 ± 2.85	2.85 ± 1.599	10.581	< 0.001[a]
PDSS	8.56 ± 3.906	N/A	N/A	N/A
PASS	6.84 ± 2.954	N/A	N/A	N/A

[a]P < 0.001.

BMI: Body mass index; PD: Panic disorder; HC: Healthy controls; HAMA: Hamilton Anxiety Rating Scale; HAMD: Hamilton Depression Rating Scale; PDSS: Panic Disorder Severity Scale; PASS: Panic-Associated Symptom Scale; N/A: Not applicable.

Behavioral performance

Descriptive statistics for reaction time and accuracy of the two groups under the two conditions are presented in Table 2. Reaction time analysis showed no significant interaction between group and task type ($F_{1, 41}$ = 1.209, P = 0.278, η_p^2 = 0.029). Task type had a significant main effect ($F_{1, 41}$ = 18.54, P < 0.001, η_p^2 = 0.311), indicating longer reaction times in the affect labeling task. The main effect of group was not significant ($F_{1, 41}$ = 2.339, P = 0.134, η_p^2 = 0.054), despite the PD group having longer reaction times in both tasks.

Accuracy analysis showed no significant interaction between group and task type ($F_{1, 41}$ = 0.453, P = 0.505, η_p^2 = 0.011). The main effect of group was not statistically significant ($F_{1, 41}$ = 0.468, P = 0.498, η_p^2 = 0.011), indicating similar accuracy between the two groups. However, there was a significant difference between the two groups in the affect labeling and gender labeling conditions ($F_{1, 41}$ = 19.174, P < 0.001, η_p^2 = 0.319), with higher accuracy in the gender labeling task.

Early LPP amplitude

The average early LPP amplitudes for both groups under the two conditions are shown in Supplementary Table 1, with waveform plots in Figure 2A and scalp topography in Figure 2B. Covariance analysis, with accuracy and reaction time as covariates, showed no significant differences in early LPP amplitudes among the groups, paradigm types, electrode locations, and their interactions (P > 0.05 for all comparisons).

Late LPP amplitude

As depicted in Figure 3A, the HC group demonstrated higher amplitudes compared to the PD group at FCz, Cz, CPz, and Pz electrode sites. We conducted an analysis of the overall average late LPP amplitude (300-1000 ms). Within the HC group, the affect labeling condition exhibited larger LPP amplitudes than the gender labeling condition [(2.77 ± 2.75 μV) *vs* (2.15 ± 2.42 μV)]. Conversely, in the PD group, there was minimal difference in late LPP amplitudes between the affect labeling and gender labeling conditions [(1.49 ± 2.29 μV) *vs* (1.79 ± 2.63 μV)], which aligns with the observed scalp voltage distribution in Figure 3B. Supplementary Table 2 provides the statistical values for the overall late LPP amplitudes.

A 2 × 2 × 5 RMANOVA was conducted to analyze overall average late LPP amplitude within the 350-630 ms time window. The results revealed significant effects. Firstly, there was a significant main effect of electrode location ($F_{1.46,63}$ = 33.68, P < 0.001, η_p^2 = 0.4394). Specifically, the FCz electrode showed significantly higher amplitudes compared to the Fz, Cz, CPz, and Pz electrodes (P < 0.01 for all comparisons). Furthermore, the analysis indicated significant differences in late LPP amplitudes between the two groups at the Cz (P = 0.015), CPz (P = 0.01), and Pz (P = 0.004) electrode sites.

Importantly, there was a significant task type × group interaction effect ($F_{1,41}$ = 6.32, P = 0.02, η_p^2= 0.14) within the 350-630 ms time window. Follow-up RMANOVA on the HC group revealed that affect labeling LPP (3.88 ± 3.60 μV) was significantly higher than gender labeling LPP (2.33 ± 3.48 μV) (P = 0.044). However, in the PD group, the difference between affect labeling LPP (3.14 ± 3.65 μV) and gender labeling LPP (2.44 ± 4.04 μV) did not reach statistical significance (P > 0.05), suggesting a lack of affect labeling effect. Late LPP amplitudes within the 630-1000 ms time window exhibited no significant differences in late LPP amplitudes across the groups, paradigm types, electrode locations, and their interactions (P > 0.05 for all comparisons).

Notably, in healthy individuals, the affect labeling LPP amplitudes were significantly higher than the gender labeling amplitudes within the 350-630 ms window, which does not indicate a decline in emotional response. However, after 630 ms, there was a trend towards convergence between the affect labeling and gender labeling LPP amplitudes. Further analysis in the 630-1000 ms window revealed a smaller difference in LPP amplitudes between affect labeling and gender labeling [(1.65 ± 2.35 μV) *vs* (1.36 ± 2.16 μV)], compared to the 350-630 ms window [(3.88 ± 3.60 μV) *vs* (2.33 ± 3.48 μV)], with no statistically significant difference of the 630-1000 ms window LPP amplitudes ($F_{1, 19}$ = 1.06, P = 0.316, η_p^2 = 0.05), indicating a decline in emotional response. This suggests that the unique nature of affect labeling led to an initial increase followed by a decrease in LPP amplitudes.

Table 2 Accuracy and reaction time (ms) of the two groups under the two tasks

	PD				HC			
	Affect labeling		Gender labeling		Affect labeling		Gender labeling	
	M	SD	M	SD	M	SD	M	SD
Reaction time	0.9271	4.62	0.9594	4.85	0.9145	13.94	0.9382	14.21
Accuracy	1389.32	221.43	1239.97	275.19	1247.50	261.76	1158.9	255.87

PD: Panic disorder; HC: Healthy controls; M: Mean.

Correlations

We performed Pearson correlation analyses to investigate the associations between late LPP amplitudes (350-630 ms) at 5 electrode sites during affect labeling and demographic data, behavioral measures, and clinical scale scores in the PD group. As shown in Figure 3C, we found significant negative correlations between late LPP amplitudes and PDSS scores at the Cz electrode site (r = -0.437, P = 0.029). Additionally, there were significant negative correlations between late LPP amplitudes and PASS scores at the same Cz electrode site (r = -0.423, P = 0.035).

DISCUSSION

This study investigated the implicit emotion regulation capacity in individuals with PD using ERP and affect labeling paradigms, while also examining the dynamic changes in affect labeling effects observed in the HC. Our findings revealed that both the PD and HC groups demonstrated prolonged reaction times and reduced accuracy in the affect labeling task compared to the gender labeling task, potentially indicating a greater demand for cognitive resources during affect labeling[22]. Additionally, the LPP amplitudes in the affect labeling condition displayed an initial increase followed by a subsequent decrease, suggesting that the process of emotion regulation through labeling is not immediate. Importantly, we observed an interaction effect between group and task condition on the late LPP. However, in the PD group, affect labeling did not result in significant neural modulation, indicating the ineffectiveness of this strategy in reducing negative emotions among PD patients and highlighting compromised implicit emotion regulation abilities in PD. Lastly, the LPP amplitudes in PD exhibited a negative correlation with PDSS and PASS scores, implying that the inability to effectively attenuate negative emotions during implicit emotion regulation may be associated with disease severity, episode frequency, and symptom intensity.

The behavioral data showed that, in the HC group, reaction times were longer for affect labeling compared to gender labeling, while accuracy was higher for gender labeling, which is in line with previous findings[23]. This performance difference can be attributed to task difficulty[24]. Moreover, the RMANOVA analysis demonstrated a significant main effect of condition but did not reveal a main effect of group, indicating that individuals with PD do not exhibit differences in reaction times and accuracy compared to HC.

The dynamic changes in LPP amplitudes during affect labeling, characterized by an initial increase followed by a decrease, reflect a distinct psychological process worthy of discussion. Torrisi *et al*[22] (2013) discovered that individuals utilize the prefrontal-amygdala circuit to suppress emotions during affect labeling, leading to the downregulation of negative emotional experiences[22]. This process involves the consumption of cognitive resources. Our study involved participants translating perceived facial emotions into verbal expressions through the affect labeling task, which required semantic processing of emotional features and the utilization of cognitive resources[23]. While both affect labeling and gender labeling tasks involve transforming features into language, affect labeling specifically deals with emotionally arousing information, representing a more complex cognitive processing[11] that demands higher cognitive resource consumption. Consequently, this is likely to lead to a more pronounced increase in LPP amplitudes during affect labeling. Furthermore, the decline in LPP amplitudes, reaching a level comparable to or even lower than gender labeling, indicates the regulatory influence of affect labeling on emotions[11,12]. However, the absence of a significant decrease in LPP amplitudes after affect labeling in this study can be attributed to the relatively lower level of arousal elicited by the negative images employed[23,25].

In this study, we observed an interaction effect between group and task type, indicating that the relationship between these factors influenced the outcomes. Specifically, when analyzing the late LPP amplitudes in the PD group, we found no significant differences between affect labeling and gender labeling tasks. These findings suggest a lack of effect of affect labeling on emotion regulation in individuals with PD. Previous research has consistently reported cognitive biases and interpretive tendencies in individuals with PD[8,26], where they exhibit a tendency to prioritize attention towards threatening stimuli and engage in catastrophic interpretations of emotional cues. This cognitive bias hinders effective downregulation of negative emotions, as individuals with PD tend to perseverate on negative aspects and struggle to mobilize sufficient cognitive resources for successful regulation of negative emotions. Furthermore, prior functional magnetic resonance imaging (fMRI) studies have consistently demonstrated compromised top-down unconscious cognitive control from the prefrontal cortex to the amygdala in individuals with PD[3,27]. Our study aligns with these findings as we did not observe a significant enhancement in the late LPP amplitude (350-630 ms) in the electro-

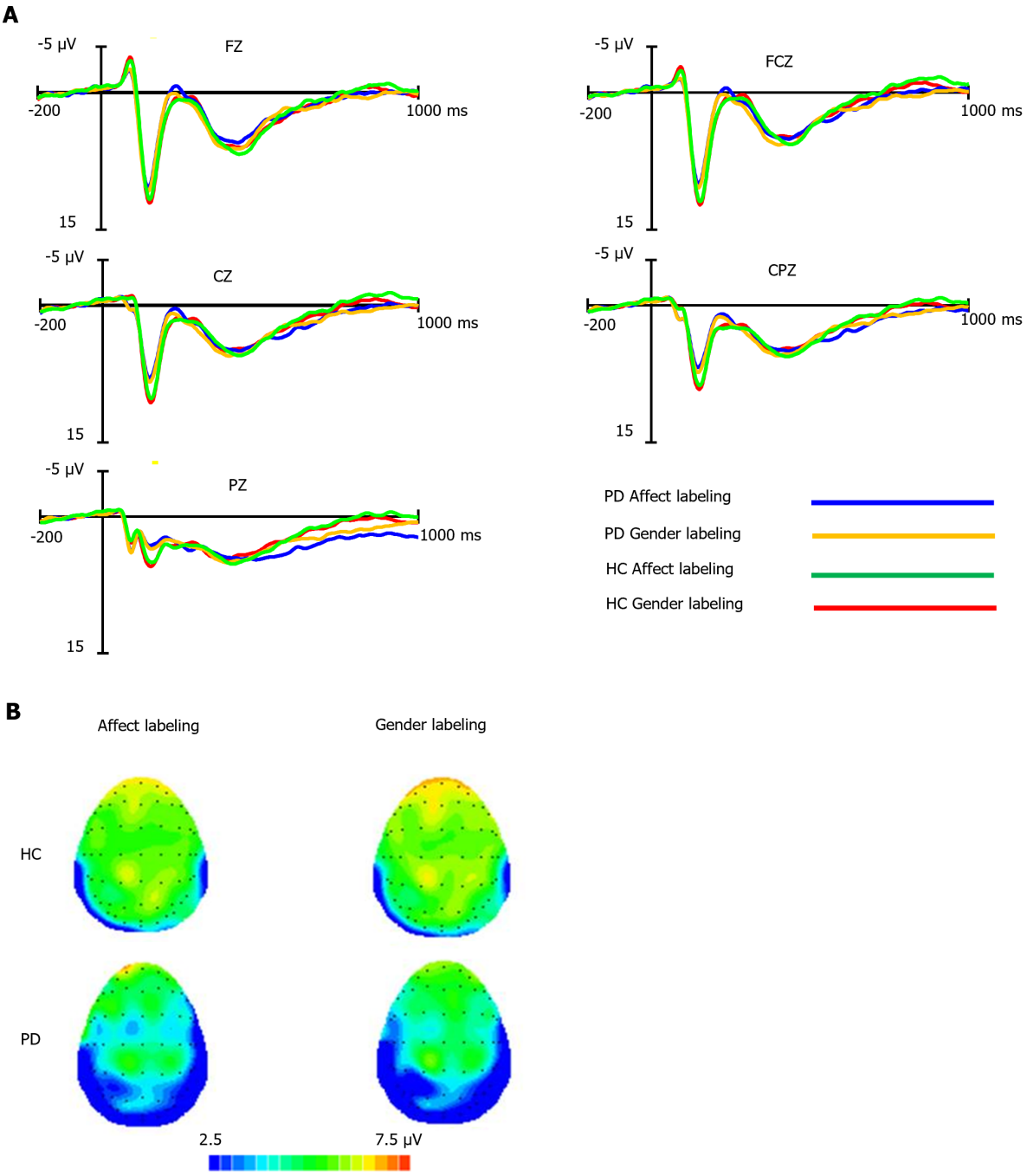

Figure 2 Early late positive potential amplitude. A: Illustrates the early late positive potential amplitudes of each electrode site for the healthy control and panic disorder groups under the affect labeling and gender labeling conditions. There were no significant main effects of group, condition, or electrode, and no significant interaction effects were observed ($P > 0.05$ for all comparisons); B: Displays the topographic maps of the two groups under the two conditions. PD: Panic disorder; HC: Healthy control; Fz: Frontal midline; FCz: Frontocentral midline; Cz: Central midline; CPz: Centroparietal midline; Pz: Parietal midline.

physiological signals, providing further support for the notion of impaired implicit emotion processing in individuals with PD.

Interestingly, we observed a significant negative correlation between disease severity and late LPP amplitudes in the PD group. Specifically, greater severity of PD symptoms in the past month or higher frequency and intensity of symptoms in the past week were associated with impaired implicit emotion regulation abilities. These findings support the potential use of LPP as an electrophysiological marker for monitoring disease progression and assessing treatment effectiveness.

This study has a few limitations. Firstly, the level of arousal elicited by the emotional stimuli was not strong enough, potentially impacting the full capture of the decline in late LPP[23,24]. However, data and waveform analysis support the existence of the regulatory process involving enhancement followed by attenuation through affect labeling. Secondly, the study exclusively utilized "negative" labels. Future research can explore more specific labels (*e.g.*, neutral and positive) to further investigate related aspects. Lastly, the study design lacked longitudinal treatment evaluations. Future studies should consider incorporating follow-up assessments of the patients to track changes over time. This would not only

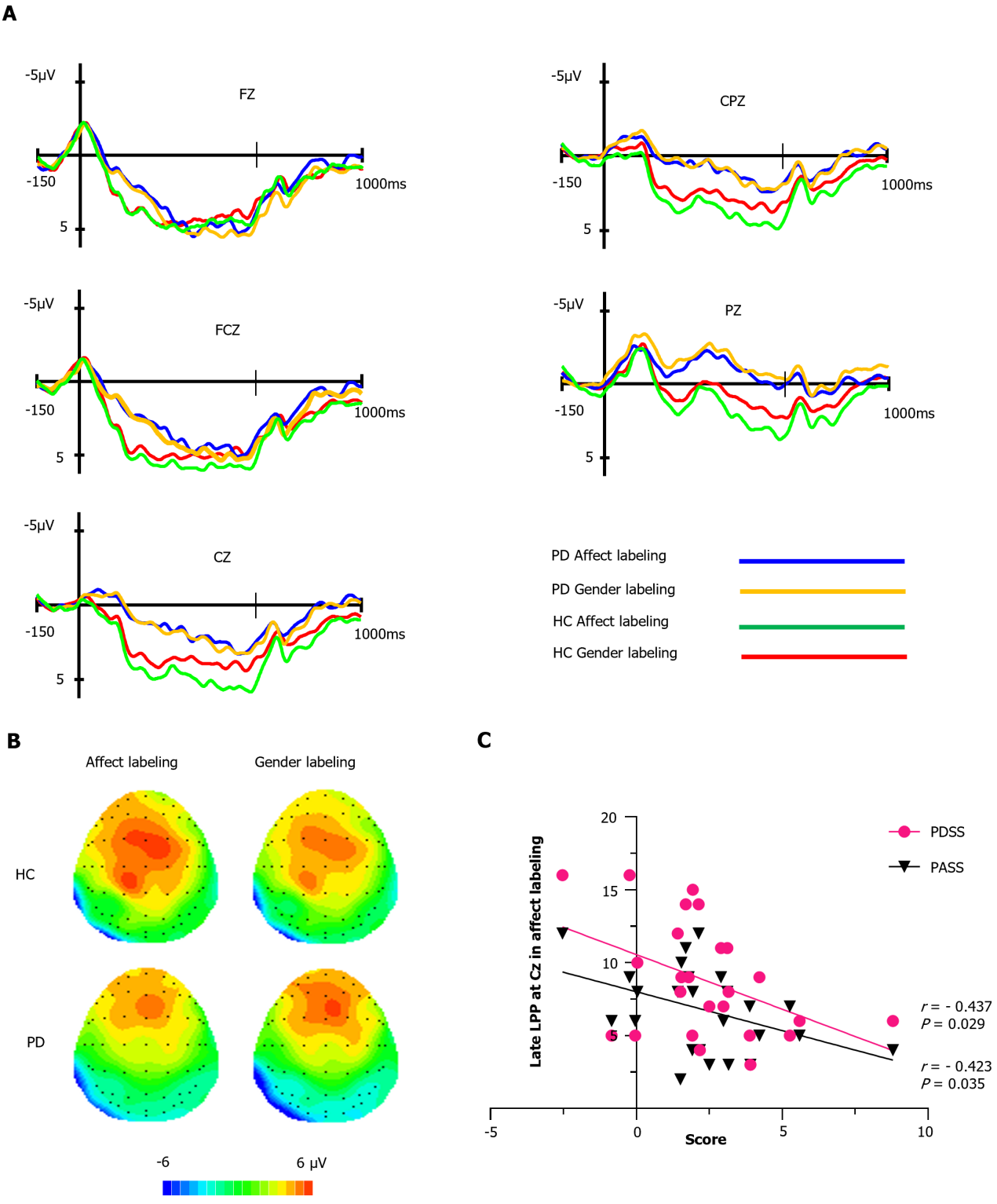

Figure 3 Late positive potential amplitude. A: Illustrates the early late positive potential (LPP) amplitudes at each electrode site for the healthy controls (HC) and panic disorder (PD) groups under affect labeling and gender labeling conditions. Firstly, a 2 × 2 × 5 repeated measures analysis of variance (350-630 ms) revealed significant main effects of electrode ($P < 0.001$) and a significant group × condition interaction effect ($P = 0.02$). Post-hoc comparisons indicated that the HC group exhibited higher LPP amplitudes in the affect labeling condition compared to the gender labeling condition ($P = 0.044$), while there was no significant difference in the PD group ($P > 0.05$). Secondly, no significant effects of electrode, condition, group, or interactions were observed in the 630-1000 ms time window ($P > 0.05$ for all comparisons); B: Presents topographic maps of the two groups under the two conditions; C: Demonstrates negative correlations between LPP amplitudes at the CZ site during affect labeling and Panic Disorder Severity Scale scores as well as Panic-Associated Symptom Scale scores in PD patients ($P = 0.029$, $P = 0.035$, respectively). PD: Panic disorder; HC: Healthy control; PDSS: Panic Disorder Severity Scale; PASS: Panic-Associated Symptom Scale; Fz: Frontal midline; FCz: Frontocentral midline; Cz: Central midline; CPz: Centroparietal midline; Pz: Parietal midline.

enhance our understanding of the causal relationship between affect labeling and neural activity changes in PD but also allow for an evaluation of whether successful treatment leads to the disappearance of the observed dysregulation.

CONCLUSION

This study reveals that the regulation process of affect labeling is not immediate, as evidenced by an initial increase followed by a decrease in LPP amplitude. Importantly, it identifies impaired implicit emotion regulation in PD patients and provides the first electrophysiological evidence of this impairment. Specifically, the diminished LPP modulation supports the abnormal affect labeling in PD patients. These findings serve as a valuable marker for future research investigating therapeutic interventions for PD that rely on implicit emotion regulation, such as cognitive behavioral therapy[28, 29], and neuromodulatory interventions like transcranial magnetic stimulation[6].

ARTICLE HIGHLIGHTS

Research background

The background of this study is rooted in clinical observations and research findings that identify emotion regulation dysfunction as a significant factor in the occurrence of panic disorder (PD). However, the neurophysiological mechanisms underlying implicit emotion regulation abnormalities in patients with PD remain unclear.

Research motivation

We aim to analyze neurophysiological changes in PD patients during implicit emotion regulation, identifying a concise and effective electrophysiological marker to assess potential anomalies in implicit emotion regulation.

Research objectives

The study aims to determine if there are anomalies in implicit emotion regulation in PD. Past research suggests abnormal Late Positive Potential (LPP) during emotion regulation in PD patients, indicating that LPP in event-related potentials (ERP) could be an effective tool for assessing implicit emotion regulation deficits.

Research methods

We assessed PD patients using clinical and psychological scales, conducting an emotion labeling task and recording behavioral and ERP data.

Research results

In the control group, late LPP initially increased, then decreased. A significant group × condition interaction effect was observed. Simple effect analysis showed reduced differences in late LPP amplitudes between affect labeling and gender labeling conditions in PD compared to controls. Additionally, under affect labeling, late LPP in PD negatively correlated with disease severity.

Research conclusions

PD patients have implicit emotion regulation impairments, and the late LPP amplitude in response to affect labeling may be a valuable clinical indicator of PD severity.

Research perspectives

Future considerations should include longitudinal treatment studies with follow-ups, assessing whether PD patients regain regulatory function post-successful treatment.

ACKNOWLEDGEMENTS

We would like to express our sincere gratitude to the patients and their families for their invaluable support in this study.

FOOTNOTES

Co-first authors: Hai-Yang Wang and Li-Zhu Li.

Author contributions: Wang HY contributed to conceptualization, visualization, initial draft writing, funding acquisition, review and editing; Li LZ contributed to investigation, data curation, review and editing; Chang Y contributed to investigation, review and editing; Pang XM contributed to investigation, review and editing; and Zhang BW contributed to review and editing, supervision, project administration, funding acquisition.

Supported by The National Natural Science Foundation of China, No. 81871080; the Key R&D Program of Jining (Major Program), No. 2023YXNS004; the National Natural Science Foundation of China, No. 81401486; the Natural Science Foundation of Liaoning Province of China, No. 20170540276; and the Medicine and Health Science Technology Development Program of Shandong Province, No. 202003070713.

Institutional review board statement: This study was approved by the Ethics Committee of the First Hospital of Dalian Medical University, No. KY2014-30.

Informed consent statement: All patients gave informed consent.

Conflict-of-interest statement: All the authors report no relevant conflicts of interest for this article.

Data sharing statement: All data generated or analyzed during this study are included in this published article.

STROBE statement: The authors have read the STROBE Statement—checklist of items, and the manuscript was prepared and revised according to the STROBE Statement—checklist of items.

Country/Territory of origin: China

ORCID number: Hai-Yang Wang 0000-0001-6148-4924; Bing-Wei Zhang 0000-0002-2331-5342.

S-Editor: Li L
L-Editor: A
P-Editor: Chen YX

REFERENCES

1 **Roy-Byrne PP**, Craske MG, Stein MB. Panic disorder. *Lancet* 2006; **368**: 1023-1032 [PMID: 16980119 DOI: 10.1016/S0140-6736(06)69418-X]
2 **Kessler RC**, Berglund P, Demler O, Jin R, Merikangas KR, Walters EE. Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication. *Arch Gen Psychiatry* 2005; **62**: 593-602 [PMID: 15939837 DOI: 10.1001/archpsyc.62.6.593]
3 **Zilverstand A**, Parvaz MA, Goldstein RZ. Neuroimaging cognitive reappraisal in clinical populations to define neural targets for enhancing emotion regulation. A systematic review. *Neuroimage* 2017; **151**: 105-116 [PMID: 27288319 DOI: 10.1016/j.neuroimage.2016.06.009]
4 **Gross JJ**, editor. Handbook of emotion regulation. 2nd ed. New York (NY): The Guilford Press, 2014
5 **Cox J**, Thakur B, Alvarado L, Shokar N, Thompson PM, Dwivedi AK. Repetitive transcranial magnetic stimulation for generalized anxiety and panic disorders: A systematic review and meta-analysis. *Ann Clin Psychiatry* 2022; **34**: e2-e24 [PMID: 35550035 DOI: 10.12788/acp.0050]
6 **Li H**, Wang J, Li C, Xiao Z. Repetitive transcranial magnetic stimulation (rTMS) for panic disorder in adults. *Cochrane Database Syst Rev* 2014; **2014**: CD009083 [PMID: 25230088 DOI: 10.1002/14651858.CD009083.pub2]
7 **Etkin A**, Büchel C, Gross JJ. The neural bases of emotion regulation. *Nat Rev Neurosci* 2015; **16**: 693-700 [PMID: 26481098 DOI: 10.1038/nrn4044]
8 **Clark DM**. A cognitive approach to panic. *Behav Res Ther* 1986; **24**: 461-470 [PMID: 3741311 DOI: 10.1016/0005-7967(86)90011-2]
9 **Chang Y**, Xu J, Pang X, Sun Y, Zheng Y, Liu Y. Mismatch negativity indices of enhanced preattentive automatic processing in panic disorder as measured by a multi-feature paradigm. *Biol Psychol* 2015; **105**: 77-82 [PMID: 25603282 DOI: 10.1016/j.biopsycho.2015.01.006]
10 **Li XL**, Wang HY. Unconscious cognitive dysfunction in emotion dysregulation and psychopathology of panic disorder: evidence from the late positive potential. *Neuroreport* 2018; **29**: 6-7 [PMID: 29194323 DOI: 10.1097/WNR.0000000000000913]
11 **Lieberman MD**, Eisenberger NI, Crockett MJ, Tom SM, Pfeifer JH, Way BM. Putting feelings into words: affect labeling disrupts amygdala activity in response to affective stimuli. *Psychol Sci* 2007; **18**: 421-428 [PMID: 17576282 DOI: 10.1111/j.1467-9280.2007.01916.x]
12 **Memarian N**, Torre JB, Haltom KE, Stanton AL, Lieberman MD. Neural activity during affect labeling predicts expressive writing effects on well-being: GLM and SVM approaches. *Soc Cogn Affect Neurosci* 2017; **12**: 1437-1447 [PMID: 28992270 DOI: 10.1093/scan/nsx084]
13 **Tabibnia G**, Lieberman MD, Craske MG. The lasting effect of words on feelings: words may facilitate exposure effects to threatening images. *Emotion* 2008; **8**: 307-317 [PMID: 18540747 DOI: 10.1037/1528-3542.8.3.307]
14 **Hajcak G**, MacNamara A, Olvet DM. Event-related potentials, emotion, and emotion regulation: an integrative review. *Dev Neuropsychol* 2010; **35**: 129-155 [PMID: 20390599 DOI: 10.1080/87565640903526504]
15 **Schupp HT**, Cuthbert BN, Bradley MM, Cacioppo JT, Ito T, Lang PJ. Affective picture processing: the late positive potential is modulated by motivational relevance. *Psychophysiology* 2000; **37**: 257-261 [PMID: 10731776 DOI: 10.1111/1469-8986.3720257]
16 **Burklund LJ**, Craske MG, Taylor SE, Lieberman MD. Altered emotion regulation capacity in social phobia as a function of comorbidity. *Soc Cogn Affect Neurosci* 2015; **10**: 199-208 [PMID: 24813437 DOI: 10.1093/scan/nsu058]
17 **First MB**, Spitzer RL, Gibbon M, Williams JBW. Structured Clinical Interview for DSM-IV-TR Axis I Disorders. New York: New York State Psychiatric Institute; 2002

18 **Shear MK**, Brown TA, Barlow DH, Money R, Sholomskas DE, Woods SW, Gorman JM, Papp LA. Multicenter collaborative panic disorder severity scale. *Am J Psychiatry* 1997; **154**: 1571-1575 [PMID: 9356566 DOI: 10.1176/ajp.154.11.1571]

19 **Argyle N**, Deltito J, Allerup P, Maier W, Albus M, Nutzinger D, Rasmussen S, Ayuso JL, Bech P. The Panic-Associated Symptom Scale: measuring the severity of panic disorder. *Acta Psychiatr Scand* 1991; **83**: 20-26 [PMID: 2011951 DOI: 10.1111/j.1600-0447.1991.tb05506.x]

20 **Gong X**, Huang YX, Wang Y, Luo YJ. [Revision of the Chinese Facial Affective Picture System]. *Zhongguo Xinli Weisheng Zazhi* 2011; **25**: 40-46 [DOI: 10.3969/j.issn.1000-6729.2011.01.011]

21 **Ferri J**, Eisendrath SJ, Fryer SL, Gillung E, Roach BJ, Mathalon DH. Blunted amygdala activity is associated with depression severity in treatment-resistant depression. *Cogn Affect Behav Neurosci* 2017; **17**: 1221-1231 [PMID: 29063521 DOI: 10.3758/s13415-017-0544-6]

22 **Torrisi SJ**, Lieberman MD, Bookheimer SY, Altshuler LL. Advancing understanding of affect labeling with dynamic causal modeling. *Neuroimage* 2013; **82**: 481-488 [PMID: 23774393 DOI: 10.1016/j.neuroimage.2013.06.025]

23 **Deng H**, Jiang Q. [When Does Labeling Happen: An ERP Study of Affect Labeling]. *Zhongguo Linchuang Xinlixue Zazhi* 2017; **25**: 231-236 [DOI: 10.16128/j.cnki.1005-3611.2017.02.008]

24 **Liang J**, Lin H. Current and lasting effects of affect labeling on late positive potential (LPP) amplitudes elicited by negative events. *Brain Behav* 2023; **13**: e3065 [PMID: 37183558 DOI: 10.1002/brb3.3065]

25 **McRae K**, Taitano EK and Lane RD. The effects of verbal labelling on psychophysiology: Objective but not subjective emotion labelling reduces skin-conductance responses to briefly presented pictures. *Cogn Emot* 2010; **24**: 829-839 [DOI: 10.1080/02699930902797141]

26 **Lang AJ**, Sarmiento J. Relationship of attentional bias to anxiety sensitivity and panic. *Depress Anxiety* 2004; **20**: 190-194 [PMID: 15390209 DOI: 10.1002/da.20030]

27 **Korgaonkar MS**, Tran J, Felmingham KL, Williams LM, Bryant RA. Neural correlates of emotional processing in panic disorder. *Neuroimage Clin* 2021; **32**: 102902 [PMID: 34911204 DOI: 10.1016/j.nicl.2021.102902]

28 **Strauss AY**, Kivity Y, Huppert JD. Emotion Regulation Strategies in Cognitive Behavioral Therapy for Panic Disorder. *Behav Ther* 2019; **50**: 659-671 [PMID: 31030881 DOI: 10.1016/j.beth.2018.10.005]

29 **Koole SL**, Webb TL and Sheeran PL. Implicit emotion regulation: feeling better without knowing why. *Curr Opin Psychol* 2015; **3**: 6-10 [DOI: 10.1016/j.copsyc.2014.12.027]

World Journal of Psychiatry

Submit a Manuscript: https://www.f6publishing.com

World J Psychiatry 2024 February 19; 14(2): 245-254

DOI: 10.5498/wjp.v14.i2.245

ISSN 2220-3206 (online)

ORIGINAL ARTICLE

Retrospective Cohort Study

Incidence and risk factors of depression in patients with metabolic syndrome

Li-Na Zhou, Xian-Cang Ma, Wei Wang

Specialty type: Psychiatry

Provenance and peer review: Invited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

Grade A (Excellent): 0
Grade B (Very good): B
Grade C (Good): 0
Grade D (Fair): 0
Grade E (Poor): 0

P-Reviewer: Alkhatib AJ, Jordan

Received: November 14, 2023
Peer-review started: November 14, 2023
First decision: December 7, 2023
Revised: December 14, 2023
Accepted: January 8, 2024
Article in press: January 8, 2024
Published online: February 19, 2024

Li-Na Zhou, Xian-Cang Ma, Wei Wang, Department of Psychiatry, The First Affiliated Hospital of Xi'an Jiaotong University, Xi'an 710061, Shaanxi Province, China

Corresponding author: Wei Wang, MD, Doctor, Department of Psychiatry, The First Affiliated Hospital of Xi'an Jiaotong University, No. 277 West Yanta Road, Xi'an 710061, Shaanxi Province, China. xianwv@sina.com

Abstract

BACKGROUND

Many studies have explored the relationship between depression and metabolic syndrome (MetS), especially in older people. China has entered an aging society. However, there are still few studies on the elderly in Chinese communities.

AIM

To investigate the incidence and risk factors of depression in MetS patients in mainland China and to construct a predictive model.

METHODS

Data from four waves of the China Health and Retirement Longitudinal Study were selected, and middle-aged and elderly patients with MetS (n = 2533) were included based on the first wave. According to the center for epidemiological survey-depression scale (CESD), participants with MetS were divided into depression (n = 938) and non-depression groups (n = 1595), and factors related to depression were screened out. Subsequently, the 2-, 4-, and 7-year follow-up data were analyzed, and a prediction model for depression in MetS patients was constructed.

RESULTS

The prevalence of depression in middle-aged and elderly patients with MetS was 37.02%. The prevalence of depression at the 2-, 4-, and 7-year follow-up was 29.55%, 34.53%, and 38.15%, respectively. The prediction model, constructed using baseline CESD and Physical Self-Maintenance Scale scores, average sleep duration, number of chronic diseases, age, and weight had a good predictive effect on the risk of depression in MetS patients at the 2-year follow-up (area under the curve = 0.775, 95% confidence interval: 0.750-0.800, P < 0.001), with a sensitivity of 68% and a specificity of 74%.

CONCLUSION

The prevalence of depression in middle-aged and elderly patients with MetS has increased over time. The early identification of and intervention for depressive symptoms requires greater attention in MetS patients.

Key Words: Depression; Metabolic syndrome; Prevalence; Risk factor

Core Tip: In this study, a 7-year follow-up of middle-aged and elderly people in China Mainland was conducted, and it was found that the incidence of depression increased in the population of metabolic syndrome.

Citation: Zhou LN, Ma XC, Wang W. Incidence and risk factors of depression in patients with metabolic syndrome. *World J Psychiatry* 2024; 14(2): 245-254
URL: https://www.wjgnet.com/2220-3206/full/v14/i2/245.htm
DOI: https://dx.doi.org/10.5498/wjp.v14.i2.245

INTRODUCTION

Metabolic syndrome (MetS) is a pathological condition characterized by abdominal obesity, insulin resistance, hypertension, and hyperlipidemia[1]. MetS has become a global problem; although its prevalence varies according to different diagnostic criteria, a high prevalence of MetS is undeniable. A cross-sectional study in China reported a MetS prevalence of 14.39%, according to diagnostic criteria defined by the Chinese Diabetes Society[2]. Another meta-analysis reported a prevalence of approximately 15.5% in China[3]. MetS is more common in the elderly[4], as it causes diabetes, stroke, and cognitive impairment, posing a serious disease burden to the middle-aged and the elderly populations[5].

MetS is also common in individuals with psychiatric disorders[6], including bipolar disorder[7], schizophrenia[8], depression[9], dementia[10], and other psychiatric disorders[11]. Moreover, MetS is becoming more common in young people with depression[9]. However, this phenomenon has received insufficient attention. This suggests that although MetS is a disease with age-related morbidity, there is still a need to focus on age groups other than the elderly, especially when there is comorbidity with psychiatric disorders.

Depression is also a disease that cannot be ignored in the elderly population. Our previous study, as well as those of others, have reported a high prevalence of depression in middle-aged and older adults[12,13], leading to significant effects on individual medical expenses[14]. As shown above, both depression and MetS have a high incidence and heavy burden in middle-aged and elderly individuals. Therefore, more attention should be paid to depression and MetS in middle-aged and elderly individuals.

Additionally, a bidirectional relationship seems to exist between depression and MetS[15], and this association is even stronger in older people[16]. On the one hand, elderly patients with MetS have a higher prevalence of depression than the general population[17]. The more MetS components the patients have, the more severe their depressive symptoms are [18]. On the other hand, elderly patients with depression also have a higher prevalence of MetS[19]. Low levels of inflammation, low levels of activity, and antidepressant use in depression patients contribute to the development of MetS[20-22], and may lead to a risk of fatalities[23]. This may be related to the fact that depression and MetS share some pathogenic factors, such as chronic low-grade inflammation[24], and the dysregulation of the hypothalamus-pituitary-adrenal axis, the autonomic nervous system, the immune system, and platelet and endothelial function[25]. However, other studies have denied a link between depression and MetS[26,27], or have simply highlighted the association between atypical depression and MetS[28].

Overall, the relationship between depression and MetS remains unclear. Large population and cohort studies need to be supplemented to analyze the association between depression and MetS, as well as the complex influencing factors. Therefore, based on a large community-based cohort study conducted in mainland China, we designed this study to investigate the incidence and risk factors of depression in MetS patients and to construct a predictive model.

MATERIALS AND METHODS

Study population

The China Health and Retirement Longitudinal Study (CHARLS) is a survey conducted in the Chinese mainland. The survey participants were those in the community who were 45 years old and above. The main contents include demographics, health, function, insurance, work, retirement, and physical examination. CHARLS has been conducting baseline surveys since 2011 and has published data from four surveys. Details such as design and sampling have been covered in previous studies[29,30]. The national baseline survey conducted during 2011-2012 consisted of 17708 individuals. The second wave was conducted in 2013-2014 for a 2-year follow-up period, and 15628 individuals were successfully re-interviewed. In 2015-2016, 14555 individuals enrolled at baseline were re-interviewed for the third wave at

the 4-year follow-up. The fourth wave survey-the most recent survey-conducted in 2018-2019, included 19744 participants who participated in their 7-year follow-up.

Study protocol

Based on the survey data from 2011 as the baseline, participants were selected according to the following inclusion criteria: (1) Meeting the diagnostic criteria for MetS; (2) center for epidemiological survey-depression scale (CESD) score, and (3) complete demographic data, health-related data, activities of daily living (ADL), social participation, *etc*. Based on the above criteria, 2533 patients were selected at baseline. Second, patients' 2-, 4-, and 7-year follow-up information was analyzed. A screening flowchart is shown in Figure 1.

MetS

According to Zhu *et al*[31], the International Diabetes Federation (IDF) definition is more pertinent than the Adult Treatment Panel III definition for screening and estimating the risk of cerebrovascular disease and diabetes in Asian American adults. Therefore, in this study, the IDF definition was selected as the diagnostic criteria for MetS, and patients were required to have at least two of the following four conditions on the basis of abdominal obesity: (1) High triglyceride (TG) level: ≥ 150 mg/dL (≥ 1.69 mmol/L); (2) reduced high-density lipoprotein (HDL) cholesterol level: < 40 mg/dL (< 1.03 mmol/L) for men, < 50 mg/dL (< 1.29 mmol/L) for women; (3) high blood pressure: ≥ 130 mmHg systolic blood pressure, ≥ 85 mmHg diastolic blood pressure (DBP), or receipt of antihypertensive medication, and (4) high fasting glucose [≥ 100 mg/dL (≥ 5.56 mmol/L)] or diabetes diagnosis. Abdominal obesity was defined as a waist circumference ≥ 90 cm in men and ≥ 80 cm in women.

Depression status

The CESD is a widely used depression assessment scale used in epidemiological surveys. The CESD comprises 10 items, and each question has a 4-level rating, respectively No, I don't have any difficulty; I have difficulty but can still do it; Yes, I have difficulty and need help; and I cannot do it. Scores of 0-3 are assigned, respectively, two of which are reverse grades. The total score is added to obtain the CESD score. The CESD has been used in a large-scale population survey in mainland China, with certain validity and reliability[32]. In this study, we labeled CESD ≥ 10 symptomatic depression, referred to as depression group, according to the criteria of Andresen *et al*[33]. And participants with CESD < 10 were defined as the non-depressed group.

ADL

The ADL was measure *via* the Physical Self-Maintenance Scale (PSMS) and Instrumental Activity of Daily Living (IADL) [34]. In this study, the PSMS included whether and how difficult it was to jog, walk, climb stairs, bend, and lift heavy objects, while the IADL included housekeeping, preparing meals, shopping, paying, and taking medications. The choices are on a 4-point scale, and they are No, I don't have any difficulty; I have difficulty but can still do it; yes, I have difficulty and need help; and I cannot do it. A score of 1 to 4 points was assigned. The higher the total score, the more severely affected the individuals' health status.

Social participation

The CHARLS investigated the type and frequency of social participation among middle-aged and elderly people. The types of social participation include: (1) Interacting with friends; (2) playing Ma-Jong, playing chess, playing cards, or attending a community club; (3) providing help to family, friends, or neighbors who do not live with you and who did not pay you for the help; (4) going to a sport, social, or other kind of club; (5) taking part in a community-related organization; (6) doing voluntary or charity work; (7) caring for a sick or disabled adult who does not live with you and who did not pay you for the help; (8) attending an educational or training course; (9) stock investment; (10) using the Internet; (11) other, and (12) none of these. They were then asked, regarding each of the selected activities: "How often have you done these social activities in the past month?" Respondents were asked to select the choice that best suited their situation from "almost every day"; "almost every week"; and "not often". We chose the frequency of activities with the highest participation as the frequency of social participation.

Health information

Physical examinations included height, weight, waist circumference, systolic blood pressure, DBP, sleep, chronic diseases, and biomarkers. The sleep aspect included a survey of the average sleep duration and nap time. The collection of blood samples required the respondents to fast for one night, and three tubes of venous blood were collected from each respondent by medically trained staff from the China Centers for Disease Control and Prevention (CDC), based on a standard protocol. After collection, these fresh venous blood samples were transported at 4 ℃, to either local CDC laboratories or township-level hospitals near the study sites, or transported to the China CDC in Beijing within 2 wk for further testing. The biomarkers tested included white blood cell count (WBC), HDL, C-reactive protein (CRP), TG, fasting blood glucose (FBG), and uric acid (UA).

Statistical analysis

All the data in this study were imported into SPSS 22.0 (SPSS Inc., Chicago, IL, United States) for analysis. First, we described the overall data and divided the patients into a depression group and a non-depression group, according to whether they met the criteria of symptomatic depression at baseline, and compared the overall data of the two groups at baseline. In this part of the results, categorical variables were expressed as *N* (%), the chi-squared test was used to

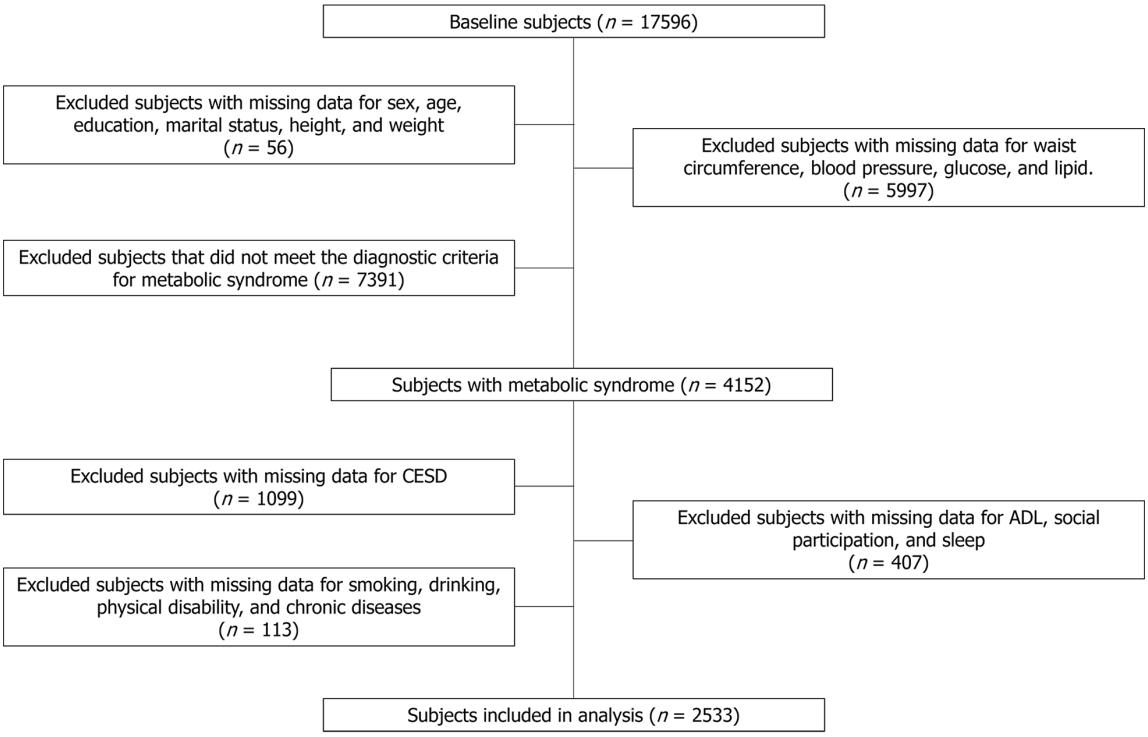

Figure 1 Selection process of participants. CESD: Center for epidemiological survey-depression; ADL: Activities of daily living scale.

compare the differences between the two groups, continuous variables were expressed as the mean [95% confidence interval (CI)], and the Kolmogorov-Smirnov test was used to compare the two groups.

To determine which factors were associated with depression in MetS patients, we performed regression analyses on baseline data. Variables with $P < 0.1$ in the comparison of the two groups were screened and included in multivariate regression analysis, with the CESD score as the dependent variable. Subsequently, we performed multiple regression analyses with significant variables obtained from multivariate regression and the CESD score at baseline as independent variables, and the CESD score at follow-up as dependent variables to screen for the factors related to symptomatic depression in MetS patients.

Finally, we used Cox regression to construct a predictive model of depression in MetS patients, with variables with $P < 0.1$ and the CESD score at baseline as independent variables, and the occurrence of depression as the outcome variable. Two-tailed $P < 0.05$ was considered statistically significant for all statistical analyses.

RESULTS

Descriptive analysis of baseline

In this study, 1595 cases in the non-depression group and 938 cases in the depression group were included, and the prevalence of depression in MetS patients was 37.02%. The detailed data are shown in Table 1.

Demographic information: There were significant differences in sex, age, education, and marital status between the two groups ($P < 0.001$). Specifically, women, younger ages, lower levels of education, and single people were overrepresented in the depression group.

Health information: Compared to the non-depression group, participants in the depression group had lower height and weight, more physical disabilities and chronic diseases, more smoking and drinking, and less average sleep and nap time ($P < 0.05$).

Physical examination: The depression group had lower serum UA and higher HDL levels ($P < 0.05$). There were no significant differences in WBC, CRP, TG, waist circumference, systolic blood pressure, DBP, or FBG between the two groups ($P > 0.05$).

ADL and social participation: The types and frequencies of social participation activities in the depression group were significantly lower than those in the control group, and the scores of PSMS and IADL were significantly higher than those in the control group ($P < 0.001$).

Table 1 Comparison of baseline data of metabolic syndrome patients with and without depression, *n* (%)

	Non-depression (*n* = 1595)	Depression (*n* = 938)	*P* value
Sex			
Male	552 (34.61)	209 (22.28)	< 0.001
Female	1043 (65.39)	729 (77.72)	
Age, yr	58.34 (57.90, 58.78)	60.23 (59.65, 60.81)	< 0.001
Education			
0 yr	403 (25.27)	352 (37.53)	< 0.001
1-6 yr	612 (38.37)	394 (42.00)	
7-12 yr	547 (34.29)	183 (19.51)	
> 12 yr	33 (2.07)	9 (0.96)	
Marital status			
Married	1457 (91.35)	783 (83.48)	< 0.001
Other	138 (8.65)	155 (16.52)	
Physical disability			
Yes	185 (11.60)	186 (19.83)	< 0.001
No	1410 (88.40)	752 (80.17)	
Number of chronic diseases	1.53 (1.46, 1.59)	2.18 (2.08, 2.29)	< 0.001
Height, cm	158.42 (157.98, 158.86)	155.53 (155.03, 156.02)	< 0.001
Weight, kg	66.76 (66.15, 67.26)	63.51 (62.79, 64.24)	< 0.001
Smoking			
Yes	469 (29.40)	719 (76.65)	< 0.001
No	1126 (70.60)	219 (23.35)	
Drinking			
Yes	314 (19.69)	108 (11.51)	< 0.001
No	1281 (80.31)	830 (88.49)	
WBC, 10^9/L	6.312 (6.215, 6.410)	6.388 (6.250, 6.527)	0.911
CRP, mg/L	3.20 (2.82, 3.58)	3.27 (2.77, 3.78)	0.864
UA, mg/dL	4.67 (4.61, 4.74)	4,43 (4.35, 4.50)	< 0.001
CESD	4.63 (4.49, 4.76)	14.77 (14.50, 15.05)	< 0.001
Waist circumference, cm	94.21 (93.83, 94.59)	93.28 (92.79, 93.76)	0.522
TG, mg/dL	193.58 (185.88, 201.29)	184.17 (175.75, 192.60)	0.266
HDL-C, mg/dL	41.80 (41.21, 42.39)	42.84 (42.09, 43.60)	0.020
SBP, mmHg	111.94 (111.16, 112.72)	112.92 (111.88, 113.96)	0.163
DBP, mmHg	80.40 (79.78, 81.02)	79.89 (79.10, 80.68)	0.359
Glu, mg/dL	122.19 (119.81, 124.57)	120.95 (117.97, 123.93)	0.522
Average sleep duration, hour	6.72 (6.64, 6.79)	5.77 (5.64, 5.90)	< 0.001
Nap time, minutes	36.52 (34.32, 38.73)	31.87 (29.20, 34.54)	0.009
Social participation			
Types of activities	0.88 (0.84, 0.93)	0.67 (0.62, 0.73)	< 0.001
Frequency of activities	1.65 (1.55, 1.75)	1.29 (1.17, 1.42)	< 0.001
PSMS	11.69 (11.53, 11.85)	15.26 (14.95, 15.58)	< 0.001
IADL	5.36 (5.29, 5.42)	6.58 (6.40, 6.77)	< 0.001

N: Number; WBC: White blood cell; CRP: C reactive protein; UA: Uric acid; CESD: Center for Epidemiological Survey-Depression Scale; TG: Triglyceride; HDL-C: High-density lipoprotein cholesterol; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; Glu: Glucose; PSMS: Physical self-maintenance scale; IADL: Instrumental activity of daily living.

Descriptive analysis of follow-up

Two-year follow-up: During the 2-year follow-up, 929 patients were lost to follow-up or died, and the remaining 1604 patients were followed up. Their average CESD score was 7.59 (95%CI: 7.30-7.88). Among this group, 474 patients (29.55%) had depression. Compared with the baseline, the CESD score did not significantly increase or decrease (P = 0.132, Figure 2), and 181 cases (17.01%, 181/1064) newly developed depression.

Four-year follow-up: During the 4-year follow-up, compared with the baseline, 998 cases were lost to follow-up or died, 1535 cases remained with an average CESD score of 8.16 (95%CI: 7.71-8.30), and 530 cases had depression, accounting for 34.53% of the cohort. There were no significant differences in CESD scores from the baseline (P = 0.163, Figure 2), and 239 cases (23.62%, 239/1,012) had newly developed depression.

Seven-year follow-up: During the 7-year follow-up, compared with the baseline period, 1,196 patients were lost to follow-up or died, and the remaining 1337 patients had an average CESD score of 8.67 (95%CI: 8.31-9.02). Compared with baseline, the CESD score was significantly increased (P = 0.004, Figure 2). A total of 510 patients (38.15%) had depression. There were 243 new cases of depression, accounting for 26.85% of the cohort (243/905).

During the overall follow-up, 1,186 patients completed the follow-up. Among them, 462 patients (38.95%) were newly diagnosed with depression, and the average time required for depression to manifest was (4.000 ± 1.978) years.

Regression analysis

Factors associated with CESD at baseline: Multivariable logistic regression analysis with baseline CESD score as the dependent variable showed that CESD at baseline was associated with PSMS, IADL, average sleep duration, marital status, number of chronic diseases, age, and weight (Table 2, $P < 0.05$).

Factors associated with CESD at follow-up: The multivariable logistic regression analysis with CESD score in the follow-up period as the dependent variable found that CESD score at the 2-year follow-up was associated with baseline CESD score, PSMS, average sleep duration, number of chronic diseases, age, and weight. CESD score at the 4-year follow-up was associated with baseline CESD, ADL, and weight, while CESD score at the 7-year follow-up was associated with baseline CESD, ADL, average sleep duration, age, and weight. The detailed data are shown in Table 2.

These factors were used as independent variables to construct the CESD prediction model during the follow-up period. The results showed that the CESD prediction model constructed during the 2-year follow-up period had a better predictive ability than other follow-up periods [area under the curve (AUC) = 0.775, 95%CI: 0.750-0.800, $P < 0.001$], with a sensitivity of 68% and a specificity of 74% (Figure 3).

Factors associated with new onset depression: Cox regression analysis showed that age [odds ratio (OR) = 0.986, 95%CI: 0.978-0.993], weight (OR = 0.487, 95%CI: 0.421-0.564), average sleep duration (OR = 0.926, 95%CI: 0.894-0.959), and ADL (OR = 1.042, 95%CI: 1.026-1.058) were associated with symptomatic depression in MetS patients within 7 years of follow-up (all $P < 0.001$).

DISCUSSION

The bidirectional relationship between depression and MetS remains questionable, especially in middle-aged and older adults, who have high rates of both conditions. This study focused on middle-aged and elderly patients with MetS in mainland China and followed them for 7 years to screen for risk factors associated with depression in MetS patients. We compared the information of people with depression and those without depression among MetS patients at baseline and found many differences, such as that those with MetS and depression included more women, lower education level, more single people, lower height and weight, more physical disabilities, more chronic diseases, more smoking and drinking, less average sleep and nap time, less frequency of social participation, impaired ability of daily living, *etc*[13,35-38]. These are all features of depression that have been reported in previous studies. However, we found that people with depression and MetS were younger than those without depression, which is related to the younger age of the current depressed population. On the one hand, the onset of depression tends to be younger, and on the other hand, a meta-analysis of observational studies found that depressive participants under 50 years of age were more likely to develop MetS than those over 50 years[34], and concluded that the odds of MetS in depressive patients decreased with age. These results suggest that the mutual worsening of MetS and depression is more significant in younger adults.

We then analyzed the follow-up data and selected the follow-up time points of 2, 4, and 7 years. It was found that the depression score at the 7-year follow-up was significantly higher than that of the baseline period, the prevalence of depression reached 38.15%, and the incidence of depression reached 26.85%, while there was no significant difference between the depression scores of the 2-year and 4-year follow-up periods and the baseline period. Akbaraly *et al*[39] proposed that the presence of MetS is associated with an increased risk of future depressive symptoms, and the results of this study further suggest that the longer the patients have MetS, the higher the risk of depression. Mulvahill *et al*[19]

Table 2 Factors associated with center for epidemiological survey-depression scale at baseline and follow-up

	Baseline		2-yr follow up		4-yr follow up		7-yr follow up	
Variables	OR (95%CI)	Beta	OR (95%CI)	Beta	OR (95%CI)	Beta	OR (95%CI)	Beta
Age	-0.551 (-0.816, -0.286)	-0.075	-0.056 (-0.086, -0.026)	-0.081	-		-0.052 (-0.093, -0.011)	-0.063
Marital status	1.893 (1.253, 2.533)	0.102	-		-		-	
Height	0.246 (0.016, 0.475)	0.084	-0.054 (-0.076, -0.031)	-0.103	-0.047 (-0.073, -0.021)	-0.082	-0.054 (-0.083, -0.025)	-0.092
Number of chronic diseases	0.448 (0.310, 0.586)	0.113	0.211 (0.039, 0.383)	0.055	-		-	
Average sleep duration	-0.664 (-0.771, -0.558)	-0.205	-0.265 (-0.406, -0.124)	-0.081	-		-0.410 (-0.596, -0.224)	-0.110
PSMS	0.46 (0.402, 0.518)	0.333	0.174 (0.103, 0.246)	0.120	0.177 (0.095, 0.258)	0.109	0.166 (0.069, 0.263)	0.094
IADL	0.293 (0.184, 0.402)	0.105	-		-		-	
Baseline CESD	-		0.424 (0.376, 0.472)	0.424	0.450 (0.393, 0.506)	0.407	0.414 (0.349, 0.478)	0.359

PSMS: Physical self-maintenance scale; IADL: Instrumental activity of daily living; CESD: Center for epidemiological survey-depression scale; OR: Odds ratio; CI: Confidence interval.

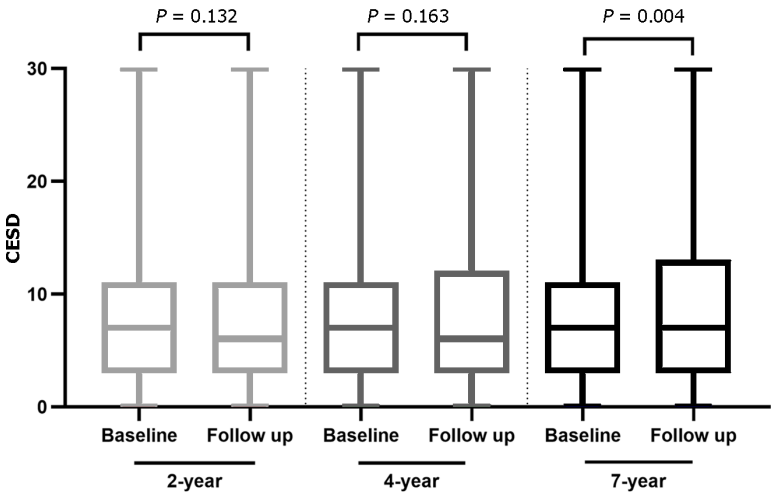

Figure 2 Center for epidemiological Survey-Depression Scale scores at 2, 4, and 7 years of follow-up. CESD: Center for epidemiological survey-depression scale.

reported that the presence of MetS in elderly patients with depression is associated with the symptom severity of depression, and that poor antidepressant responses are observed in MetS patients. This indicates that the changes brought about by MetS not only increase the risk of depression but also affect the treatment efficacy. Therefore, patients must be identified and managed as early as possible to improve their outcomes.

Although the prevalence of depression in MetS patients was the highest after 7 years of follow-up, the predictive effect of the model established with the screened baseline information on the risk of depression in MetS patients after 7 years is limited. We found that the prediction model constructed by baseline CESD, PSMS, average sleep duration, number of chronic diseases, age, and weight had a good predictive effect on the risk of depression at the 2-year follow-up. It is worth noting that there are also complex interactions between these factors, such as depression and sleep duration, depression and chronic disease, chronic disease and ADL, and depression and ADL[40,41]. This suggests that paying attention to individuals who already have depressive symptoms, especially those with sleep problems and chronic diseases, is important for reducing the development of depression in MetS patients.

This study had some limitations. First, the patients in this study were from a community population, and the assessment of depressive symptoms was carried out with the self-rating scale used in a large epidemiological survey; therefore, the selected depression could not completely replace a diagnosis of depression. In addition, in the follow-up, to avoid too many influencing factors, we started from the data at 2 years, 4 years, and 7 years, instead of continuous analysis of the same group of patients. However, the prediction efficiency of the model constructed by this analysis method worsened with a longer follow-up time, indicating that the influencing factors within the follow-up years play a

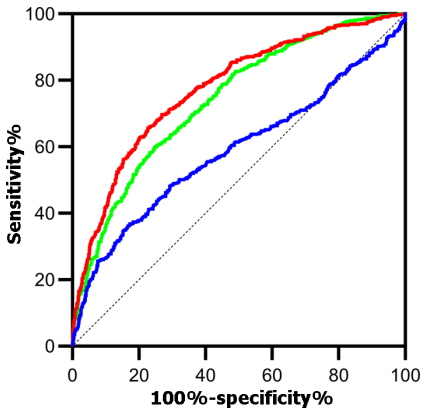

Figure 3 Depression prediction models at 2 -, 4 -, and 7-year follow-up. The red line is 2-year follow up, the green line is 4-year follow up, and the blue line is 7-year follow up.

certain role. Finally, antidepressants may affect metabolism, but the use of antidepressants was not analyzed in this study; therefore, the results regarding the association between MetS and depression may have been affected.

CONCLUSION

In conclusion, this study described changes in the prevalence of depression in MetS patients over a 7-year period, screened out factors associated with the development of depression in MetS patients, and constructed a 2-year model to predict the risk of depression. The early identification of depression and the provision of interventions can improve patient outcomes.

ARTICLE HIGHLIGHTS

Research background

Metabolic syndrome (MetS) is also common in individuals with psychiatric disorders and becoming more common in young people with depression. However, the relationship between depression and MetS remains unclear.

Research motivation

Many studies have explored the relationship between depression and MetS, especially in older people. China has entered an aging society. However, there are still few studies on the elderly in Chinese communities.

Research objectives

Based on a large community-based cohort study conducted in mainland China, we designed this study to address the following: (1) The prevalence of depression in MetS patients; (2) the changing trajectory of the prevalence of MetS during the 7-year follow-up; and (3) the risk factors for the development of depression in MetS patients and the construction of predictive models.

Research methods

This study analyzed 7 years of follow-up data from the CHARLS database, screened the risk factors for depression in patients with metabolic syndrome, and constructed a predictive model for depression in patients with metabolic syndrome by regression analysis.

Research results

People with metabolic syndrome had a higher incidence of depression, which increased with the extension of follow-up time. The predictive model of baseline depression level, sleep duration, chronic disease, age, and weight was significant for depression risk after 2 years in patients with metabolic syndrome.

Research conclusions

All in all, this study shows the prevalence of depression in middle-aged and elderly patients with MetS increases over time. More attention should be paid to early identification and intervention of depressive symptoms in MetS patients.

Research perspectives

Mechanisms of depression in patients with MetS, early predictors and intervention modalities.

FOOTNOTES

Author contributions: Zhou LN, Wang W contributed to conception and design of the study, acquisition and interpretation of data, drafting the article, final approval of the version to be published; Ma XC contributed to conception and design of the study, and reflect the design and recruit subjects.

Supported by Shaanxi Provincial Key Research and Development Program, No. 2023-YBSF-517; and National Natural Science Foundation of China, No. 82301737.

Institutional review board statement: This study only adopted publicly available data. Ethical review and approval were not required for this study in accordance with the local legislation and institutional requirements.

Informed consent statement: This study only adopted publicly available data. Signed informed consent form or document were not applicable for this study.

Conflict-of-interest statement: We have no financial relationships to disclose.

Data sharing statement: No additional data are available.

Country/Territory of origin: China

ORCID number: Li-Na Zhou 0000-0003-0688-8162; Wei Wang 0009-0003-1326-5390.

S-Editor: Qu XL
L-Editor: A
P-Editor: Chen YX

REFERENCES

1 **Saklayen MG**. The Global Epidemic of the Metabolic Syndrome. *Curr Hypertens Rep* 2018; **20**: 12 [PMID: 29480368 DOI: 10.1007/s11906-018-0812-z]
2 **Lan Y**, Mai Z, Zhou S, Liu Y, Li S, Zhao Z, Duan X, Cai C, Deng T, Zhu W, Wu W, Zeng G. Prevalence of metabolic syndrome in China: An up-dated cross-sectional study. *PLoS One* 2018; **13**: e0196012 [PMID: 29668762 DOI: 10.1371/journal.pone.0196012]
3 **Wang Y**, Mi J, Shan XY, Wang QJ, Ge KY. Is China facing an obesity epidemic and the consequences? The trends in obesity and chronic disease in China. *Int J Obes (Lond)* 2007; **31**: 177-188 [PMID: 16652128 DOI: 10.1038/sj.ijo.0803354]
4 **Akbulut G**, Köksal E, Bilici S, Acar Tek N, Yildiran H, Karadag MG, Sanlier N. Metabolic syndrome (MS) in elderly: a cross sectional survey. *Arch Gerontol Geriatr* 2011; **53**: e263-e266 [PMID: 21163537 DOI: 10.1016/j.archger.2010.11.021]
5 **Alberti KG**, Zimmet P, Shaw J; IDF Epidemiology Task Force Consensus Group. The metabolic syndrome--a new worldwide definition. *Lancet* 2005; **366**: 1059-1062 [PMID: 16182882 DOI: 10.1016/S0140-6736(05)67402-8]
6 **Asaye S**, Bekele S, Tolessa D, Cheneke W. Metabolic syndrome and associated factors among psychiatric patients in Jimma University Specialized Hospital, South West Ethiopia. *Diabetes Metab Syndr* 2018; **12**: 753-760 [PMID: 29729979 DOI: 10.1016/j.dsx.2018.04.037]
7 **McElroy SL**, Keck PE Jr. Metabolic syndrome in bipolar disorder: a review with a focus on bipolar depression. *J Clin Psychiatry* 2014; **75**: 46-61 [PMID: 24502861 DOI: 10.4088/JCP.13r08634]
8 **Lin YC**, Lai CL, Chan HY. The association between rehabilitation programs and metabolic syndrome in chronic inpatients with schizophrenia. *Psychiatry Res* 2018; **260**: 227-232 [PMID: 29216485 DOI: 10.1016/j.psychres.2017.11.081]
9 **Moreira FP**, Jansen K, Cardoso TA, Mondin TC, Vieira IS, Magalhães PVDS, Kapczinski F, Souza LDM, da Silva RA, Oses JP, Wiener CD. Metabolic syndrome, depression and anhedonia among young adults. *Psychiatry Res* 2019; **271**: 306-310 [PMID: 30522000 DOI: 10.1016/j.psychres.2018.08.009]
10 **Borshchev YY**, Uspensky YP, Galagudza MM. Pathogenetic pathways of cognitive dysfunction and dementia in metabolic syndrome. *Life Sci* 2019; **237**: 116932 [PMID: 31606384 DOI: 10.1016/j.lfs.2019.116932]
11 **Penninx BWJH**, Lange SMM. Metabolic syndrome in psychiatric patients: overview, mechanisms, and implications. *Dialogues Clin Neurosci* 2018; **20**: 63-73 [PMID: 29946213 DOI: 10.31887/DCNS.2018.20.1/bpenninx]
12 **Sjöberg L**, Karlsson B, Atti AR, Skoog I, Fratiglioni L, Wang HX. Prevalence of depression: Comparisons of different depression definitions in population-based samples of older adults. *J Affect Disord* 2017; **221**: 123-131 [PMID: 28645024 DOI: 10.1016/j.jad.2017.06.011]
13 **Zhou L**, Ma X, Wang W. Relationship between Cognitive Performance and Depressive Symptoms in Chinese Older Adults: The China Health and Retirement Longitudinal Study (CHARLS). *J Affect Disord* 2021; **281**: 454-458 [PMID: 33360747 DOI: 10.1016/j.jad.2020.12.059]
14 **Sun X**, Zhou M, Huang L, Nuse B. Depressive costs: medical expenditures on depression and depressive symptoms among rural elderly in China. *Public Health* 2020; **181**: 141-150 [PMID: 32032922 DOI: 10.1016/j.puhe.2019.12.011]
15 **Pan A**, Keum N, Okereke OI, Sun Q, Kivimaki M, Rubin RR, Hu FB. Bidirectional association between depression and metabolic syndrome: a systematic review and meta-analysis of epidemiological studies. *Diabetes Care* 2012; **35**: 1171-1180 [PMID: 22517938 DOI: 10.2337/dc11-2055]

16 **Repousi N**, Masana MF, Sanchez-Niubo A, Haro JM, Tyrovolas S. Depression and metabolic syndrome in the older population: A review of evidence. *J Affect Disord* 2018; **237**: 56-64 [PMID: 29772477 DOI: 10.1016/j.jad.2018.04.102]

17 **Sekita A**, Arima H, Ninomiya T, Ohara T, Doi Y, Hirakawa Y, Fukuhara M, Hata J, Yonemoto K, Ga Y, Kitazono T, Kanba S, Kiyohara Y. Elevated depressive symptoms in metabolic syndrome in a general population of Japanese men: a cross-sectional study. *BMC Public Health* 2013; **13**: 862 [PMID: 24044502 DOI: 10.1186/1471-2458-13-862]

18 **Liaw FY**, Kao TW, Hsueh JT, Chan YH, Chang YW, Chen WL. Exploring the Link between the Components of Metabolic Syndrome and the Risk of Depression. *Biomed Res Int* 2015; **2015**: 586251 [PMID: 26770976 DOI: 10.1155/2015/586251]

19 **Mulvahill JS**, Nicol GE, Dixon D, Lenze EJ, Karp JF, Reynolds CF 3rd, Blumberger DM, Mulsant BH. Effect of Metabolic Syndrome on Late-Life Depression: Associations with Disease Severity and Treatment Resistance. *J Am Geriatr Soc* 2017; **65**: 2651-2658 [PMID: 29235659 DOI: 10.1111/jgs.15129]

20 **Zhang M**, Chen J, Yin Z, Wang L, Peng L. The association between depression and metabolic syndrome and its components: a bidirectional two-sample Mendelian randomization study. *Transl Psychiatry* 2021; **11**: 633 [PMID: 34903730 DOI: 10.1038/s41398-021-01759-z]

21 **Hiles SA**, Révész D, Lamers F, Giltay E, Penninx BW. Bidirectional prospective associations of metabolic syndrome components with depression, anxiety, and antidepressant use. *Depress Anxiety* 2016; **33**: 754-764 [PMID: 27120696 DOI: 10.1002/da.22512]

22 **Silić A**, Karlović D, Serretti A. Increased inflammation and lower platelet 5-HT in depression with metabolic syndrome. *J Affect Disord* 2012; **141**: 72-78 [PMID: 22391518 DOI: 10.1016/j.jad.2012.02.019]

23 **Lemche AV**, Chaban OS, Lemche E. Depression contributing to dyslipidemic cardiovascular risk in the metabolic syndrome. *J Endocrinol Invest* 2017; **40**: 539-546 [PMID: 28012071 DOI: 10.1007/s40618-016-0601-y]

24 **Chan KL**, Cathomas F, Russo SJ. Central and Peripheral Inflammation Link Metabolic Syndrome and Major Depressive Disorder. *Physiology (Bethesda)* 2019; **34**: 123-133 [PMID: 30724127 DOI: 10.1152/physiol.00047.2018]

25 **Marazziti D**, Rutigliano G, Baroni S, Landi P, Dell'Osso L. Metabolic syndrome and major depression. *CNS Spectr* 2014; **19**: 293-304 [PMID: 24103843 DOI: 10.1017/S1092852913000667]

26 **Dekker IP**, Marijnissen RM, Giltay EJ, van der Mast RC, Oude Voshaar RC, Rhebergen D, Rius Ottenheim N. The role of metabolic syndrome in late-life depression over 6 years: The NESDO study. *J Affect Disord* 2019; **257**: 735-740 [PMID: 31386966 DOI: 10.1016/j.jad.2019.07.060]

27 **Ribeiro RP**, Marziale MH, Martins JT, Ribeiro PH, Robazzi ML, Dalmas JC. Prevalence of Metabolic Syndrome among nursing personnel and its association with occupational stress, anxiety and depression. *Rev Lat Am Enfermagem* 2015; **23**: 435-440 [PMID: 26155007 DOI: 10.1590/0104-1169.0383.2573]

28 **Takeuchi T**, Nakao M, Kachi Y, Yano E. Association of metabolic syndrome with atypical features of depression in Japanese people. *Psychiatry Clin Neurosci* 2013; **67**: 532-539 [PMID: 24152284 DOI: 10.1111/pcn.12104]

29 **Zhao Y**, Hu Y, Smith JP, Strauss J, Yang G. Cohort profile: the China Health and Retirement Longitudinal Study (CHARLS). *Int J Epidemiol* 2014; **43**: 61-68 [PMID: 23243115 DOI: 10.1093/ije/dys203]

30 **Chen X**, Crimmins E, Hu PP, Kim JK, Meng Q, Strauss J, Wang Y, Zeng J, Zhang Y, Zhao Y. Venous Blood-Based Biomarkers in the China Health and Retirement Longitudinal Study: Rationale, Design, and Results From the 2015 Wave. *Am J Epidemiol* 2019; **188**: 1871-1877 [PMID: 31364691 DOI: 10.1093/aje/kwz170]

31 **Zhu L**, Spence C, Yang JW, Ma GX. The IDF Definition Is Better Suited for Screening Metabolic Syndrome and Estimating Risks of Diabetes in Asian American Adults: Evidence from NHANES 2011-2016. *J Clin Med* 2020; **9** [PMID: 33260754 DOI: 10.3390/jcm9123871]

32 **Chen H**, Mui AC. Factorial validity of the Center for Epidemiologic Studies Depression Scale short form in older population in China. *Int Psychogeriatr* 2014; **26**: 49-57 [PMID: 24125553 DOI: 10.1017/S1041610213001701]

33 **Andresen EM**, Malmgren JA, Carter WB, Patrick DL. Screening for depression in well older adults: evaluation of a short form of the CES-D (Center for Epidemiologic Studies Depression Scale). *Am J Prev Med* 1994; **10**: 77-84 [PMID: 8037935]

34 **Moradi Y**, Albatineh AN, Mahmoodi H, Gheshlagh RG. The relationship between depression and risk of metabolic syndrome: a meta-analysis of observational studies. *Clin Diabetes Endocrinol* 2021; **7**: 4 [PMID: 33648597 DOI: 10.1186/s40842-021-00117-8]

35 **Chan S**, Jia S, Chiu H, Chien WT, R Thompson D, Hu Y, Lam L. Subjective health-related quality of life of Chinese older persons with depression in Shanghai and Hong Kong: relationship to clinical factors, level of functioning and social support. *Int J Geriatr Psychiatry* 2009; **24**: 355-362 [PMID: 18773498 DOI: 10.1002/gps.2129]

36 **Yuan MZ**, Fang Q, Liu GW, Zhou M, Wu JM, Pu CY. Risk Factors for Post-Acute Coronary Syndrome Depression: A Meta-analysis of Observational Studies. *J Cardiovasc Nurs* 2019; **34**: 60-70 [PMID: 30312193 DOI: 10.1097/JCN.0000000000000520]

37 **Tsuboi Y**, Ueda Y, Sugimoto T, Naruse F, Ono R. Association between metabolic syndrome and disability due to low back pain among care workers. *Int J Occup Med Environ Health* 2018; **31**: 165-172 [PMID: 28967647 DOI: 10.13075/ijomeh.1896.01004]

38 **Moussavi S**, Chatterji S, Verdes E, Tandon A, Patel V, Ustun B. Depression, chronic diseases, and decrements in health: results from the World Health Surveys. *Lancet* 2007; **370**: 851-858 [PMID: 17826170 DOI: 10.1016/S0140-6736(07)61415-9]

39 **Akbaraly TN**, Kivimäki M, Brunner EJ, Chandola T, Marmot MG, Singh-Manoux A, Ferrie JE. Association between metabolic syndrome and depressive symptoms in middle-aged adults: results from the Whitehall II study. *Diabetes Care* 2009; **32**: 499-504 [PMID: 19106378 DOI: 10.2337/dc08-1358]

40 **Maresova P**, Javanmardi E, Barakovic S, Barakovic Husic J, Tomsone S, Krejcar O, Kuca K. Consequences of chronic diseases and other limitations associated with old age - a scoping review. *BMC Public Health* 2019; **19**: 1431 [PMID: 31675997 DOI: 10.1186/s12889-019-7762-5]

41 **Jiang CH**, Zhu F, Qin TT. Relationships between Chronic Diseases and Depression among Middle-aged and Elderly People in China: A Prospective Study from CHARLS. *Curr Med Sci* 2020; **40**: 858-870 [PMID: 33123901 DOI: 10.1007/s11596-020-2270-5]

World Journal of Psychiatry

Submit a Manuscript: https://www.f6publishing.com

World J Psychiatry 2024 February 19; 14(2): 255-265

DOI: 10.5498/wjp.v14.i2.255

ISSN 2220-3206 (online)

ORIGINAL ARTICLE

Retrospective Study

Analysis of risk factors leading to anxiety and depression in patients with prostate cancer after castration and the construction of a risk prediction model

Rui-Xiao Li, Xue-Lian Li, Guo-Jun Wu, Yong-Hua Lei, Xiao-Shun Li, Bo Li, Jian-Xin Ni

Specialty type: Urology and nephrology

Provenance and peer review: Unsolicited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

Grade A (Excellent): 0
Grade B (Very good): B
Grade C (Good): C
Grade D (Fair): 0
Grade E (Poor): 0

P-Reviewer: Pak H, Turkey; Sunanda T, United States

Received: November 3, 2023
Peer-review started: November 3, 2023
First decision: November 16, 2023
Revised: November 29, 2023
Accepted: January 16, 2024
Article in press: January 16, 2024
Published online: February 19, 2024

Rui-Xiao Li, Guo-Jun Wu, Yong-Hua Lei, Xiao-Shun Li, Bo Li, Jian-Xin Ni, Urology Hospital, Xi'an People's Hospital (Xi'an Fourth Hospital), Xi'an 710199, Shaanxi Province, China

Xue-Lian Li, Department of Surgery, Xi'an Hospital of Traditional Chinese Medicine, Xi'an 710199, Shaanxi Province, China

Corresponding author: Jian-Xin Ni, MM, Doctor, Urology Hospital, Xi'an People's Hospital (Xi'an Fourth Hospital), Intersection of Hangtian East Road and Hangtuo Road, Chang'an District, Xi'an 710199, Shaanxi Province, China. nijianxin@tom.com

Abstract

BACKGROUND

Cancer patients often suffer from severe stress reactions psychologically, such as anxiety and depression. Prostate cancer (PC) is one of the common cancer types, with most patients diagnosed at advanced stages that cannot be treated by radical surgery and which are accompanied by complications such as bodily pain and bone metastasis. Therefore, attention should be given to the mental health status of PC patients as well as physical adverse events in the course of clinical treatment.

AIM

To analyze the risk factors leading to anxiety and depression in PC patients after castration and build a risk prediction model.

METHODS

A retrospective analysis was performed on the data of 120 PC cases treated in Xi'an People's Hospital between January 2019 and January 2022. The patient cohort was divided into a training group (n = 84) and a validation group (n = 36) at a ratio of 7:3. The patients' anxiety symptoms and depression levels were assessed 2 wk after surgery with the Self-Rating Anxiety Scale (SAS) and the Self-rating Depression Scale (SDS), respectively. Logistic regression was used to analyze the risk factors affecting negative mood, and a risk prediction model was constructed.

RESULTS

In the training group, 35 patients and 37 patients had an SAS score and an SDS

score greater than or equal to 50, respectively. Based on the scores, we further subclassified patients into two groups: a bad mood group (n = 35) and an emotional stability group (n = 49). Multivariate logistic regression analysis showed that marital status, castration scheme, and postoperative Visual Analogue Scale (VAS) score were independent risk factors affecting a patient's bad mood ($P < 0.05$). In the training and validation groups, patients with adverse emotions exhibited significantly higher risk scores than emotionally stable patients ($P < 0.0001$). The area under the curve (AUC) of the risk prediction model for predicting bad mood in the training group was 0.743, the specificity was 70.96%, and the sensitivity was 66.03%, while in the validation group, the AUC, specificity, and sensitivity were 0.755, 66.67%, and 76.19%, respectively. The Hosmer-Lemeshow test showed a χ^2 of 4.2856, a P value of 0.830, and a C-index of 0.773 (0.692-0.854). The calibration curve revealed that the predicted curve was basically consistent with the actual curve, and the calibration curve showed that the prediction model had good discrimination and accuracy. Decision curve analysis showed that the model had a high net profit.

CONCLUSION

In PC patients, marital status, castration scheme, and postoperative pain (VAS) score are important factors affecting postoperative anxiety and depression. The logistic regression model can be used to successfully predict the risk of adverse psychological emotions.

Key Words: Prostate cancer; Castration; Anxiety and depression; Risk factors; Risk prediction model

Core Tip: Postoperative anxiety and depression are common and serious psychological problems in patients with prostate cancer, and marital status, castration scheme, and postoperative pain score have been identified as important factors leading to these psychological problems. Establishing a predictive model based on logistic regression can facilitate effective evaluation of patients' psychological risk and provide guidance for individualized intervention measures. By paying attention to patients' mental health, health care professionals can improve the quality of life and prognosis of patients. However, further research is needed to validate these findings and continue to explore other possible influencing factors, with the objective of developing more precise intervention strategies and support measures to meet the mental health needs of prostate cancer patients.

Citation: Li RX, Li XL, Wu GJ, Lei YH, Li XS, Li B, Ni JX. Analysis of risk factors leading to anxiety and depression in patients with prostate cancer after castration and the construction of a risk prediction model. *World J Psychiatry* 2024; 14(2): 255-265
URL: https://www.wjgnet.com/2220-3206/full/v14/i2/255.htm
DOI: https://dx.doi.org/10.5498/wjp.v14.i2.255

INTRODUCTION

Prostate cancer (PC) is a common malignancy affecting older men[1]. Worldwide, PC ranks second in the incidence of male malignancies and fifth in mortality[2]. In the United States, the incidence of PC has risen to the top of the list as the tumor that poses the greatest threat to men's health[3]. Although less prevalent than in Europe and America, PC shows an increasing incidence year by year in China and has become the main type of urinary system malignancy since 2008[4]. There are many therapeutic strategies for PC, including surgery, radiotherapy, and androgen deprivation therapy (ADT)[5]. ADT is the major treatment for PC patients due to the atypical early symptoms of the disease that result in disease progression to a higher stage when diagnosed[2]. For ADT, castration can be performed either surgically by removing both testicles or medically by using drugs to block the production of male hormones in the testicles. Surgical castration is usually a simple procedure with few side effects, but for many men, it is a major decision concerning body image and gender identity[6]. Although medical castration can store male hormone production after treatment discontinuation, it may cause some side effects, such as flushing, decreased libido, and impotence[7]. Nevertheless, surgical castration may still be an effective treatment option for PC patients who are ineligible for drug treatment.

The stress that PC patients experience comes not only from the physical symptoms of the disease and the side effects of treatment but also from the psychological and social issues associated with stigma[8]. While methods such as surgery and endocrine therapy can improve survival in PC patients, they may have a serious negative impact on their physical and mental health[9]. The medical model is shifting from a single physiological level to a comprehensive psychological, social and physiological model that extends beyond physical symptoms; therefore, more attention is expected to be given to patients' psychological conditions, such as anxiety and depression, when treating PC[10]. Malignant tumors, surgical trauma, and postoperative complications may bring enormous mental pressure to patients, resulting in important negative emotions such as anxiety, depression, and pessimism[11]. Therefore, in the process of treating PC, doctors and medical teams need to pay close attention to patients' mental health and provide timely psychological counseling and support to help patients cope with various challenges brought by the disease.

Risk prediction models play a central role in many fields, including but not limited to medical care, finance, insurance, and industry[12]. Their major function is to support decision-making. For example, doctors can use models to evaluate patients' disease risk and develop personalized treatment and prevention plans accordingly. In this study, we built a risk prediction model to predict anxiety and depression in PC patients after surgical castration, providing a reference for clinical treatment and intervention.

MATERIALS AND METHODS

Sample information

After obtaining approval from the Xi'an People's Hospital Medical Ethics Committee, a retrospective analysis was conducted on the data of 148 PC patients who received treatment in Xi'an People's Hospital between January 2019 and January 2022.

Eligibility and exclusion criteria

The inclusion criteria are listed as follows: Age range: 30-75; confirmed diagnosis of PC by prostate puncture or postoperative pathology; clear mind, good cooperation, and ability to independently complete various questionnaires; intact clinical data.

The exclusion criteria were as follows: Serious dysfunction of vital organs such as the heart and lung; history of organic brain diseases or mental illness; concomitant other tumors; and life expectancy ≤ 6 months.

Sample screening and grouping

One hundred and twenty PC patients were selected after rigorous screening according to the patient eligibility and exclusion criteria mentioned above. They were assigned to a training group (n = 84) and a validation group (n = 36) at a ratio of 7:3. Furthermore, they were assessed by the Self-rating Anxiety and Depression Scale (SAS/SDS)[13] for anxiety symptoms and depression levels two weeks after surgery, with a score of more than 50 on both scales indicating the presence of anxiety and depression.

Clinical data collection

By reviewing patients' electronic medical records, we collected the following clinical data: Age, education level, marital status, employment, body mass index (BMI), smoking history, alcoholism history, hypertension, diabetes, castration scheme, monthly income, and postoperative pain level. In addition, SAS and SDS scores were collected after 2 wk of treatment.

Statistical analysis

The data collected were analyzed and processed by SPSS 26.0. Continuous variables conforming to a normal distribution are described as the mean ± SD and were analyzed by the two independent samples t test. Categorical variables, expressed as percentages (%), were tested by the χ^2 test. Variables with a P value less than 0.05 in the univariate analysis were included in the multivariate logistic regression analysis, and the independent risk factors for anxiety and depression in PC patients were screened using the stepwise regression procedure. Using R software and the RMS package, a nomogram for the prediction of bad mood in PC patients was established; the operating characteristic (ROC) curves of the subjects were drawn, and the areas under the curve (AUCs) were calculated. The calibration curve and decision curve were plotted to verify the effectiveness of the model. Statistical significance was indicated by P values less than $P < 0.05$.

RESULTS

Evaluation of patients' bad mood

Patients' anxiety and depression were evaluated by the SAS and SDS at 2 wk after treatment. The results showed that 35 patients had SAS scores greater than or equal to 50 points, and 37 patients had SDS scores greater than or equal to 50 points (Figure 1). By further comparing patients' baseline data between the training and validation sets, we found no statistical difference between the two groups ($P > 0.05$). Based on the scores, we further assigned the patients to a bad mood group (n = 35) and an emotional stability group (n = 49) for univariate analysis (Table 1).

Analysis of factors affecting patients' bad mood

Clinical data were evaluated after patients were grouped according to their scores. Statistical differences were present in marital status, castration scheme, monthly income, and postoperative Visual Analogue Scale (VAS) score between patients with bad mood and those with emotional stability ($P < 0.05$; Table 2), while no significant difference was identified in age, education level, employment, BMI, smoking history, alcoholism history, hypertension, or diabetes ($P > 0.05$).

Multivariate analysis of patients' bad mood

According to the results, we assigned values to marital status, castration scheme, monthly income, and postoperative

Table 1 Comparison of the baseline data between the training group and the validation group

Factors		Training group (*n* = 84)	Validation group (*n* = 36)	*P* value
Age				0.871
	≥ 60 years old	34	14	
	< 60 years old	50	22	
Education level				0.274
	≥ High school	37	12	
	< High school	47	24	
Marital status				0.999
	Married	56	24	
	Divorced/unmarried	28	12	
Employment				0.545
	Employed	19	10	
	Retired	65	26	
BMI				0.668
	≥ 25 kg/m^2	18	9	
	< 25 kg/m^2	66	27	
Smoking history				0.624
	With	62	25	
	Without	22	11	
History of alcoholism				0.373
	With	13	8	
	Without	71	28	
Hypertension				0.593
	With	15	5	
	Without	69	31	
Diabetes mellitus				0.451
	With	18	10	
	Without	66	26	
Castration scheme				0.778
	Surgery	35	16	
	Medication	49	20	
Monthly income				0.807
	≥ 4500 RMB	33	15	
	< 4500 RMB	51	21	
Postoperative VAS score				0.777
	≥ 5 points	19	9	
	< 5 points	65	27	
Unhealthy emotions				
	Bad mood group	35	15	
	Emotional stability group	49	21	0.999

BMI: Body mass index; VAS: Visual Analogue Scale.

Table 2 Univariate analysis

Factors		Bad mood group (*n* = 35)	Emotional stability group (*n* = 49)	*P* value
Age				
	≥ 60 years old	15	19	0.645
	< 60 years old	20	30	
Education level				
	≥ High school	18	19	0.249
	< High school	17	30	
Marital status				
	Married	28	28	0.034[a]
	Divorced/unmarried	7	21	
Employment				
	Employed	7	12	0.591
	Retired	28	37	
BMI				
	≥ 25 kg/m^2	8	10	0.787
	< 25 kg/m^2	27	39	
Smoking history				
	With	25	37	0.675
	Without	10	12	
History of alcoholism				
	With	4	9	0.454
	Without	31	40	
Hypertension				
	With	5	10	0.556
	Without	30	39	
Diabetes mellitus				
	With	6	12	0.446
	Without	29	37	
Castration scheme				
	Surgery	21	14	0.003[b]
	Medication	14	35	
Monthly income				
	≥ 4500 RMB	8	25	0.010[a]
	< 4500 RMB	27	24	
Postoperative VAS score				
	≥ 5 points	13	6	0.007[a]
	< 5 points	22	43	

[a]$P < 0.05$.
[b]$P < 0.01$.
BMI: Body mass index; VAS: Visual Analogue Scale.

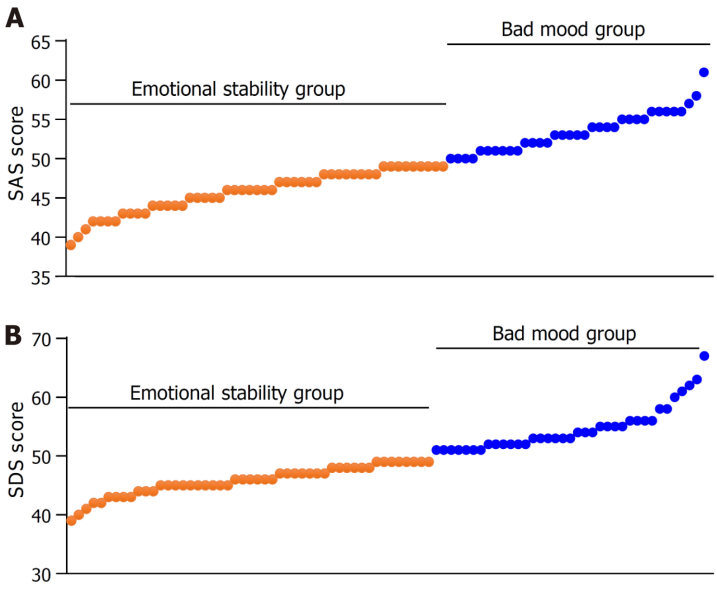

Figure 1 Assessment of patients' bad mood. A: Self-Rating Anxiety Scale scores of patients in training group; B: Self-Rating Depression Scale scores of patients in training group. SAS: Self-Rating Anxiety Scale; SDS: Self-Rating Depression Scale.

VAS score (Table 3). Then, multivariate logistic regression was used to analyze the independent factors for patients' negative mood. Marital status, castration scheme, and postoperative VAS score were identified as independent risk factors for adverse mood (Table 4; $P < 0.05$).

Construction of a risk prediction model for the prediction of bad mood

Based on the β coefficient of logistic regression, we constructed a risk scoring formula: 1.284* marital status + 1.224* castration scheme + 1.792* postoperative VAS score. By calculating the risk score of each patient, we found that the risk score of patients in the bad mood group was significantly higher than that of patients in the emotional stability group ($P < 0.0001$; Figure 2). Moreover, ROC curve analysis showed that the AUC of the risk prediction model for predicting patients' bad mood was 0.743, the specificity was 70.96%, and the sensitivity was 66.03%.

Validation of the risk prediction model

There were 15 patients in the validation group with adverse emotions. According to the risk scoring formula, we substituted the clinical data of the validation group into the formula for calculation and found that the risk score of patients with bad mood in the validation group was significantly higher than that of patients in the emotional stability group ($P < 0.0001$; Figure 3 and Table 5). Through ROC curve analysis, the AUC, specificity, and sensitivity of the risk prediction model for the prediction of adverse mood in the validation group were 0.755, 66.67%, and 76.19%, respectively.

Construction and validation of a nomogram for the prediction of bad mood in PC patients

The three independent risk factors were used to establish a nomogram for the prediction of bad mood in PC patients (Figure 4). The corresponding score was given to each indicator, depending on the specific condition, and the total score, and the scores were added together to obtain the total score. A vertical line from the total score to the probability axis of bad mood risk was the occurrence risk of bad mood. The Hosmer-Lemeshow test revealed a χ^2 value of 4.2856, a P value of 0.830, and a C-index of 0.773 (0.692-0.854). The calibration curve showed basic consistency between the predicted and actual curves (Figure 4), indicating that the model had good discrimination and accuracy. The analysis of the decision curve revealed that the model had a high net benefit (Figure 4).

DISCUSSION

Cancer-related anxiety and depression are common clinical reactions to serious psychophysiological stress. The incidence of anxiety and depression varies among patients with different types of cancer[14]. This study found that the incidence rates of anxiety and depression in PC patients were 41.66% and 44.04%, respectively, which is basically consistent with foreign research[15,16]. Most PC patients in China have progressed to the middle and late stages upon diagnosis, which is unsuitable for radical surgery. Meanwhile, they are often complicated with physical pain and bone metastasis, which can impose heavy physical and mental burdens on them[17,18]. Therefore, during PC treatment, we should not only pay attention to physical adverse events but also attach sufficient importance to the occurrence of adverse psychological symptoms such as anxiety and depression to improve patient prognosis.

Table 3 Assignment table

Factors	Assignment
Marital status	Married = 1; unmarried/divorced = 0
Castration scheme	Surgery = 1; medication = 0
Monthly income	≥ 4500 RMB = 0; < 4500 RMB = 1
Postoperative VAS score	≥ 5 points = 1; < 5 points = 0
Bad mood	Bad mood = 1; emotional stability = 0

VAS: Visual Analogue Scale.

Table 4 Logistic multivariate regression analysis

Factors	β	Standard error	χ^2	*P* value	OR	95%CI	
						Lower bound	Upper bound
Marital status	1.284	0.602	4.554	0.033[a]	3.611	1.110	11.742
Castration scheme	1.224	0.508	5.805	0.016[a]	3.401	1.256	9.203
Monthly income	0.614	0.561	1.200	0.273	1.848	0.616	5.547
Postoperative VAS score	1.792	0.646	7.701	0.006[b]	6.000	1.693	21.27

[a]*P* < 0.05.
[b]*P* < 0.01.
VAS: Visual Analogue Scale.

Table 5 Comparison of the risk scores

Groups	Training group (*n* = 84)	Groups	Validation group (*n* = 36)
Bad mood group (*n* = 35)	2.43 ± 1.00	Bad mood group (*n* = 15)	2.56 ± 1.14
Emotional stability group (*n* = 49)	1.30 ± 1.09	Emotional stability group (*n* = 21)	1.34 ± 1.16
t value	4.813	*t* value	3.132
P value	< 0.001[c]	*P* value	0.004[b]

[b]*P* < 0.01.
[c]*P* < 0.001.

In this study, we analyzed the risk factors for postoperative anxiety and depression in PC patients undergoing surgical castration. Marital status, castration scheme, and postoperative VAS score were identified as important factors affecting postoperative anxiety and depression. In addition, research has found that widowed men have a higher risk of developing PC than those who are married or in a relationship. This may mean that social support in marriage or partnership may help to promote a healthy lifestyle and active attention to medical care, which in turn affects PC risk and prognosis. We believe that castration treatment of PC, especially surgical castration, can cause a sharp drop in male hormone levels in physiological terms, which is a possible cause of the above effects. The testicles are the organs that primarily produce male hormones such as testosterone, which play an important role in regulating mood and psychological state. After surgical castration, male patients may experience a physiological reaction of decreased testosterone levels, which will lead to emotional changes such as mood swings, anxiety, and depression. Such a physiological change may trigger physical and psychological discomfort, including mood swings, insomnia and fatigue, contributing to anxiety and depression. In addition, castration treatment may lead to sexual dysfunction, such as erectile dysfunction and decreased libido, all of which may adversely influence patients' self-esteem and self-confidence, triggering anxiety and depression. Furthermore, castration therapy can cause changes that affect a patient's body image, such as weight gain and breast hypertrophy, which may affect one's feelings of self-image and self-identity, leading to anxiety and depression. Somatic pain seriously affects the quality of daily life of PC patients, and the stress response triggered by pain may induce anxiety and depression. Moreover, patients undergoing surgical castration are affected by the operation, which increases the stress of the body.

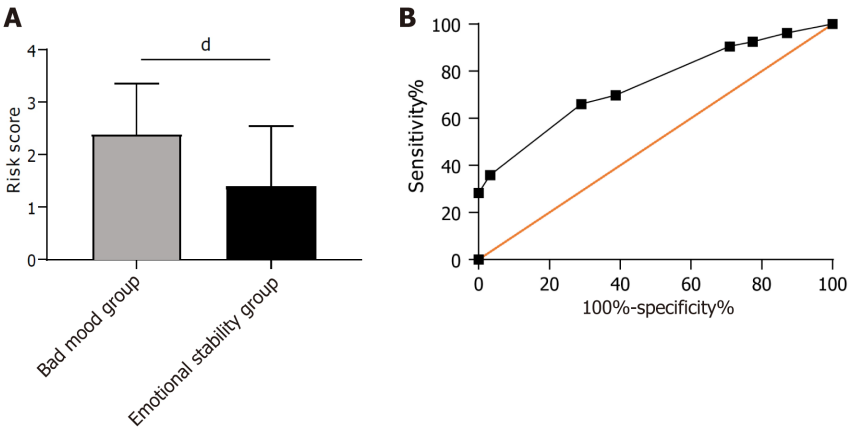

Figure 2 Construction of a risk prediction model for bad mood in patients in the training group. A: The risk score of patients with bad mood in the training group; B: The area under the curve of the risk score in predicting bad mood in patients with bad mood in the training group. $^{d}P < 0.0001$.

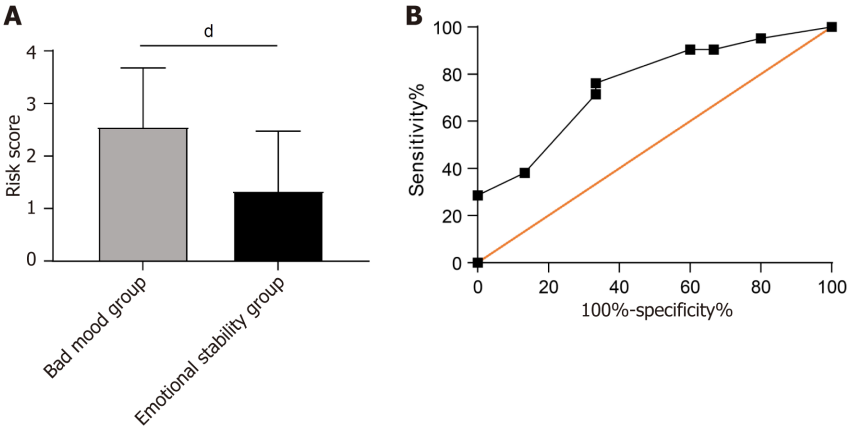

Figure 3 Risk prediction model construction for bad mood in patients in the validation group. A: The risk score in patients with bad mood in the validation group; B: The area under the curve of risk score in predicting bad mood in patients with bad mood in the validation group. $^{d}P < 0.0001$.

By collecting and analyzing relevant clinical features and predictive variables, regression models can be used to predict the probability or risk of a specific event. These events may include disease development, therapeutic response, complications, disease risk assessment, personalized medicine, screening and early intervention, and decision support. The logistic regression model is a regression model for establishing binary classification problems, which is suitable for continuous and discrete features due to the advantages of interpretability, probability prediction, simplicity, and efficiency. This model is widely used in various practical applications, helping to estimate the probability of binary outcome variables and providing an explanation of the degree of influence of features on target variables. Through the establishment of a logistic regression model, we found that the risk score constructed based on marital status, castration scheme, and postoperative VAS score successfully predicted the occurrence of bad mood in PC patients after castration treatment with an AUC of 0.743. In addition, through data validation, the AUC of the model for predicting bad mood in validation group patients was found to be 0.755, indicating the high generalization potential of the model. Based on the results of multivariate analysis, the nomograph integrates multiple clinically relevant variables into line segments with scales, visualizing and graphically presenting the influence of each variable on clinical outcomes, which makes it easy and intuitive to be applied in hospitals for calculating clinical outcome probabilities. At the end of the study, we drew a nomogram and found through the calibration curve that the predicted curve was basically consistent with the actual curve. Furthermore, the decision curve revealed a high net benefit of the model, suggesting good prediction efficiency; this implies that it will be helpful for medical staff in predicting the adverse emotion risk of PC patients individually and accurately.

Although this study identified the risk factors for the occurrence of bad mood in PC patients after castration treatment, there are still some limitations. First, since we did not collect the prognostic data of patients, more data are needed to support the analysis of the impact of bad mood on patients' long-term outcomes. Second, the sample size is small, and whether this will lead to bias in the data analysis needs further exploration. Finally, as this is a single-center study, more data are needed to verify the feasibility of the model for generalization in other centers. Therefore, we hope to cooperate in follow-up research and collect more data to validate our model.

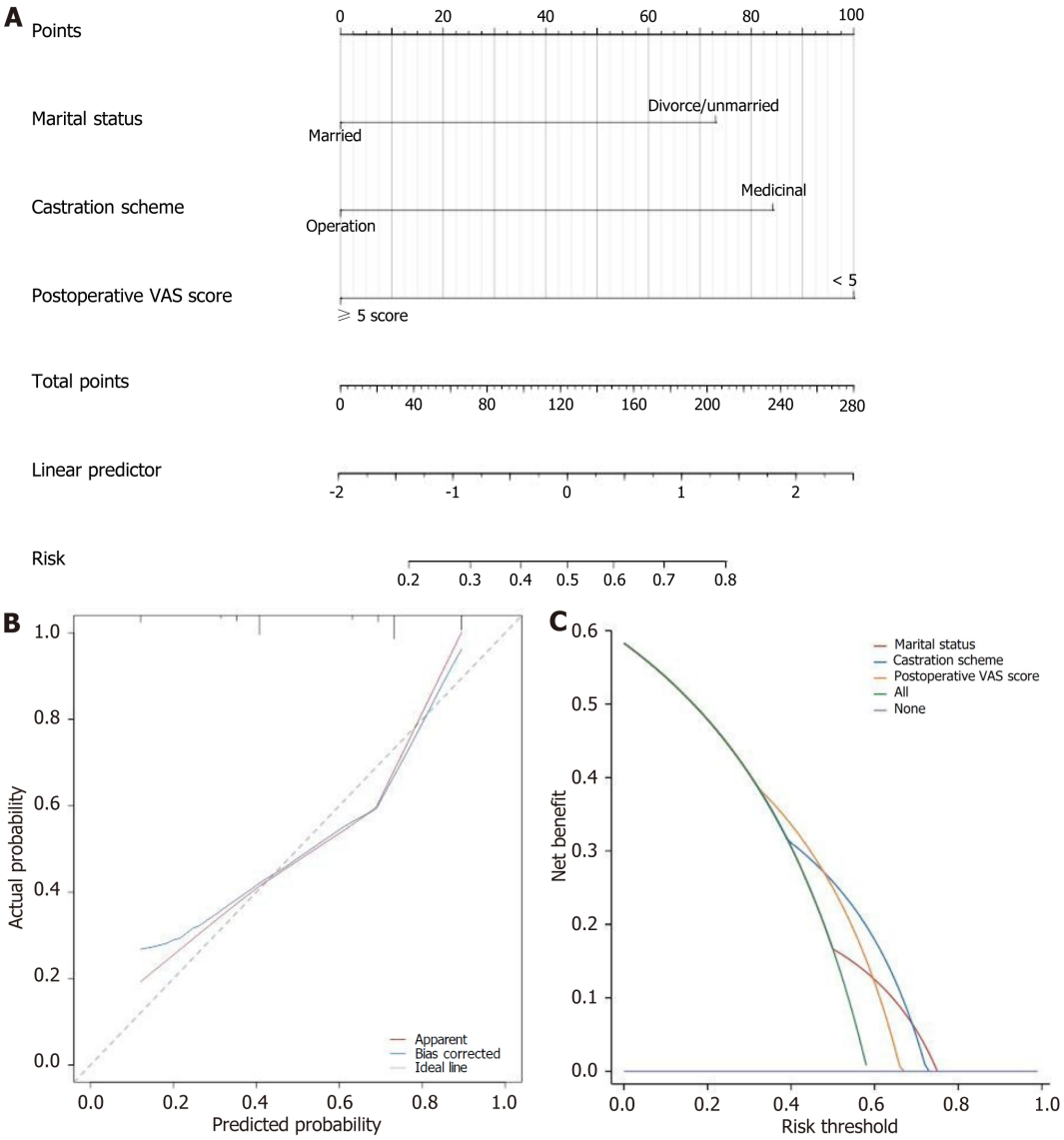

Figure 4 Construction and validation of the nomogram. A: A nomogram of bad mood in prostate cancer patients; B: Calibration curve of bad mood in prostate cancer patients; C: Decision curve of bad mood in prostate cancer patients. VAS: Visual Analogue Scale.

CONCLUSION

In patients with PC, marital status, castration scheme, and postoperative pain (VAS) score are important factors affecting postoperative anxiety and depression. A logistic regression model can be used to successfully predict the risk of adverse psychological emotions. Through an individualized risk assessment, health care professionals can intervene in advance to improve patients' mental health and outcomes. However, further validation and sample size extension are needed to deepen the understanding of the psychological problems of PC patients and to look for other possible influencing factors that may provide more precise intervention strategies and support measures.

ARTICLE HIGHLIGHTS

Research background

Cancer-related anxiety and depression are common severe psychological stress reactions in clinical practice, with their incidence rates varying among patients with different types of cancer. Prostate cancer (PC), a common type of cancer that is usually diagnosed in the advanced stages, makes radical surgery impossible. In addition, the disease is accompanied by complications such as physical pain and bone metastasis, which brings a heavy physical and mental burden to patients. Therefore, in the clinical treatment of PC, we should pay attention to not only the adverse reactions of the body, but also the occurrence of psychological symptoms such as anxiety and depression, so as to improve the prognosis of patients.

Research motivation

The motivation for this study is to understand the factors that influence postoperative anxiety and depression in PC patients, based on which healthcare professionals can develop effective intervention and support strategies to meet the mental health needs of these patients.

Research objectives

The objective of this study is to analyze the risk factors affecting postoperative anxiety and depression in PC patients, and to explore the effects of marital status, castration scheme, and postoperative Visual Analogue Scale (VAS score) on anxiety and depression. In addition, the study aims to establish a prediction model using logistic regression analysis to evaluate the risk of adverse emotional outcomes of these patients.

Research methods

In this study, retrospective analysis was used to investigate the relationship between various clinical factors and postoperative anxiety and depression in PC patients. Data such as marital status, castration scheme, and postoperative VAS score were collected and analyzed. Using the logistic regression model, a risk scoring system was developed to predict the occurrence of adverse emotional outcomes.

Research results

Marital status, castration scheme, and postoperative VAS score were identified to be important factors affecting postoperative anxiety and depression in PC patients. The logistic regression model successfully predicted the risk of adverse emotional outcomes, with an area under the curve of 0.743. The model exhibited high generalization with a verified area under the curve of 0.755.

Research conclusions

The findings highlight the importance of psychological symptoms, especially anxiety and depression, in the clinical management of patients with PC. Marital status, castration scheme, and postoperative VAS score are identified as important predictors of adverse emotional outcomes. The logistic regression model shows good accuracy, which is helpful to individualize and improve the predictive ability of psychological risk in PC patients.

Research perspectives

Although this study successfully identified the risk factors and developed a risk prediction model, there are still some limitations. Further research is needed to explore the long-term outcomes of patients and the impact of adverse emotional outcomes on patient prognosis, and to validate the generalization of the model with more data. Future research collaborations and data collection are important to further understand and apply this predictive model in PC.

FOOTNOTES

Co-first authors: Rui-Xiao Li and Xue-Lian Li.

Author contributions: Li RX and Li XL contributed equally to this work and are co-first authors; Li RX, Li XL and Ni JX designed the research and wrote the first manuscript; Li RX, Li XL, Wu GJ, Lei YH and Ni JX contributed to conceiving the research and analyzing data; Li RX, Li XL, Li XS, Li B and Ni JX conducted the analysis and provided guidance for the research; all authors reviewed and approved the final manuscript.

Institutional review board statement: This study was approved by the Ethic Committee of Xi'an People's Hospital (Approval No. KJLL-Z-K-2023055).

Informed consent statement: All study participants, or their legal guardian, provided informed written consent prior to study enrollment.

Conflict-of-interest statement: There is no conflict of interest.

Data sharing statement: All data and materials are available from the corresponding author.

Country/Territory of origin: China

ORCID number: Jian-Xin Ni 0009-0007-6007-4000.

S-Editor: Yan JP
L-Editor: A

P-Editor: Zhang YL

REFERENCES

1 **Desai K**, McManus JM, Sharifi N. Hormonal Therapy for Prostate Cancer. *Endocr Rev* 2021; **42**: 354-373 [PMID: 33480983 DOI: 10.1210/endrev/bnab002]

2 **Sekhoacha M**, Riet K, Motloung P, Gumenku L, Adegoke A, Mashele S. Prostate Cancer Review: Genetics, Diagnosis, Treatment Options, and Alternative Approaches. *Molecules* 2022; **27** [PMID: 36080493 DOI: 10.3390/molecules27175730]

3 **Wang G**, Zhao D, Spring DJ, DePinho RA. Genetics and biology of prostate cancer. *Genes Dev* 2018; **32**: 1105-1140 [PMID: 30181359 DOI: 10.1101/gad.315739.118]

4 **Liu J**, Dong L, Zhu Y, Dong B, Sha J, Zhu HH, Pan J, Xue W. Prostate cancer treatment - China's perspective. *Cancer Lett* 2022; **550**: 215927 [PMID: 36162714 DOI: 10.1016/j.canlet.2022.215927]

5 **Teo MY**, Rathkopf DE, Kantoff P. Treatment of Advanced Prostate Cancer. *Annu Rev Med* 2019; **70**: 479-499 [PMID: 30691365 DOI: 10.1146/annurev-med-051517-011947]

6 **Menges D**, Yebyo HG, Sivec-Muniz S, Haile SR, Barbier MC, Tomonaga Y, Schwenkglenks M, Puhan MA. Treatments for Metastatic Hormone-sensitive Prostate Cancer: Systematic Review, Network Meta-analysis, and Benefit-harm assessment. *Eur Urol Oncol* 2022; **5**: 605-616 [PMID: 35599144 DOI: 10.1016/j.euo.2022.04.007]

7 **Boevé LMS**, Hulshof MCCM, Vis AN, Zwinderman AH, Twisk JWR, Witjes WPJ, Delaere KPJ, Moorselaar RJAV, Verhagen PCMS, van Andel G. Effect on Survival of Androgen Deprivation Therapy Alone Compared to Androgen Deprivation Therapy Combined with Concurrent Radiation Therapy to the Prostate in Patients with Primary Bone Metastatic Prostate Cancer in a Prospective Randomised Clinical Trial: Data from the HORRAD Trial. *Eur Urol* 2019; **75**: 410-418 [PMID: 30266309 DOI: 10.1016/j.eururo.2018.09.008]

8 **Naser AY**, Hameed AN, Mustafa N, Alwafi H, Dahmash EZ, Alyami HS, Khalil H. Depression and Anxiety in Patients With Cancer: A Cross-Sectional Study. *Front Psychol* 2021; **12**: 585534 [PMID: 33935849 DOI: 10.3389/fpsyg.2021.585534]

9 **Wang YH**, Li JQ, Shi JF, Que JY, Liu JJ, Lappin JM, Leung J, Ravindran AV, Chen WQ, Qiao YL, Shi J, Lu L, Bao YP. Depression and anxiety in relation to cancer incidence and mortality: a systematic review and meta-analysis of cohort studies. *Mol Psychiatry* 2020; **25**: 1487-1499 [PMID: 31745237 DOI: 10.1038/s41380-019-0595-x]

10 **Charalambous A**, Giannakopoulou M, Bozas E, Paikousis L. Parallel and serial mediation analysis between pain, anxiety, depression, fatigue and nausea, vomiting and retching within a randomised controlled trial in patients with breast and prostate cancer. *BMJ Open* 2019; **9**: e026809 [PMID: 30679301 DOI: 10.1136/bmjopen-2018-026809]

11 **Duarte V**, Araújo N, Lopes C, Costa A, Ferreira A, Carneiro F, Oliveira J, Braga I, Morais S, Pacheco-Figueiredo L, Ruano L, Tedim Cruz V, Pereira S, Lunet N. Anxiety and Depression in Patients with Prostate Cancer, at Cancer Diagnosis and after a One-Year Follow-Up. *Int J Environ Res Public Health* 2022; **19** [PMID: 35897487 DOI: 10.3390/ijerph19159122]

12 **Nissen ER**, O'Connor M, Kaldo V, Højris I, Borre M, Zachariae R, Mehlsen M. Internet-delivered mindfulness-based cognitive therapy for anxiety and depression in cancer survivors: A randomized controlled trial. *Psychooncology* 2020; **29**: 68-75 [PMID: 31600414 DOI: 10.1002/pon.5237]

13 **Yue T**, Li Q, Wang R, Liu Z, Guo M, Bai F, Zhang Z, Wang W, Cheng Y, Wang H. Comparison of Hospital Anxiety and Depression Scale (HADS) and Zung Self-Rating Anxiety/Depression Scale (SAS/SDS) in Evaluating Anxiety and Depression in Patients with Psoriatic Arthritis. *Dermatology* 2020; **236**: 170-178 [PMID: 31434087 DOI: 10.1159/000498848]

14 **Irusen H**, Fernandez P, Van der Merwe A, Suliman S, Esterhuizen T, Lazarus J, Parkes J, Seedat S. Depression, Anxiety, and Their Association to Health-Related Quality of Life in Men Commencing Prostate Cancer Treatment at Tertiary Hospitals in Cape Town, South Africa. *Cancer Control* 2022; **29**: 10732748221125561 [PMID: 36112984 DOI: 10.1177/10732748221125561]

15 **Huang T**, Su H, Zhang S, Huang Y. Reminiscence therapy-based care program serves as an optional nursing modality in alleviating anxiety and depression, improving quality of life in surgical prostate cancer patients. *Int Urol Nephrol* 2022; **54**: 2467-2476 [PMID: 35841489 DOI: 10.1007/s11255-022-03282-6]

16 **Kaushik D**, Shah PK, Mukherjee N, Ji N, Dursun F, Kumar AP, Thompson IM Jr, Mansour AM, Jha R, Yang X, Wang H, Darby N, Ricardo Rivero J, Svatek RS, Liss MA. Effects of yoga in men with prostate cancer on quality of life and immune response: a pilot randomized controlled trial. *Prostate Cancer Prostatic Dis* 2022; **25**: 531-538 [PMID: 34815548 DOI: 10.1038/s41391-021-00470-w]

17 **Conant KJ**, Huynh HN, Chan J, Le J, Yee MJ, Anderson DJ, Kaye AD, Miller BC, Drinkard JD, Cornett EM, Gomelsky A, Urits I. Racial Disparities and Mental Health Effects Within Prostate Cancer. *Health Psychol Res* 2022; **10**: 39654 [PMID: 36425236 DOI: 10.52965/001c.39654]

18 **Popiolek A**, Brzoszczyk B, Jarzemski P, Piskunowicz M, Jarzemski M, Borkowska A, Bieliński M. Quality of Life of Prostate Cancer Patients Undergoing Prostatectomy and Affective Temperament. *Cancer Manag Res* 2022; **14**: 1743-1755 [PMID: 35620062 DOI: 10.2147/CMAR.S358054]

World Journal of Psychiatry

Submit a Manuscript: https://www.f6publishing.com

World J Psychiatry 2024 February 19; 14(2): 266-275

DOI: 10.5498/wjp.v14.i2.266

ISSN 2220-3206 (online)

ORIGINAL ARTICLE

Retrospective Study

Sepsis one-hour bundle management combined with psychological intervention on negative emotion and sleep quality in patients with sepsis

Ming Xia, Guang-Yan Dong, Shi-Chao Zhu, Huan-Min Xing, Li-Ming Li

Specialty type: Psychiatry

Provenance and peer review: Unsolicited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

Grade A (Excellent): 0
Grade B (Very good): 0
Grade C (Good): C
Grade D (Fair): 0
Grade E (Poor): 0

P-Reviewer: Kotera Y, United Kingdom

Received: November 30, 2023
Peer-review started: November 30, 2023
First decision: December 15, 2023
Revised: December 26, 2023
Accepted: January 22, 2024
Article in press: January 22, 2024
Published online: February 19, 2024

Ming Xia, Guang-Yan Dong, Shi-Chao Zhu, Huan-Min Xing, Department of Intensive Care Unit, Henan Provincial Key Medicine Laboratory of Nursing, Henan Provincial People's Hospital, Zhengzhou University People's Hospital, Zhengzhou 450003, Henan Province, China

Li-Ming Li, Department of Nursing, Henan Provincial Key Medicine Laboratory of Nursing, Henan Provincial People's Hospital, Zhengzhou University People's Hospital, Zhengzhou 450003, Henan Province, China

Corresponding author: Li-Ming Li, MPhil, Chief Nurse, Department of Nursing, Henan Provincial Key Medicine Laboratory of Nursing, Henan Provincial People's Hospital, Zhengzhou University People's Hospital, No. 7 Weiwu Road, Jinshui District, Zhengzhou 450003, Henan Province, China. lilimingand@163.com

Abstract

BACKGROUND

Sepsis is a serious infectious disease caused by various systemic inflammatory responses and is ultimately life-threatening. Patients usually experience depression and anxiety, which affect their sleep quality and post-traumatic growth levels.

AIM

To investigate the effects of sepsis, a one-hour bundle (H1B) management was combined with psychological intervention in patients with sepsis.

METHODS

This retrospective analysis included 300 patients with sepsis who were admitted to Henan Provincial People's Hospital between June 2022 and June 2023. According to different intervention methods, the participants were divided into a simple group (SG, n = 150) and combined group (CG, n = 150). H1B management was used in the SG and H1B management combined with psychological intervention was used in the CG. The changes of negative emotion, sleep quality and post-traumatic growth and prognosis were compared between the two groups before (T0) and after (T1) intervention.

RESULTS

After intervention (T1), the scores of the Hamilton Anxiety scale and Hamilton

Depression scale in the CG were significantly lower than those in the SG ($P < 0.001$). Sleep time, sleep quality, sleep efficiency, daytime dysfunction, sleep disturbance dimension score, and the total score in the CG were significantly lower than those in the SG ($P < 0.001$). The appreciation of life, mental changes, relationship with others, personal strength dimension score, and total score of the CG were significantly higher than those of the SG ($P < 0.001$). The scores for mental health, general health status, physiological function, emotional function, physical pain, social function, energy, and physiological function in the CG were significantly higher than those in the SG ($P < 0.001$). The mechanical ventilation time, intensive care unit stay time, and 28-d mortality of the CG were significantly lower than those of the SG ($P < 0.05$).

CONCLUSION

H1B management combined with psychological intervention can effectively alleviate the negative emotions of patients with sepsis and increase their quality of sleep and life.

Key Words: Cluster management; Psychological intervention; Sepsis; Negative emotions; Sleep quality; Post-traumatic growth

Core Tip: This study investigated changes in negative emotions, quality of life, and prognosis of patients with sepsis after one-hour bundle (H1B) management and psychological intervention. The results showed that the Hamilton Anxiety scale, Hamilton Depression scale, and Pittsburgh Sleep Quality Index scores of the patients were significantly lower after the intervention, and the Post Traumatic Growth Inventory scores were higher than those before the intervention. These results indicate that H1B management combined with psychological intervention can effectively improve negative emotions, sleep quality, post-traumatic growth levels, and quality of life in patients with sepsis.

Citation: Xia M, Dong GY, Zhu SC, Xing HM, Li LM. Sepsis one-hour bundle management combined with psychological intervention on negative emotion and sleep quality in patients with sepsis. *World J Psychiatry* 2024; 14(2): 266-275
URL: https://www.wjgnet.com/2220-3206/full/v14/i2/266.htm
DOI: https://dx.doi.org/10.5498/wjp.v14.i2.266

INTRODUCTION

Sepsis is a clinical syndrome characterized by dysregulated systemic, metabolic, and pathological host responses to infection. Sepsis is associated with the release of a large number of inflammatory mediators, which exert their effects through the neuroendocrine-immune regulatory network and may lead to septic shock and organ failure in severe cases [1]. At present, sepsis is the leading cause of death from critical illness worldwide[2]. It is conservatively estimated that approximately 31.5 million patients are affected by sepsis and its complications each year, resulting in approximately 5.3 million deaths globally[3]. In China, a downward trend in the fatality rate of sepsis has been observed with technological advancements and improvements in the management of medical conditions; nonetheless, the reported incidence and fatality rate of sepsis are approximately 28% and 70%, respectively[4]. Therefore, the treatment and clinical management of patients with sepsis have become critical issues that urgently need addressing.

Currently, the clinical treatment of sepsis mainly focuses on infection control, early fluid resuscitation, and correction of the pathophysiological state. Previous studies[5] have shown that patients with sepsis are emotionally depressed and have a poor overall sleep status during treatment, which has a significant impact on their prognosis. In 2018, researchers at Brown University in the United States proposed a sepsis one-hour bundle (H1B) management for patients with sepsis, which included lactic acid level detection, blood cultures for broad-spectrum antibacterial drug use, administration of antibiotics, and fluid resuscitation within the first hour of treatment. Compared with conventional 3-h and 6-h management intervention, H1B management may be more efficient[6]. More generally, cluster management is a new method that includes evidence-based treatments, personalized interventions, and nursing measures that target challenging diseases. Studies[7] have shown that cluster management interventions for patients with severe sepsis can improve patient compliance and prognosis. Other studies have shown that psychological interventions for patients with sepsis can alleviate anxiety and depression, effectively prevent the occurrence of post-traumatic stress disorder, and improve the long-term prognosis of patients. However, the effect of H1B management combined with psychological interventions on sepsis remains unclear. This study investigated changes in negative emotions, sleep quality, and prognosis of patients with sepsis following H1B management combined with psychological intervention.

MATERIALS AND METHODS

Clinical data

In a retrospective analysis, patients with sepsis admitted to Henan Provincial People's Hospital between June 2022 and June 2023 were selected as study participants. After rigorous screening, 300 patients with sepsis were included in this study. Participants were classified into two groups according to the intervention methods used: a simple group (SG; n = 150) and a combined group (CG; n = 150). Patients in the SG underwent H1B management only, whereas those in the CG underwent H1B management combined with psychological intervention.

The inclusion criteria were as follows: (1) Patients between 18 and 75 years old; (2) patients meeting the diagnostic criteria for sepsis[1,8]; (3) all patients were admitted to the intensive care unit (ICU); (4) the baseline data, clinical characteristics and laboratory indices of all patients were complete; and (5) all participants indicated that they were willing and able to actively cooperate with the clinical nursing intervention. The following exclusion criteria applied: (1) Patients with cardiovascular disease, autoimmune disease, or malignant tumor; (2) pregnant or lactating women; (3) patients with abnormal liver, kidney, and other organ functions and mental abnormalities; and (4) patients who died, were brain-dead, or abandoned treatment within 24 h of admission.

The following diagnostic criteria for sepsis applied[1,8]: presence of organ dysfunction, quick Sequential Organ Failure Assessment (qSOFA) ≥ 2 score indicates sepsis; Sepsis 3.0 = infection + SOFA ≥ 2 score. The qSOFA score is based on the following items[9]: (1) Respiratory rate ≥ 22 times/min; (2) altered state of consciousness; (3) systolic blood pressure ≤ 100 mmHg. One point is allocated for each item and a score ≥ 2 points is considered suspected sepsis.

Intervention method

H1B management: The H1B intervention team is composed of 1 deputy chief physician, 1 attending physician, 2 physicians, and 8 nurses. The teams were divided into four groups that cooperated with each other in the nursing process of patients. All nurses underwent training in sepsis education, pharmacotherapy of sepsis, physiological function, role function, psychological intervention applied in this study, and identifying categories of patient behavior. Patient management involved the following: (1) Communication with the attending physician within 1 h after admission and blood gas analysis, blood cultures, administration of antibiotics, blood resuscitation, and vasoactive drug use within 1h of admission; (2) administration of anti-infection therapy, explaining to the patient the use of antibiotics and vasoactive drugs, with timely contact with the pharmacy to prepare a sufficient quantity of common antibiotics, including imipenem, piperacillin, vancomycin, cefoperazone, and sulbactam; and (3) mechanical ventilation in cases of hypoxia, tachycardia, hypotension, poor systemic perfusion, and pyrexia, with fluid resuscitation, and drugs such as milrinone to enhance cardiac function, vasopressors, subcutaneous pumping of insulin to lower blood sugar, and furosemide. A central venous catheter was placed for central venous pressure monitoring.

Psychological intervention: Psychological intervention is conducted after the patient's life is out of danger and involves several steps: (1) Obtaining the trust of the patient involves considering factors such as the patient's cultural background, their personality, and psychological characteristics, using honest communication, and conveying a warm attitude to establish a good relationship with the patient; (2) the psychological intervention plan requires an analysis of the psychological problems of the patients and the formulation of an intervention tailored to the psychological characteristics of the patient. Effective psychological intervention should be provided to patients as early as possible; and (3) implementation of the plan requires good communication with patients, the provision of care, and demonstrating a warm demeanor to reduce the patient's sense of loneliness. Through health education, sepsis knowledge promotion, and the distribution of informational leaflets, patients can develop an accurate understanding of sepsis. By explaining cases of successful treatment, patients can properly understand their disease and manage unnecessary worries and doubts. Prolonged hospitalization may prevent the patient from fulfilling their role in the family and society. Responsible nursing staff should enhance communication with patients, try to maintain the pre-admission healthy living habits of patients, meet their reasonable needs as much as possible, and help patients become familiar with the ward environment as soon as possible to reduce discomfort. This approach allows negative emotions to be effectively alleviated and enables patients to actively cooperate with clinical treatment, adopt an optimistic attitude towards completing rehabilitation goals at each stage, and achieve physical recovery.

Observational indicators

Baseline characteristics, including sex, age, body mass index (BMI), and type of sepsis, were compared between the two groups.

The emotional scores of the two groups were compared before (T0) and after (T1) the intervention. The Hamilton Anxiety scale (HAMA) and the Hamilton Depression scale (HAMD) were used to evaluate anxiety, depression, and mood [10]. The HAMA score rates the severity of anxiety as follows: < 7 indicates no anxiety, ≥ 7 indicates possible anxiety, ≥ 14 indicates certain anxiety, ≥ 21 indicates obvious anxiety, and > 29 indicates severe anxiety. The HAMD score rates the severity of depression as follows: < 7 indicates no depression, ≥ 7 indicates probable depression, ≥ 17 indicates certain depression, and > 24 indicates severe depression.

The sleep conditions at T0 and T1 were compared between the two groups. The Pittsburgh Sleep Quality Index (PSQI) [11] was used to evaluate sleep quality. The PSQI includes seven dimensions: time to fall asleep, sleep time, sleep quality, sleep efficiency, hypnotic drugs, daytime dysfunction, and sleep disorders. A 0- to 3-point scale is used with higher scores indicating worse sleep quality.

The post-traumatic growth levels at T0 and T1 were compared between the groups. Post Traumatic Growth Inventory (PTGI)[12] assesses levels of post-traumatic growth. PTGI evaluated the level of post-traumatic growth according to five dimensions: Appreciation of life, new possibilities, spiritual changes, relationships with others, and personal strength, with a total of 20 items. Each item is rated on a 0 to 5-point Likert scale, with 0 indicating that no such changes were experienced after trauma and 5 indicating considerable changes after trauma. The total score ranges from 0 to 100 with a higher score indicating more changes in post-traumatic growth.

The health survey status at T0 and T1 were compared between the groups. The MOS36-item short-form health survey (SF-36)[13] assesses quality of life according to eight aspects: mental health, general health status, physiological function, emotional function, physical pain, social function, energy, and physiological function. The final score of each aspect is calculated as follows: Final score = (actual score - lowest possible score for that aspect)/difference between lowest and highest possible scores for that aspect × 100%. The actual score is the sum of all the scores for a particular aspect and each dimension is scored on a scale from 0 to 100.

Comparison of prognosis between the groups. Differences in mechanical ventilation time, ICU stay time, and 28-d mortality between the two groups were compared.

Statistical analysis

Statistical analyses were performed using IBM SPSS statistics for Windows, version 26.0. The measurement data conforming to normal distribution are represented as mean ± SD, using a t test. Counting data are expressed as percentage of frequency (n%), by χ^2 test. A P value < 0.05 was considered statistically significant.

RESULTS

Baseline data comparison

A flowchart of the analysis in this study is presented in Figure 1. Sex, age, disease duration, BMI, and infection type were compared between the two groups (P > 0.05; Table 1).

HAMA and HAMD scores

At T1, the HAMA and HAMD scores of the two groups were significantly lower than those at T0 (P < 0.05), and the scores of the CG group were lower than those of the SG group (P < 0.05; Figure 2).

PSQI scores

At T1, the time to fall asleep, sleep time, sleep quality, sleep efficiency, hypnotic drugs, daytime dysfunction, sleep disturbance dimension score, and total PSQI score in the two groups were lower than those at T0 (P < 0.05). Each dimension score was lower in the CG group than that in the SG group (P < 0.05; Table 2).

PTGI scores

At T1, the appreciation of life, new possibilities, spiritual changes, relationships with others, and personal power dimension scores of the PTGI in the two groups were higher than those at T0 (P < 0.05). Each dimension score was higher in the CG group than that in the SG group (P < 0.05) (Table 3).

SF-36 scores

In both groups, the SF-36 scores for mental health, general health status, physiological function, emotional function, physical pain, social function, energy, and physiological function were higher at T1 than those at T0 (P < 0.05). CG were higher than SG (P < 0.05) (Table 4).

Prognosis comparison

The mechanical ventilation time of the CG group was (6.08 ± 2.07) d, ICU hospitalization time was (8.25 ± 1.13) d, and the 28-d mortality rate was 4.67%, which were significantly lower than those of the SG group [(7.96 ± 2.12) d, (10.15 ± 1.28) d, 11.33%] (P < 0.05; Figure 3).

DISCUSSION

Sepsis is a serious infection, which can cause host response disorders and lead to organ dysfunction. Without timely and effective treatment, severe sepsis and septic shock can develop, which are associated with high mortality[14]. The sepsis inflammatory response generates many inflammatory mediators through a cascade effect, causing infiltration of human tissues and organs, resulting in functional failure and shock to multiple organs, or death[15]. Optimal intervention is crucial to prevent organ dysfunction and improve patient quality of life and prognosis. Studies have shown[16] that cluster management can promote prognosis and improve the quality of life of critically ill patients, and psychological intervention with cocoa can alleviate anxiety and depression in patients with sepsis, effectively preventing the occurrence of post-traumatic stress disorder, and improving the long-term prognosis of patients. Therefore, to understand the emotional state, sleep status, and post-traumatic growth level of patients with sepsis, we explored the effect of a 1-h

Table 1 Comparison of baseline data [*n* (%), (mean ± SD)]

Index	CG (*n* = 150)	SG (*n* = 150)	χ^2/t value	*P* value
Sex			0.054	0.817
Male	81 (54.00)	79 (52.67)		
Female	69 (46.00)	71 (47.33)		
Age (yr)	58.27 ± 4.36	58.33 ± 4.51	-0.130	0.897
BMI (kg/m^2)	25.33 ± 1.57	25.29 ± 1.47	0.172	0.864
Infection type			0.272	0.965
Abdominal infection	39 (26.00)	42 (28.00)		
Respiratory tract infection	60 (40.00)	58 (38.67)		
Bacteremia	32 (21.33)	33 (22.00)		
Miscellaneous	19 (12.67)	17 (11.33)		

CG: Combined group; SG: Simple group; BMI: Body mass index.

Table 2 Comparison of Pittsburgh Sleep Quality Index scores (mean ± SD)

Dimensional	CG (*n* = 150)				SG (*n* = 150)			
	T0	T1	*t* value	*P* value	T0	T1	*t* value	*P* value
Time to fall asleep	2.72 ± 0.47	1.19 ± 0.53[c]	0.058	< 0.001	2.72 ± 0.50	1.75 ± 0.56	15.722	< 0.001
Sleep time	2.65 ± 0.59	1.12 ± 0.38[c]	26.512	< 0.001	2.68 ± 0.47	1.83 ± 0.37	17.309	< 0.001
Sleep quality	1.97 ± 0.37	1.09 ± 0.33[c]	22.165	< 0.001	1.94 ± 0.31	1.70 ± 0.46	5.292	< 0.001
Sleep efficiency	2.38 ± 0.53	1.22 ± 0.50[c]	19.259	< 0.001	2.45 ± 0.51	1.78 ± 0.42	12.494	< 0.001
Hypnotic drugs	2.38 ± 0.48	1.34 ± 0.48[c]	18.717	< 0.001	2.38 ± 0.48	1.84 ± 0.37	10.836	< 0.001
Daytime dysfunction	2.17 ± 0.38	1.35 ± 0.48[c]	16.416	< 0.001	2.17 ± 0.38	1.66 ± 0.48	10.334	< 0.001
Dyssomnia	2.53 ± 0.50	1.23 ± 0.42[c]	24.126	< 0.001	2.52 ± 0.50	1.65 ± 0.48	15.332	< 0.001
Total score	16.80 ± 1.23	8.545 ± 1.18[c]	59.284	< 0.001	16.87 ± 1.22	12.22 ± 1.24	32.709	< 0.001

[c]*P* < 0.001 *vs* SG.
CG: Combined group; SG: Simple group; T0: Before intervention; T1: After intervention.

Table 3 Comparison of Post Traumatic Growth Inventory scores between the combined group and simple group (mean ± SD)

Dimension	CG (*n* = 150)				SG (*n* = 150)			
	T0	T1	*t* value	*P* value	T0	T1	*t* value	*P* value
Appreciation of life	15.33 ± 2.47	21.36 ± 3.28[c]	-17.984	< 0.001	15.28 ± 2.53	17.55 ± 2.86	-7.272	< 0.001
New possibilities	8.54 ± 1.26	10.37 ± 1.75[c]	-10.401	< 0.001	8.62 ± 1.18	9.13 ± 1.42	-3.409	< 0.001
Mental changes	4.76 ± 1.14	6.15 ± 1.28[c]	-9.966	< 0.001	4.69 ± 1.16	5.12 ± 1.09	-3.282	< 0.001
Relations with others	16.27 ± 2.52	21.48 ± 3.35[c]	-15.204	< 0.001	16.33 ± 2.48	18.67 ± 2.18	-8.680	< 0.001
Individual force	14.39 ± 2.25	17.65 ± 2.84[c]	1-0.991	< 0.001	14.41 ± 2.27	15.72 ± 2.53	-4.707	< 0.001
Total score	59.30 ± 4.51	77.01 ± 5.71[c]	-29.802	0.001	59.34 ± 4.47	66.19 ± 4.72	-12.913	< 0.001

[c]*P* < 0.001 *vs* SG.
CG: Combined group; SG: Simple group; T0: Before intervention; T1: After intervention.

Table 4 Comparison of MOS36-item short-form health survey scores (mean ± SD)

Dimension	CG (*n* = 150)				SG (*n* = 150)			
	T0	T1	*t* value	*P* value	T0	T1	*t* value	*P* value
Mental health	67.59 ± 6.73	81.13 ± 7.94[c]	-15.932	< 0.001	68.15 ± 6.82	73.59 ± 7.24	-6.706	< 0.001
General health status	61.28 ± 6.35	85.21 ± 7.65[c]	-29.446	< 0.001	61.57 ± 6.23	72.13 ± 7.08	-13.728	< 0.001
Physiological functions	59.37 ± 5.86	78.42 ± 7.53[c]	-24.444	< 0.001	58.76 ± 5.94	64.53 ± 6.17	-8.247	< 0.001
Emotional function	53.45 ± 5.72	81.22 ± 7.52[c]	-36.013	< 0.001	52.33 ± 5.68	74.28 ± 7.06	-29.664	< 0.001
Body pain	62.57 ± 6.18	82.54 ± 7.93[c]	-24.334	< 0.001	62.49 ± 6.20	73.45 ± 7.18	-14.145	< 0.001
Social function	63.54 ± 6.20	85.70 ± 7.01[c]	-28.986	< 0.001	62.87 ± 6.25	74.33 ± 6.95	-15.007	< 0.001
Energy	68.93 ± 6.84	84.51 ± 7.55[c]	-18.725	< 0.001	68.79 ± 6.86	75.62 ± 7.34	-8.317	< 0.001
Physiologic function	80.82 ± 7.58	93.82 ± 3.69[c]	-18.890	< 0.001	80.98 ± 7.68	86.15 ± 7.87	-5.753	< 0.001

[c]*P* < 0.001 *vs* SG.

CG: Combined group; SG: Simple group; T0: Before intervention; T1: After intervention.

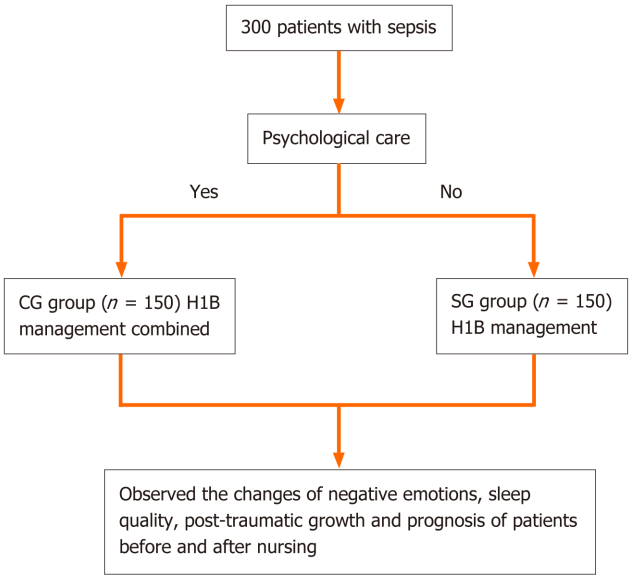

Figure 1 Number of patients included, flow chart of analysis method. CG: Combined group; SG: Simple group.

cluster management combined with psychological intervention in patients with sepsis. Cluster management nursing is an emerging clinical nursing model using various evidence-based intervention methods to improve nursing outcomes. Compared with the traditional model, cluster management has the characteristics of scientific validity, feasibility, and high efficiency, which reduces the blindness of clinical nursing and makes it more easily accepted by patients[17,18]. In this study, the HAMA and HAMD scores of patients in the CG group were significantly lower than those of the patients in the SG group, suggesting that 1-h cluster management combined with psychological intervention can effectively alleviate the negative mood of patients with sepsis. In this study, detection of lactic acid level was completed sequentially through H1B management intervention; blood culture specimens were obtained; and antibiotics, fluid resuscitation, and vasopressor therapy were administered. H1B management intervention also promotes knowledge about health and sepsis among patients, thereby improving their disease awareness levels. Furthermore, patient medication management and anti-infection care should be optimized to eliminate concerns about the disease. Treatment and nursing care were combined with psychological intervention to help patients face their disease and cooperate with the intervention, and with counseling to relieve anxiety and depression[19].

Our study also found that at T1, the PSQI scores of the CG group were markedly lower than those of the SG group, suggesting that H1B management combined with psychological intervention can improve sleep quality in patients admitted to the ICU with sepsis. This finding may be explained by the fact that negative emotions and respiratory dysfunction are the main reasons affecting sleep quality[20]. The combination of cluster management and psychological intervention improves patient understanding of the disease, and anti-infective drugs are prepared in advance to provide timely and effective treatment[21]. Careful monitoring of the patient's condition and timely and effective management of hypoxia, hypotension, and poor systemic perfusion should also be performed. In addition to the psychological inter-

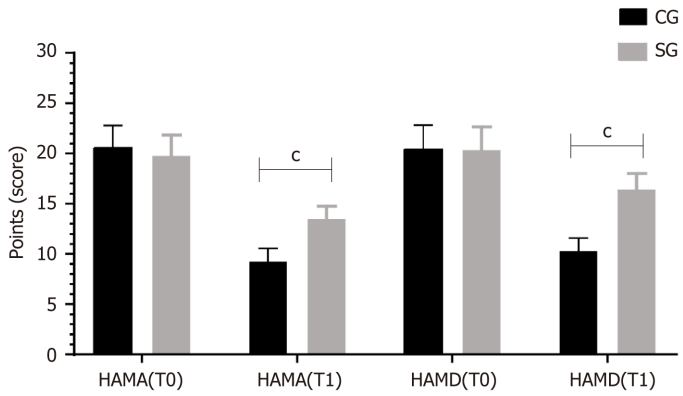

Figure 2 Comparison of Hamilton Anxiety scale and Hamilton Depression scale scores between the two groups. $^{c}P < 0.001$. HAMA: Hamilton Anxiety scale; HAMD: Hamilton Depression scale; CG: Combined group; SG: Simple group; T0: Before intervention; T1: After intervention.

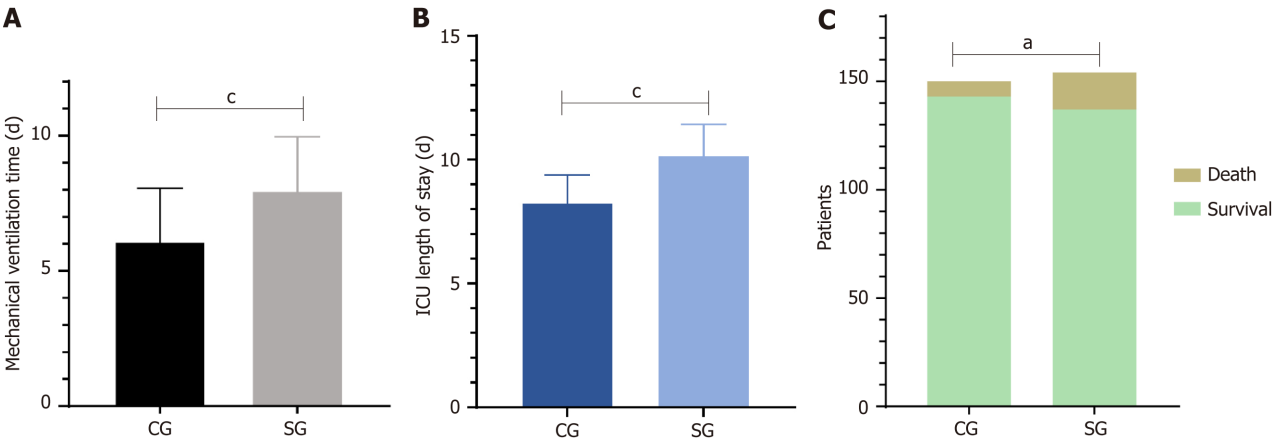

Figure 3 Prognosis. A: Duration of mechanical ventilation; B: Duration of intensive care unit hospitalization; C: 28-d fatality rate. $^{a}P < 0.05$, $^{c}P < 0.001$. CG: Combined group; SG: Simple group.

vention, explaining successful cases of treatment, strengthening patient confidence, optimizing communication with patients, creating a comfortable ward environment, keeping patients happy, and improving negative emotions are also paramount[22]. Furthermore, intervention to reduce oxygen consumption and relieve shortness of breath is also important to improve sleep quality. In this study, at T1, the PTGI scores of the CG were markedly higher than those of the SG, indicating that H1B management combined with psychological intervention can accelerate the post-traumatic growth of patients with sepsis. Research has shown[23] that anxiety and depression in patients with cancer are closely related to post-traumatic growth; that is, lower levels of anxiety and depression promote post-traumatic growth in patients. Therefore, the post-traumatic growth of patients with sepsis may be related to cluster management and psychological interventions to improve negative emotions. Post-traumatic growth is closely related to coping styles and social support. Psychological nursing intervention can regulate the negative emotions of patients and improve patient understanding of the disease, providing them with the knowledge and confidence to cope with and overcome the disease[24].

By analyzing the quality of life of patients based on their health status, our study also found that at T1, the scores of each dimension of the SF-36 scale in the CG group were higher than those in the SG group, indicating that H1B management with psychological intervention can increase the quality of life of patients with sepsis. Quality of life involves mental, physiological, psychological, and social aspects and is one of the new criteria for evaluating the prognosis of critically ill patients[25,26]. In addition, negative emotions and post-traumatic growth also have a considerable influence on quality of life. Psychological interventions can adjust the negative emotions of patients, eliminate fear of the disease, increase adaptability to the disease, improve psychological resilience, and promote post-traumatic growth, thereby improving quality of life. Prognostic analysis of the two groups showed that the mechanical ventilation time, ICU stay time and 28-d mortality of the CG were significantly lower than those of the SG. This indicates that professional skills, professional knowledge, and the personnel ratio of medical staff also have an impact on patient prognosis[27]. H1B management combined with psychological nursing intervention for patients with sepsis reduced the length of hospital stay and mechanical ventilation time and effectively improved patient prognosis[28]. Some limitations of this study should be acknowledged. First, due to time and sample size limitations, all the selected participants were admitted to a single hospital. Further multicenter studies with a larger sample size should conducted to validate these results.

CONCLUSION

In summary, H1B management combined with psychological nursing intervention can effectively alleviate negative emotions in patients with sepsis, increase sleep quality, and enhance post-traumatic growth and quality of life.

ARTICLE HIGHLIGHTS

Research background

Cluster management has been rapidly developing and increasingly recognized in the clinical care of critically ill patients. Psychological interventions have considerable impact on the mood, sleep, and quality of life of critically ill patients. Therefore, we analyzed the influence of one-hour bundle (H1B) management combined with psychological interventions in patients with sepsis.

Research motivation

Severe cases of sepsis are often accompanied by mood and sleep disorders. We postulate that H1B management combined with psychological interventions may have an important impact on patients with sepsis.

Research objectives

The purpose of this research was to discuss the effects of H1B management combined with psychological intervention on negative emotions, sleep quality, and post-traumatic growth in patients with sepsis and to provide a reference for clinical treatment.

Research methods

Patients were divided into a group undergoing H1B management only (simple group, SG) and a group undergoing H1B management combined with psychological intervention (combination group, CG). The clinical data were retrospectively analyzed to compare the influence of negative emotions, sleep quality, post-traumatic growth, and prognosis of patients in the two groups before (T0) and after (T1) intervention.

Research results

At T1, the Hamilton Anxiety scale and Hamilton Depression scale scores of the CG group were significantly lower than those of the SG group. The Pittsburgh Sleep Quality Index score of the CG group was significantly lower than that of the SG group. The Post Traumatic Growth Inventory score of the CG group was significantly higher than that of the SG group. The MOS36-item short-form health survey scores of the CG group were higher than those of the SG group. The mechanical ventilation time, intensive care unit stay time, and 28-d mortality of the CG group were lower than those of the SG group. These differences were significant ($P < 0.05$).

Research conclusions

H1B management combined with psychological nursing interventions can effectively alleviate the adverse emotions of patients with sepsis, increase quality of sleep, and enhance the level of post-traumatic growth and quality of life.

Research perspectives

Future research should further explore the impact of H1B management combined with psychological intervention on patients with sepsis from the perspective of negative emotions, sleep quality, post-traumatic growth, and prognosis. These findings may provide a reference for nursing management and treatment strategies for patients with sepsis.

FOOTNOTES

Author contributions: Xia M designed and performed the research; Li LM designed the research and supervised the report; Dong GY, Zhu SC and Xing HM collected and analyzed data; all authors approved the final manuscript.

Supported by Key R&D and Promotion Special Project (Science and Technology Research) in Henan Province in 2023, No. 232102310089.

Institutional review board statement: This study was reviewed and approved by the Henan Provincial People's Hospital Institutional Review Board.

Informed consent statement: Because of the retrospective nature of the study and the anonymization of data, applied for application for exemption from informed consent form.

Conflict-of-interest statement: The authors declare no conflict of interest.

Data sharing statement: The clinical data used in this study can be obtained from the corresponding author upon reasonable request.

Country/Territory of origin: China

ORCID number: Ming Xia 0009-0005-2183-5917; Guang-Yan Dong 0009-0001-3536-7027; Shi-Chao Zhu 0009-0007-3861-8024; Huan-Min Xing 0009-0007-1831-6926; Li-Ming Li 0009-0004-9020-8004.

S-Editor: Gong ZM
L-Editor: A
P-Editor: Zhang YL

REFERENCES

1 **Fernando SM**, Rochwerg B, Seely AJE. Clinical implications of the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *CMAJ* 2018; **190**: E1058-E1059 [PMID: 30201611 DOI: 10.1503/cmaj.170149]
2 **Komorowski M**, Celi LA, Badawi O, Gordon AC, Faisal AA. The Artificial Intelligence Clinician learns optimal treatment strategies for sepsis in intensive care. *Nat Med* 2018; **24**: 1716-1720 [PMID: 30349085 DOI: 10.1038/s41591-018-0213-5]
3 **Fleischmann C**, Scherag A, Adhikari NK, Hartog CS, Tsaganos T, Schlattmann P, Angus DC, Reinhart K; International Forum of Acute Care Trialists. Assessment of Global Incidence and Mortality of Hospital-treated Sepsis. Current Estimates and Limitations. *Am J Respir Crit Care Med* 2016; **193**: 259-272 [PMID: 26414292 DOI: 10.1164/rccm.201504-0781OC]
4 **Pei F**, Yao RQ, Ren C, Bahrami S, Billiar TR, Chaudry IH, Chen DC, Chen XL, Cui N, Fang XM, Kang Y, Li WQ, Li WX, Liang HP, Lin HY, Liu KX, Lu B, Lu ZQ, Maegele M, Peng TQ, Shang Y, Su L, Sun BW, Wang CS, Wang J, Wang JH, Wang P, Xie JF, Xie LX, Zhang LN, Zingarelli B, Guan XD, Wu JF, Yao YM; Shock and Sepsis Society of Chinese Research Hospital Association; China Critical Care Immunotherapy Research Group; International Federation of the Shock Societies (IFSS). Expert consensus on the monitoring and treatment of sepsis-induced immunosuppression. *Mil Med Res* 2022; **9**: 74 [PMID: 36567402 DOI: 10.1186/s40779-022-00430-y]
5 **Shen G**, He Y, Ni J, Jiang L, Xia Z, Liu H, Pan S, Wang H, Hu W, Li X. Effects of comprehensive nursing on negative emotion and prognosis of patients with sepsis. *Am J Transl Res* 2021; **13**: 8221-8227 [PMID: 34377309]
6 **Yang H**, Wang W, Li Y, Tian L, Jing M, Hu Y. [Application effect of 1-hour bundle in the treatment of patients with sepsis]. *Zhonghua Wei Zhong Bing Ji Jiu Yi Xue* 2019; **31**: 1087-1090 [PMID: 31657330 DOI: 10.3760/cma.j.issn.2095-4352.2019.09.006]
7 **Jorgensen AL**. Nurse Influence in Meeting Compliance With the Centers for Medicare and Medicaid Services Quality Measure: Early Management Bundle, Severe Sepsis/Septic Shock (SEP-1). *Dimens Crit Care Nurs* 2019; **38**: 70-82 [PMID: 30702476 DOI: 10.1097/DCC.0000000000000340]
8 **Esposito S**, De Simone G, Boccia G, De Caro F, Pagliano P. Sepsis and septic shock: New definitions, new diagnostic and therapeutic approaches. *J Glob Antimicrob Resist* 2017; **10**: 204-212 [PMID: 28743646 DOI: 10.1016/j.jgar.2017.06.013]
9 **Singer M**, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, Bellomo R, Bernard GR, Chiche JD, Coopersmith CM, Hotchkiss RS, Levy MM, Marshall JC, Martin GS, Opal SM, Rubenfeld GD, van der Poll T, Vincent JL, Angus DC. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *JAMA* 2016; **315**: 801-810 [PMID: 26903338 DOI: 10.1001/jama.2016.0287]
10 **Zhang S**, Chen H, Zhang M, Sun X, Liu X. Reduction of depression symptoms in laryngeal cancer patients receiving psychology services. *Am J Transl Res* 2020; **12**: 6637-6645 [PMID: 33194060]
11 **Zhang C**, Zhang H, Zhao M, Li Z, Cook CE, Buysse DJ, Zhao Y, Yao Y. Reliability, Validity, and Factor Structure of Pittsburgh Sleep Quality Index in Community-Based Centenarians. *Front Psychiatry* 2020; **11**: 573530 [PMID: 33110414 DOI: 10.3389/fpsyt.2020.573530]
12 **Cormio C**, Muzzatti B, Romito F, Mattioli V, Annunziata MA. Posttraumatic growth and cancer: a study 5 years after treatment end. *Support Care Cancer* 2017; **25**: 1087-1096 [PMID: 28013416 DOI: 10.1007/s00520-016-3496-4]
13 **Ware JK**, Owens BD, Akelman MR, Karamchedu NP, Fadale PD, Hulstyn MJ, Shalvoy RM, Badger GJ, Fleming BC. Preoperative KOOS and SF-36 Scores Are Associated With the Development of Symptomatic Knee Osteoarthritis at 7 Years After Anterior Cruciate Ligament Reconstruction. *Am J Sports Med* 2018; **46**: 869-875 [PMID: 29401408 DOI: 10.1177/0363546517751661]
14 **Marchand EP**, Villemure JG, Rubin J, Robitaille Y, Ethier R. Solitary osteochondroma of the thoracic spine presenting as spinal cord compression. A case report. *Spine (Phila Pa 1976)* 1986; **11**: 1033-1035 [PMID: 3576338 DOI: 10.1164/rccm.202112-2743OC]
15 **Font MD**, Thyagarajan B, Khanna AK. Sepsis and Septic Shock - Basics of diagnosis, pathophysiology and clinical decision making. *Med Clin North Am* 2020; **104**: 573-585 [PMID: 32505253 DOI: 10.1016/j.mcna.2020.02.011]
16 **Sanghvi S**, Podlog M, Aycock RD. Does the Severe Sepsis and Septic Shock Early Management Bundle (SEP-1) Improve Survival in Septic Adults? *Ann Emerg Med* 2019; **73**: 363-365 [PMID: 30482516 DOI: 10.1016/j.annemergmed.2018.09.009]
17 **Chen X**, Deng C, Tan G, Zheng H, Yang T, Zhang X. Application efficacy of bundled nursing management in care of elderly patients with pressure ulcers. *Am J Transl Res* 2021; **13**: 6738-6744 [PMID: 34306420]
18 **Pun BT**, Balas MC, Barnes-Daly MA, Thompson JL, Aldrich JM, Barr J, Byrum D, Carson SS, Devlin JW, Engel HJ, Esbrook CL, Hargett KD, Harmon L, Hielsberg C, Jackson JC, Kelly TL, Kumar V, Millner L, Morse A, Perme CS, Posa PJ, Puntillo KA, Schweickert WD, Stollings JL, Tan A, D'Agostino McGowan L, Ely EW. Caring for Critically Ill Patients with the ABCDEF Bundle: Results of the ICU Liberation Collaborative in Over 15,000 Adults. *Crit Care Med* 2019; **47**: 3-14 [PMID: 30339549 DOI: 10.1097/CCM.0000000000003482]
19 **Uffen JW**, Oosterheert JJ, Schweitzer VA, Thursky K, Kaasjager HAH, Ekkelenkamp MB. Interventions for rapid recognition and treatment of sepsis in the emergency department: a narrative review. *Clin Microbiol Infect* 2021; **27**: 192-203 [PMID: 32120030 DOI: 10.1016/j.cmi.2020.02.022]
20 **Simor P**, Harsányi A, Csigó K, Miklós G, Lázár AS, Demeter G. Eveningness is associated with poor sleep quality and negative affect in

obsessive-compulsive disorder. *J Behav Addict* 2018; **7**: 10-20 [PMID: 29415552 DOI: 10.1556/2006.7.2018.07]

21 **Odawara K**. [Biochemical study of diphenylhydantoin gingival hyperplasia--effect of DPH on intermolecular cross-links of rat gingival collagen]. *Kanagawa Shigaku* 1987; **21**: 519-528 [PMID: 3504534 DOI: 10.1016/j.jhin.2022.01.004]

22 **Ding X**, Yao J. Peer Education Intervention on Adolescents' Anxiety, Depression, and Sleep Disorder during the COVID-19 Pandemic. *Psychiatr Danub* 2020; **32**: 527-535 [PMID: 33370763 DOI: 10.24869/psyd.2020.527]

23 **Gori A**, Topino E, Sette A, Cramer H. Pathways to post-traumatic growth in cancer patients: moderated mediation and single mediation analyses with resilience, personality, and coping strategies. *J Affect Disord* 2021; **279**: 692-700 [PMID: 33190121 DOI: 10.1016/j.jad.2020.10.044]

24 **Shi G**, Shi T, Liu Y, Cai Y. Relationships between dyadic coping, intimate relationship and post-traumatic growth in patients with breast cancer: A cross-sectional study. *J Adv Nurs* 2021; **77**: 4733-4742 [PMID: 34227131 DOI: 10.1111/jan.14946]

25 **Nannan Panday RS**, Minderhoud TC, Chantalou DS, Alam N, Nanayakkara PWB. Health related quality of life in sepsis survivors from the Prehospital Antibiotics Against Sepsis (PHANTASi) trial. *PLoS One* 2019; **14**: e0222450 [PMID: 31574094 DOI: 10.1371/journal.pone.0222450]

26 **Rababa M**, Bani Hamad D, Hayajneh AA. Sepsis assessment and management in critically Ill adults: A systematic review. *PLoS One* 2022; **17**: e0270711 [PMID: 35776738 DOI: 10.1371/journal.pone.0270711]

27 **Lasater KB**, Sloane DM, McHugh MD, Cimiotti JP, Riman KA, Martin B, Alexander M, Aiken LH. Evaluation of hospital nurse-to-patient staffing ratios and sepsis bundles on patient outcomes. *Am J Infect Control* 2021; **49**: 868-873 [PMID: 33309843 DOI: 10.1016/j.ajic.2020.12.002]

28 **Seymour CW**, Gesten F, Prescott HC, Friedrich ME, Iwashyna TJ, Phillips GS, Lemeshow S, Osborn T, Terry KM, Levy MM. Time to Treatment and Mortality during Mandated Emergency Care for Sepsis. *N Engl J Med* 2017; **376**: 2235-2244 [PMID: 28528569 DOI: 10.1056/NEJMoa1703058]

World Journal of Psychiatry

Submit a Manuscript: https://www.f6publishing.com

World J Psychiatry 2024 February 19; 14(2): 276-286

DOI: 10.5498/wjp.v14.i2.276

ISSN 2220-3206 (online)

ORIGINAL ARTICLE

Retrospective Study

Neuropathological characteristics of abnormal white matter functional signaling in adolescents with major depression

Xin-Lin Huang, Ju Gao, Yong-Ming Wang, Feng Zhu, Jing Qin, Qian-Nan Yao, Xiao-Bin Zhang, Hong-Yan Sun

Specialty type: Psychiatry

Provenance and peer review: Unsolicited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

Grade A (Excellent): 0
Grade B (Very good): B
Grade C (Good): 0
Grade D (Fair): 0
Grade E (Poor): 0

P-Reviewer: Bernstein HG, Germany

Received: November 23, 2023
Peer-review started: November 23, 2023
First decision: December 6, 2023
Revised: December 13, 2023
Accepted: January 8, 2024
Article in press: January 8, 2024
Published online: February 19, 2024

Xin-Lin Huang, Qian-Nan Yao, Imaging and Nuclear Medicine, Jiamusi University, Jiamusi 154000, Heilongjiang Province, China

Ju Gao, Feng Zhu, Xiao-Bin Zhang, Department of Psychiatry, The Affiliated Guangji Hospital of Soochow University, Suzhou 215137, Jiangsu Province, China

Yong-Ming Wang, School of Biology & Basic Medical Sciences, Medical College of Soochow University, Suzhou 215137, Jiangsu Province, China

Jing Qin, Department of Radiology, Shanghai Anting Hospital, Shanghai 20000, China

Hong-Yan Sun, Department of Radiology, The Affiliated Guangji Hospital of Soochow University, Suzhou 215137, Jiangsu Province, China

Corresponding author: Hong-Yan Sun, MD, PhD, Chief Doctor, Department of Radiology, The Affiliated Guangji Hospital of Soochow University, No. 11 Guangqian Road, Suzhou 215137, Jiangsu Province, China. hoya12@126.com

Abstract

BACKGROUND

Major depression disorder (MDD) constitutes a significant mental health concern. Epidemiological surveys indicate that the lifetime prevalence of depression in adolescents is much higher than that in adults, with a corresponding increased risk of suicide. In studying brain dysfunction associated with MDD in adolescents, research on brain white matter (WM) is sparse. Some researchers even mistakenly regard the signals generated by the WM as noise points. In fact, studies have shown that WM exhibits similar blood oxygen level-dependent signal fluctuations. The alterations in WM signals and their relationship with disease severity in adolescents with MDD remain unclear.

AIM

To explore potential abnormalities in WM functional signals in adolescents with MDD.

METHODS

This study involved 48 adolescent patients with MDD and 31 healthy controls (HC). All participants were assessed using the Patient Health Questionnaire-9 Scale and the mini international neuropsychiatric interview (MINI) suicide

inventory. In addition, a Siemens Skyra 3.0T magnetic resonance scanner was used to obtain the subjects' image data. The DPABI software was utilized to calculate the WM signal of the fractional amplitude of low frequency fluctuations (fALFF) and regional homogeneity, followed by a two-sample *t*-test between the MDD and HC groups. Independent component analysis (ICA) was also used to evaluate the WM functional signal. Pearson's correlation was performed to assess the relationship between statistical test results and clinical scales.

RESULTS

Compared to HC, individuals with MDD demonstrated a decrease in the fALFF of WM in the corpus callosum body, left posterior limb of the internal capsule, right superior corona radiata, and bilateral posterior corona radiata [$P < 0.001$, family-wise error (FWE) voxel correction]. The regional homogeneity of WM increased in the right posterior limb of internal capsule and left superior corona radiata, and decreased in the left superior longitudinal fasciculus ($P < 0.001$, FWE voxel correction). The ICA results of WM overlapped with those of regional homogeneity. The fALFF of WM signal in the left posterior limb of the internal capsule was negatively correlated with the MINI suicide scale ($P = 0.026$, $r = -0.32$), and the right posterior corona radiata was also negatively correlated with the MINI suicide scale ($P = 0.047$, $r = -0.288$).

CONCLUSION

Adolescents with MDD involves changes in WM functional signals, and these differences in brain regions may increase the risk of suicide.

Key Words: White matter; Regional homogeneity; The fractional amplitude of low-frequency fluctuations; Independent component analysis; Adolescents; Major depression disorders

Core Tip: This groundbreaking study investigates white matter (WM) functional signals in adolescents with major depressive disorder (MDD), an area often overlooked in research. Utilizing advanced imaging techniques, the study identifies specific abnormalities in WM signals, revealing decreased fractional amplitude of low frequency fluctuations in key regions and altered regional homogeneity and independent component analysis patterns. Notably, these changes correlate with suicidality scales, indicating a potential link between WM anomalies and severity of depression. The study pioneers a crucial shift in understanding MDD's neuropathogenesis, offering novel insights and support for future research and predictive measures.

Citation: Huang XL, Gao J, Wang YM, Zhu F, Qin J, Yao QN, Zhang XB, Sun HY. Neuropathological characteristics of abnormal white matter functional signaling in adolescents with major depression. *World J Psychiatry* 2024; 14(2): 276-286
URL: https://www.wjgnet.com/2220-3206/full/v14/i2/276.htm
DOI: https://dx.doi.org/10.5498/wjp.v14.i2.276

INTRODUCTION

Major depressive disorder (MDD) is a widespread psychiatric condition across the globe, with an estimated lifetime prevalence rate of approximately 11% among adolescents[1,2]. It has been reported that over half of adolescent suicide victims had a depressive disorder[3]. MDD in adolescents is associated with an increased risk of suicide, and the disorder often persists into adulthood[4]. Therefore, the increasing incidence of depression among adolescents requires urgent attention[5]. The recognition and treatment of MDD in adolescence are crucial; however, our current grasp of the physiological and pathological underpinnings of the condition remains incomplete.

Functional magnetic resonance imaging (fMRI) is a non-invasive technique, and it can be used to indirectly measure neuronal activity *via* the blood oxygenation level-dependent (BOLD) signal[6]. In recent years, the development and progress of magnetic resonance imaging (MRI) technology have provided an opportunity to study the pathophysiology of MDD using various resting state fMRI (rs-fMRI) techniques. These techniques have been extensively utilized in the exploration of the physiological and pathological foundations of the brain in mental disorders. The changes in the resting state of gray matter (GM) found in most studies are often used as biomarkers for neuropsychiatric disorders[7-9], while white matter (WM) tends to be ignored[10,11], even though the volume of WM in the human brain accounts for approximately 40%-45%[12].

To date, various approaches are used to analyze spontaneous BOLD signals, such as the amplitude of low frequency fluctuations (ALFF), the fractional ALFF (fALFF), regional homogeneity (ReHo), and independent component analysis (ICA)[13]. The fALFF[14] is a metric believed to capture spontaneous neural activity and has been demonstrated to correlate with regional brain glucose metabolism[15-17], which effectively mitigates physiological noise when compared to ALFF[14]. ReHo, a data-driven approach, implies that the time series of spatially adjacent voxels exhibit greater temporal similarity when the brain region is engaged in a specific condition[18]. ICA is also a data-driven method, it can

decompose fMRI data into spatially independent and functionally connected brain networks[19]. ReHo and ICA can acquire a greater amount of information than methods driven by models[18,20]. Using these data analysis methods, Liu *et al*[21] discovered the alterations in ReHo and ALFF in the precentral gyrus, postcentral gyrus, and paracentral gyrus in MDD[21]. In addition, a meta-analysis found a correlation between amygdala activity and depression[22]. These findings may indicate the pathological and physiological processes associated with MDD.

Recent studies have shown the presence of functional brain activity related to neuronal activity in the WM, including connectivity and interconnection functions[23,24]. In task related studies, activation of brain regions can be detected in the inner capsule and corpus callosum (CC)[25,26]. Additional studies showed that fMRI activity within particular WM pathways is remarkably consistent during the resting state, and indicated that these WM signals exhibit features reminiscent of hemodynamic (BOLD) alterations linked to neuronal activity[27,28]. Furthermore, a recent study employing ICA and hierarchical clustering revealed the presence of clusters of correlated activity within the WM[29]. These findings reveal that WM may play a crucial role in resting states. We hope to provide more information in order to understand the underlying pathological mechanisms of adolescent severe depression by revealing the fluctuation characteristics of WM functional signals.

Therefore, we decided to use the GM analysis method to explore changes in WM, using a combination of multiple features, including fALFF, ReHo, and ICA. These three analytical methods present a progressive relationship layer by layer, from individual, to local, and finally to component networks. The combination of multiple analytical methods is used to explore the functional differences of WM in adolescents with MDD. This method is expected to reveal the characteristics and potential biological mechanisms of abnormal brain activity in adolescents with MDD during the resting state, filling the current incomplete understanding of the physiological and pathological basis of the disease. From this study, we may not only better understand the pathogenesis of MDD in adolescents, but also provide more targeted methods for future diagnosis and treatment, thereby more effectively addressing this global health problem.

MATERIALS AND METHODS

Participants

A total of 84 subjects, including 51 adolescents with MDD and 33 healthy controls (HC) matched by age, gender, education and right-handedness were initially recruited from Suzhou Guangji Hospital. Using the mini international neuropsychiatric interview (MINI), patients were diagnosed by two trained psychiatrists above the attending level who conducted a structured interview. The inclusion criteria were: (1) The patients had not received systematic medication treatment prior to the MRI scan; (2) Patient Health Questionnaire-9 (PHQ-9) scores ≥ 20; (3) Right-handed; (4) Met the criteria of the Diagnostic and Statistical Manual of Mental Disorders, 5th edition; and (5) Aged 11 to 18 years. The exclusion criteria were: (1) Contrain-dications to MRI; (2) Any other psychiatric disorders such as bipolar disorder and schizophrenia; (3) Individuals with organic brain diseases, as identified by imaging; and (4) 32-item Hypomania Checklist (HCL-32) scores < 14.

This study was approved by the Ethics Committee of Suzhou Guangji Hospital, and each subject signed a written informed consent form. For participants under age 18, at least one legal guardian signed an informed consent form on their behalf.

Clinical assessments

Two attending psychiatrists with specialized training assessed the clinical symptoms of the participants and performed a reliability assessment. The PHQ-9 is a reliable and valid screening tool for depression[30,31], derived from the depression section of the Patient Health Questionnaire developed by Spitzer *et al*[32]. All participants completed the MINI suicidality subscale (MINISS), a user-friendly and highly accurate tool for predicting suicide risk[33] and the HCL-32, a self-assessment tool for hypomanic symptoms[34].

MRI acquisition

All participants' image data were obtained on a 3.0T Siemens Skyra scanner at Suzhou Guangji Hospital, equipped with a head/neck 20 channel coil. The scanning parameters of rs-fMRI are as follows: Repetition time = 2000 ms, echo time = 30 ms, slice thickness = 3.5 mm, 32 slices, slice gap = 0.875 mm, filed of view = 224 mm × 224 mm, flip angle = 90°, matrix size = 64 voxels × 64 voxels, acquisition time = 8.04 min. During the scan procedure, each subject was asked to lie flat in the machine, and close their eyes but not to fall asleep. While the subjects were being scanned, a sponge pad was placed on each person's head to prevent head movement and obtain clear images.

Data preprocessing

The MRI data of each subject were preprocessed by The Data Processing & Analysis for (Resting-state) Brain Imaging (DPABI)[35] and Statistical Parametric Map-ping (SPM12, http://www.fil.ion.ucl.ac.uk/spm) toolkit in MATLAB 2016b. This was based on the following steps: (1) Conversion data format from DICOM to NIFTI; (2) the first 10 time points were removed in order to stabilize the data; (3) slice timing and realignment of head motion correction (any participant whose head motion exceeded 2.0 mm or rotation exceeded 2.0° was excluded); (4) the T1 images were registered to functional images and segmentation into WM and GM and cerebrospinal fluid using the New Segment algorithm; (5) apply white mask to functional images; (6) normalize the functional image space to a standard space (Montreal Neurological Institute) using DARTEL, and resampled to a voxel size of 3 mm × 3 mm × 3 mm; and (7) extraction of individual-level WM 4D

images[36]. Five participants were excluded due to head motion > 2 mm or 2°. Finally, 48 MDD and 31 HC were included for further analysis in the current study.

fALFF and ReHo of WM calculation

Using a fast Fourier transform at each voxel, we computed the power of the BOLD signal of WM within the low-frequency range of 0.01–0.10 Hz and subsequently divided it by the entire frequency range to calculate the fALFF of WM [14].

The calculation of ReHo of WM values was performed as follows: Firstly, a low-pass filter (0.01–0.1 Hz) was used to mitigate the effects of high-frequency noise and low-frequency drift. Then, Kendall's Coefficient of Concordance[18], also known as the ReHo value, was utilized to assess the similarity between an individual voxel and its neighboring 27 voxels. Subsequently, in order to minimize individual variance, the ReHo value for each voxel was normalized by dividing it by the global mean ReHo value.

Extraction of WM-fMRI signals via ICA

On the basis of the aforementioned WM signal preprocessing, the preprocessed imaging data in each group was used to perform group ICA analysis using the fMRI toolbox (GIFT, version 3.0C, http://mialab.mrn.org/software/gift)[37]. Firstly, the pre-processed data's dimensionality was reduced, which was followed by application of the Infomax algorithm for spatial ICA on this data. In addition, component stability was attained by running 100 iterations in a software package called ICASSO[38]. A total of 6 components were estimated. Finally, we selected an interesting independent component that was related to the alteration of WM in MDD for further evaluation.

Statistical analysis

Differences in demographics between the two participant groups were assessed using SPSS version 29.0, sex differences were assessed using the chi-squared test, while other parameters were compared between the two groups using a two-sample t-test.

Voxel-based comparisons of fALFF and ReHo of WM maps between the patient and control groups were performed using the two-sample *t*-test in DPABI software with age, sex, education, head-motion included as covariates, and with a threshold setting at $P < 0.001$, FWE voxel correction for multiple comparisons. Additionally, sex, age, education, and head motion were controlled for during the analysis of ICA maps. The selected component of interest was then compared between the patient and control groups (FWE voxel correction for multiple comparisons).

Correlational analyses were performed to investigate the association between fALFF, ReHo values of MW in regions exhibiting group differences and clinical variables, including the PHQ-9 and the MINI Suicide Inventory.

RESULTS

Demographic and clinical variables

The demographic and clinical characteristics of the adolescents with MDD and HC are summarized in Table 1. There were no significant differences in sex, age, education and head-motion between the two groups.

fALFF and ReHo of WM alterations in adolescents with MDD

WM brain regions that exhibited disparities between the groups in the fALFF and ReHo analyses were identified and reported using the JHU-ICBM WM label atlas (provided by Wakana *et al*[39] and Hua *et al*[40] from the Laboratory of Brain Anatomical MRI at Johns Hopkins University)[39,40]. With regard to the fALFF calculation, patients with MDD showed decreased fALFF in the left posterior limb of the internal capsule (PLIC), posterior corona radiata (PCR), right PCR, superior corona radiata (SCR), and CC body ($P < 0.001$, FWE voxel correction for multiple comparisons). With regard to the ReHo computation, MDD patients displayed decreased ReHo values in the left superior longitudinal fasciculus (SLF), and higher ReHo values in the right PLIC and the left SCR ($P < 0.001$, FWE voxel correction for multiple comparisons). These results are presented in Table 2 and Figure 1.

Spatial ICA of rs-fMRI signals of the WM

We investigated the spatiotemporal patterns in rs-WM-fMRI data using ICA. Six spatially independent components were estimated and extracted from the time series of all WM voxels. Subsequent analyses of the 6 components showed decreased connectivity of the left SLF and higher connectivity of the right PLIC in MDD patients relative to HC ($P < 0.001$, FWE voxel correction for multiple comparisons; Table 2 and Figure 1).

Correlation analysis

The fALFF and ReHo values were extracted from WM regions that displayed significant differences between adolescents with MDD and the HC group, and correlation analyses between these region's values and clinical characteristics were conducted. We found there is no correlation between significant differential brain regions and PHQ-9 scales. A negative correlation between the fALFF values in the left PLIC and the MINI suicide scale ($P = 0.026$, r = -0.320; Figure 2A), as well as between the right PCR and the MINI suicide scale ($P = 0.047$, r = -0.288; Figure 2B).

Table 1 Demographic and clinical characteristics of the included subjects

	MDD (n = 48)	HC (n = 31)	χ^2/t	P value
Sex (male/female)	8/40	6/25	0.093	0.771
Age (yr)	14.15 (1.79)	14.71 (2.00)	-1.306	0.195
Education (yr)	8.44 (1.73)	8.87 (1.77)	-1.081	0.283
Head-motion	0.08 (0.04)	0.07 (0.03)	0.234	0.815
PHQ-9 scores	23.02 (2.39)	-	-	-
HCL-32 scores	6.94 (2.77)	-	-	-
MINISS scores	22.44 (9.61)	-	-	-

PHQ-9: Patient Health Questionnaire-9; HCL-32: The 32-item Hypomania Checklist; MINISS: The mini international neuropsychiatric interview suicidality subscale; MDD: Major depression disorders; HC: Healthy controls.

Table 2 Brain regions with significant differences in fractional amplitude of low frequency fluctuations, regional homogeneity and independent component analysis between adolescents with major depression disorders and healthy controls

Indices	Anatomical region	MNI coordinates, x, y, z	Peak intensity	Cluster size
fALFF of WM	Posterior limb of the internal capsule L	21, -18, 3	-6.12	27
	Posterior corona radiata R	-24, -39, 33	-5.57	36
	Body of the corpus callosum	12, 15, 30	-5.75	62
	Superior corona radiata R	-18, -21, 51	-5.44	71
	Posterior corona radiata L	24, -36, 39	-6.39	106
ReHo of WM	Posterior limb of the internal capsule R	27, 0, 18	5.40	60
	Superior corona radiata L	-27, 3, 39	4.55	23
	Superior longitudinal fasciculus L	-30, -39, 42	-5.33	18
	Superior longitudinal fasciculus L	-24, -24, 48	-4.76	14
ICA of WM	Posterior limb of the internal capsule R	27, -15, 12	4.30	26
	Superior longitudinal fasciculus L	-24, -24, 45	-5.80	25

The significance threshold was set at $P < 0.001$, FWE voxel correction for multiple comparisons. fALFF: Fractional amplitude of low frequency fluctuations; WM: White matter; ReHo: Regional homogeneity; ICA: Independent component analysis; L: Left; R: Right; MNI: Montreal neurological institute.

DISCUSSION

In this study, we demonstrated functional changes of WM by employing several distinct rs-fMRI techniques (ReHo, fALFF, and ICA), for the first time, on datasets from healthy subjects, and MDD patients. We found that adolescent patients with MDD showed significant differences in the CC body, left SLF, bilateral PLIC, PCR and SCR compared with the HC group. We also investigated the relationship between functional changes in regions of WM and the clinical features in patients with MDD. These results indicated that resting state functional metrics of WM can be valuable in investigating the pathophysiologic basis of MDD.

In the fALFF results, significant differences in MDD patients were mainly observed in the CC, PLIC, and corona radiata, when compared with the HC group. The CC is a dense bundle of nerve fibers that plays a crucial role in connecting different regions of the neocortex. It facilitates neural circuits involved in cognitive and emotional processing [41,42]. In addition, the CC body contains fibers connecting the cingulate cortex, insular cortex, and temporal cortex[43], these areas are often associated with depression[44-46]. A lower fALFF value indicates a decrease in WM integrity of the CC, which may hinder the interaction between the cerebral hemispheres and cause emotional processing disorders in depression. It is worth noting that in this study, we found that adolescent patients with severe depression experienced abnormal activation of brain regions in the posterior limbs of the inner capsule using various analytical methods. This may be because the core symptom of MDD is low mood, and the PLIC participates in the formation of a neural network by connecting structures such as the cerebral cortex and hypothalamus. Its subcortical area belongs to the frontal striatal

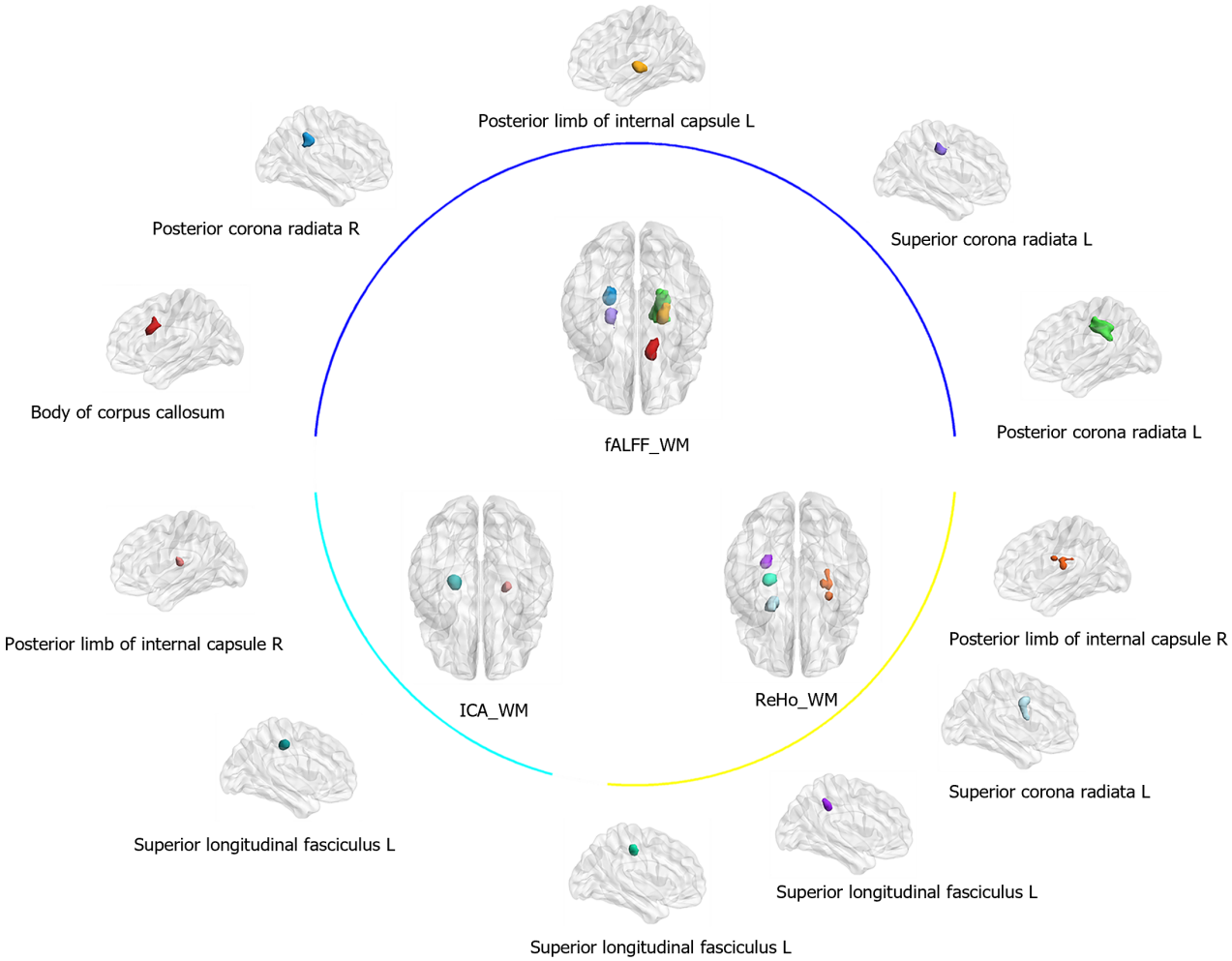

Figure 1 White matter regions with significant differences in fractional amplitude of low frequency fluctuations, regional homogeneity and independent component analysis in adolescents with major depression disorders compared to healthy controls. Maps a threshold at $P < 0.001$, FWE voxel correction. fALFF: Fractional amplitude of low frequency fluctuations; WM: White matter; ReHo: Regional homogeneity; ICA: Independent component analysis; L: Left; R: Right; MDD: Major depression disorders.

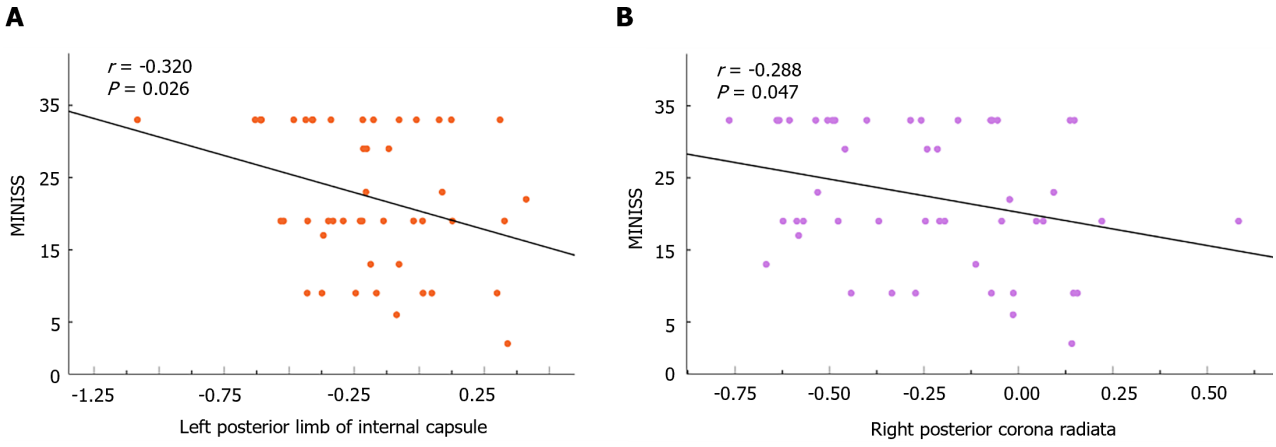

Figure 2 Correlations between clinical psychiatric symptoms and white matter regions with significant differences in the major depression disorders and healthy controls groups. A: It is a significant brain region left posterior limb of internal capsule in fractional amplitude of low frequency fluctuations (fALFF) of white matter (WM); B: It is a significant brain region right posterior corona radiata in fALFF of WM. MINISS: The mini international neuropsychiatric interview suicidality subscale.

circuit[47], and these two circuits play a crucial role in emotional, cognitive, and motor functions[48]. Interestingly, in this study, MDD patients showed significantly lower fALFF values in the PLIC. In addition, Sisti *et al*[49] also found that cognitive decline was not only related to local brain lesions, but may also be related to the destruction of WM fibers and impaired connectivity in these brain regions[49]. Therefore, this discovery may explain the cognitive style of adolescent patients with depression. The corona radiata is composed of ascending and descending fibers that transmit information to the cerebral cortex and functionally involve emotions and executive processing[50,51]. Furthermore, in the correlation analysis, there was a negative correlation between the fALFF values of the PLIC and the PCR and the suicide scale. Some studies have found that impaired executive function may be a risk factor for suicide[52]. This may indicate that as brain dysfunction increases, the risk of suicide also increases.

The upper longitudinal bundle is considered the largest associative fiber bundle system in the brain[53], connecting the frontal and parietal lobes[54]. It is considered a higher-order multi-sensory associative system and is often reported to be related to executive function and emotions[55]. Previous studies have shown that the degree of damage to the SLF in patients with anxiety related depression may be more severe than in patients with non-anxiety related depression, which may lead to cognitive and emotional impairment[56]. This is consistent with the findings of this study in relation to WM ReHo. In a study of mild cognitive impairment (MCI), the left upper corona showed a lower fractional anisotropy value, suggesting that changes in WM in this brain area may be a potential biomarker of MCI[57]. Therefore, an abnormality of the SLF may indicate that patients with depression have more severe depression.

In this study, the ICA method was used to calculate the differences in the brain network of the components of interest. The brain regions overlapped with ReHo, and the direction of changes in the signal values of the brain regions was consistent. This may be because ReHo measures the local connectivity of spontaneous fMRI signals[18,58], and ICA studies measure inter-regional connectivity. These two methods are complementary to each other in a sense, which is why there is an abnormal overlap of activated brain regions. MDD patients also showed an increase in ReHo values in the left WM and a decrease in fALFF values on the right side in bilateral corona radiata lesions in this study, which may be due to the non-flow coupling metabolism of fALFF and ReHo.

Correlation analysis showed that significant correlations were observed between fALFF values, ReHo values, and clinical features in several WM regions. The left PLIC and the right PCR were negatively correlated with suicide. Research found that the bilateral PCR was associated with cognitive impairment in several different diseases[59-61]. There are many studies on the relationship between cognitive impairment and suicidal behavior[62,63]. In the study of suicidal ideation in schizophrenia, it is mentioned that the PCR may be associated with biological processes leading to depression and increased suicidal ideation[64]. This is consistent with the correlation between the PCR and the MINISS found in our study. In addition, studies have shown that impaired executive function may be a risk factor for suicide[52]. Therefore, we speculate that the abnormal activity of the right PCR and the left posterior limb brain area of the inner capsule may be potential biomarkers that trigger suicidal ideation in patients. There are multiple neural circuits within the inner capsule, and the corona radiata and fiber bundles within the capsule project from the cortex to the thalamus and pons nuclei[65]. The thalamus plays an important role in emotional regulation[66], and changes in the inner capsule may interfere with the connection between the thalamus and cortex, leading to abnormal emotional regulation and increasing the occurrence of manic symptoms.

There are some limitations in this study. Firstly, this was a cross-sectional study that failed to reveal the dynamic changes in WM functional signals over time in adolescents with severe depression. Further longitudinal research will help us understand the principles of this disease. Secondly, the sample size in this study was relatively small, and further research and verification are needed in a larger sample size. In addition, studies have also indicated that the relationship between BOLD signals observed in WM and neuronal related activities is still unclear[67]. We require more evidence in future work to demonstrate the importance of BOLD signals observed in WM.

CONCLUSION

Our research findings suggest that changes in WM functional signals may provide new insights into the neurophysiological mechanisms of severe depression in adolescents, and that changes in WM functional signals may serve as biomarkers for predicting future trends in suicide in this disease.

ARTICLE HIGHLIGHTS

Research background

White matter (WM) is composed of various functional nerve fibers and plays an indispensable role in the central nervous system. However, the WM signal changes and their correlation with major depression disorder (MDD) in adolescents are still unclear.

Research motivation

An increasing number of studies have confirmed the functional organization of WM by the resting state functional magnetic imaging (rs-fMRI), indicating its feasibility of studying WM function in adolescents with MDD.

Research objectives
The purpose of this study is to explore the functional changes in the WM of adolescents with MDD.

Research methods
We collected rs-fMRI data and clinical scale information from the adolescent group with MDD and the healthy control group, and analyzed the correlation between WM function signals and clinical scales in the two groups.

Research results
We found significant changes in the functional signals of WM in adolescents with MDD, using the fractional amplitude of low frequency fluctuations, regional homogeneity, and independent component analysis. There are two brain regions, the left posterior limb of the inner capsule and the right posterior corona radiata, which are negatively correlated with the mini international neuropsychiatric interview suicide scales.

Research conclusions
The discovery of changes in WM functional signals in adolescents with MDD is of great significance for understanding the neuropathogenesis of depression.

Research perspectives
Our research findings may serve as biomarkers for predicting the risk of MDD and suicide in adolescents.

ACKNOWLEDGEMENTS

The corresponding author would like to thank all participants and all authors in the study for guidance and support.

FOOTNOTES

Co-first authors: Xin-Lin Huang and Ju Gao.

Co-corresponding authors: Xiao-Bin Zhang and Hong-Yan Sun.

Author contributions: Huang XL, Sun HY, Gao J and Zhang XB conceived the study and drafted the manuscript; Huang XL and Yao QN completed all data collection; Huang XL and Wang YM participated in data analysis and acquired imaging data; Qin J and Zhu F conducted the literature search; All authors contributed to writing and revision of the manuscript, and approved the final version to be published. Huang XL and Gao J, they share co-first authorship, and they have made equal contributions to this paper. They undertook responsibilities for explored research ideas, data collection, data curation, and the writing of the original draft. Sun HY and Zhang XB, they share co-corresponding authorship, and they have made equal contributions to this paper. They were involved in conceptualization, securing funding, supervision, editing and modifying.

Supported by the Suzhou Clinical Medical Center for Mood Disorders, No. Szlcyxzx202109; and Jiangsu Provincial Department of Science and Technology for Social Development-General Project, No. BE2022735.

Institutional review board statement: The study was approved by the Ethics Committee of Suzhou Guangji Hospital.

Informed consent statement: All patients gave informed consent.

Conflict-of-interest statement: All the authors report no relevant conflicts of interest for this article.

Data sharing statement: No additional data are available.

Country/Territory of origin: China

ORCID number: Xin-Lin Huang 0009-0005-8660-5469; Xiao-Bin Zhang 0000-0002-0577-5951; Hong-Yan Sun 0009-0009-2030-1103.

S-Editor: Li L
L-Editor: A
P-Editor: Chen YX

REFERENCES

1 **Stallwood E**, Monsour A, Rodrigues C, Monga S, Terwee C, Offringa M, Butcher NJ. Systematic Review: The Measurement Properties of the Children's Depression Rating Scale-Revised in Adolescents With Major Depressive Disorder. *J Am Acad Child Adolesc Psychiatry* 2021; **60**: 119-133 [PMID: 33130251 DOI: 10.1016/j.jaac.2020.10.009]

2 **Avenevoli S**, Swendsen J, He JP, Burstein M, Merikangas KR. Major depression in the national comorbidity survey-adolescent supplement: prevalence, correlates, and treatment. *J Am Acad Child Adolesc Psychiatry* 2015; **54**: 37-44.e2 [PMID: 25524788 DOI: 10.1016/j.jaac.2014.10.010]

3 **Hawton K**, van Heeringen K. Suicide. *Lancet* 2009; **373**: 1372-1381 [PMID: 19376453 DOI: 10.1016/S0140-6736(09)60372-X]

4 **Weissman MM**, Wolk S, Goldstein RB, Moreau D, Adams P, Greenwald S, Klier CM, Ryan ND, Dahl RE, Wickramaratne P. Depressed adolescents grown up. *JAMA* 1999; **281**: 1707-1713 [PMID: 10328070 DOI: 10.1001/jama.281.18.1707]

5 **Barbeito S**, Vega P, Sánchez-Gutiérrez T, Becerra JA, González-Pinto A, Calvo A. A systematic review of suicide and suicide attempts in adolescents with psychotic disorders. *Schizophr Res* 2021; **235**: 80-90 [PMID: 34332428 DOI: 10.1016/j.schres.2021.07.029]

6 **Ogawa S**, Lee TM, Kay AR, Tank DW. Brain magnetic resonance imaging with contrast dependent on blood oxygenation. *Proc Natl Acad Sci U S A* 1990; **87**: 9868-9872 [PMID: 2124706 DOI: 10.1073/pnas.87.24.9868]

7 **Reuveni I**, Bonne O, Giesser R, Shragai T, Lazarovits G, Isserles M, Schreiber S, Bick AS, Levin N. Anatomical and functional connectivity in the default mode network of post-traumatic stress disorder patients after civilian and military-related trauma. *Hum Brain Mapp* 2016; **37**: 589-599 [PMID: 26536845 DOI: 10.1002/hbm.23051]

8 **Finke C**, Kopp UA, Scheel M, Pech LM, Soemmer C, Schlichting J, Leypoldt F, Brandt AU, Wuerfel J, Probst C, Ploner CJ, Prüss H, Paul F. Functional and structural brain changes in anti-N-methyl-D-aspartate receptor encephalitis. *Ann Neurol* 2013; **74**: 284-296 [PMID: 23686722 DOI: 10.1002/ana.23932]

9 **Yan CG**, Chen X, Li L, Castellanos FX, Bai TJ, Bo QJ, Cao J, Chen GM, Chen NX, Chen W, Cheng C, Cheng YQ, Cui XL, Duan J, Fang YR, Gong QY, Guo WB, Hou ZH, Hu L, Kuang L, Li F, Li KM, Li T, Liu YS, Liu ZN, Long YC, Luo QH, Meng HQ, Peng DH, Qiu HT, Qiu J, Shen YD, Shi YS, Wang CY, Wang F, Wang K, Wang L, Wang X, Wang Y, Wu XP, Wu XR, Xie CM, Xie GR, Xie HY, Xie P, Xu XF, Yang H, Yang J, Yao JS, Yao SQ, Yin YY, Yuan YG, Zhang AX, Zhang H, Zhang KR, Zhang L, Zhang ZJ, Zhou RB, Zhou YT, Zhu JJ, Zou CJ, Si TM, Zuo XN, Zhao JP, Zang YF. Reduced default mode network functional connectivity in patients with recurrent major depressive disorder. *Proc Natl Acad Sci U S A* 2019; **116**: 9078-9083 [PMID: 30979801 DOI: 10.1073/pnas.1900390116]

10 **Marchitelli R**, Paillère-Martinot ML, Bourvis N, Guerin-Langlois C, Kipman A, Trichard C, Douniol M, Stordeur C, Galinowski A, Filippi I, Bertschy G, Weibel S, Granger B, Limosin F, Cohen D, Martinot JL, Artiges E. Dynamic Functional Connectivity in Adolescence-Onset Major Depression: Relationships With Severity and Symptom Dimensions. *Biol Psychiatry Cogn Neurosci Neuroimaging* 2022; **7**: 385-396 [PMID: 34051395 DOI: 10.1016/j.bpsc.2021.05.003]

11 **Hu L**, Xiao M, Ai M, Wang W, Chen J, Tan Z, Cao J, Kuang L. Disruption of resting-state functional connectivity of right posterior insula in adolescents and young adults with major depressive disorder. *J Affect Disord* 2019; **257**: 23-30 [PMID: 31299401 DOI: 10.1016/j.jad.2019.06.057]

12 **Black SE**. Imaging white matter and the burden of small vessel disease. *Brain Cogn* 2007; **63**: 192-193 [DOI: 10.1016/j.bandc.2006.08.010]

13 **Lan H**, Suo X, Li W, Li N, Li J, Peng J, Lei D, Sweeney JA, Kemp GJ, Peng R, Gong Q. Abnormalities of intrinsic brain activity in essential tremor: A meta-analysis of resting-state functional imaging. *Hum Brain Mapp* 2021; **42**: 3156-3167 [PMID: 33769638 DOI: 10.1002/hbm.25425]

14 **Zou QH**, Zhu CZ, Yang Y, Zuo XN, Long XY, Cao QJ, Wang YF, Zang YF. An improved approach to detection of amplitude of low-frequency fluctuation (ALFF) for resting-state fMRI: fractional ALFF. *J Neurosci Methods* 2008; **172**: 137-141 [PMID: 18501969 DOI: 10.1016/j.jneumeth.2008.04.012]

15 **Jiao F**, Gao Z, Shi K, Jia X, Wu P, Jiang C, Ge J, Su H, Guan Y, Shi S, Zang YF, Zuo C. Frequency-Dependent Relationship Between Resting-State fMRI and Glucose Metabolism in the Elderly. *Front Neurol* 2019; **10**: 566 [PMID: 31191447 DOI: 10.3389/fneur.2019.00566]

16 **Aiello M**, Salvatore E, Cachia A, Pappatà S, Cavaliere C, Prinster A, Nicolai E, Salvatore M, Baron JC, Quarantelli M. Relationship between simultaneously acquired resting-state regional cerebral glucose metabolism and functional MRI: a PET/MR hybrid scanner study. *Neuroimage* 2015; **113**: 111-121 [PMID: 25791784 DOI: 10.1016/j.neuroimage.2015.03.017]

17 **Marchitelli R**, Aiello M, Cachia A, Quarantelli M, Cavaliere C, Postiglione A, Tedeschi G, Montella P, Milan G, Salvatore M, Salvatore E, Baron JC, Pappatà S. Simultaneous resting-state FDG-PET/fMRI in Alzheimer Disease: Relationship between glucose metabolism and intrinsic activity. *Neuroimage* 2018; **176**: 246-258 [PMID: 29709628 DOI: 10.1016/j.neuroimage.2018.04.048]

18 **Zang Y**, Jiang T, Lu Y, He Y, Tian L. Regional homogeneity approach to fMRI data analysis. *Neuroimage* 2004; **22**: 394-400 [PMID: 15110032 DOI: 10.1016/j.neuroimage.2003.12.030]

19 **Pamilo S**, Malinen S, Hlushchuk Y, Seppä M, Tikka P, Hari R. Functional subdivision of group-ICA results of fMRI data collected during cinema viewing. *PLoS One* 2012; **7**: e42000 [PMID: 22860044 DOI: 10.1371/journal.pone.0042000]

20 **La C**, Mossahebi P, Nair VA, Bendlin BB, Birn R, Meyerand ME, Prabhakaran V. Age-Related Changes in Inter-Network Connectivity by Component Analysis. *Front Aging Neurosci* 2015; **7**: 237 [PMID: 26733864 DOI: 10.3389/fnagi.2015.00237]

21 **Liu P**, Tu H, Zhang A, Yang C, Liu Z, Lei L, Wu P, Sun N, Zhang K. Brain functional alterations in MDD patients with somatic symptoms: A resting-state fMRI study. *J Affect Disord* 2021; **295**: 788-796 [PMID: 34517253 DOI: 10.1016/j.jad.2021.08.143]

22 **Nawaz H**, Shah I, Ali S. The amygdala connectivity with depression and suicide ideation with suicide behavior: A meta-analysis of structural MRI, resting-state fMRI and task fMRI. *Prog Neuropsychopharmacol Biol Psychiatry* 2023; **124**: 110736 [PMID: 36842608 DOI: 10.1016/j.pnpbp.2023.110736]

23 **Nasrallah IM**, Pajewski NM, Auchus AP, Chelune G, Cheung AK, Cleveland ML, Coker LH, Crowe MG, Cushman WC, Cutler JA, Davatzikos C, Desiderio L, Doshi J, Erus G, Fine LJ, Gaussoin SA, Harris D, Johnson KC, Kimmel PL, Kurella Tamura M, Launer LJ, Lerner AJ, Lewis CE, Martindale-Adams J, Moy CS, Nichols LO, Oparil S, Ogrocki PK, Rahman M, Rapp SR, Reboussin DM, Rocco MV, Sachs BC, Sink KM, Still CH, Supiano MA, Snyder JK, Wadley VG, Walker J, Weiner DE, Whelton PK, Wilson VM, Woolard N, Wright JT Jr, Wright CB, Williamson JD, Bryan RN; SPRINT MIND Investigators for the SPRINT Research Group. Association of Intensive *vs* Standard Blood Pressure Control With Cerebral White Matter Lesions. *JAMA* 2019; **322**: 524-534 [PMID: 31408137 DOI: 10.1001/jama.2019.10551]

24 **Zhao B**, Li T, Yang Y, Wang X, Luo T, Shan Y, Zhu Z, Xiong D, Hauberg ME, Bendl J, Fullard JF, Roussos P, Li Y, Stein JL, Zhu H. Common genetic variation influencing human white matter microstructure. *Science* 2021; **372** [PMID: 34140357 DOI: 10.1126/science.abf3736]

25 **Gawryluk JR**, Mazerolle EL, Brewer KD, Beyea SD, D'Arcy RC. Investigation of fMRI activation in the internal capsule. *BMC Neurosci* 2011; **12**: 56 [PMID: 21672250 DOI: 10.1186/1471-2202-12-56]

26 **Mazerolle EL**, D'Arcy RC, Beyea SD. Detecting functional magnetic resonance imaging activation in white matter: interhemispheric transfer across the corpus callosum. *BMC Neurosci* 2008; **9**: 84 [PMID: 18789154 DOI: 10.1186/1471-2202-9-84]

27 **Ding Z**, Newton AT, Xu R, Anderson AW, Morgan VL, Gore JC. Spatio-temporal correlation tensors reveal functional structure in human brain. *PLoS One* 2013; **8**: e82107 [PMID: 24339997 DOI: 10.1371/journal.pone.0082107]

28 **Ding Z**, Xu R, Bailey SK, Wu TL, Morgan VL, Cutting LE, Anderson AW, Gore JC. Visualizing functional pathways in the human brain using correlation tensors and magnetic resonance imaging. *Magn Reson Imaging* 2016; **34**: 8-17 [PMID: 26477562 DOI: 10.1016/j.mri.2015.10.003]

29 **Marussich L**, Lu KH, Wen H, Liu Z. Mapping white-matter functional organization at rest and during naturalistic visual perception. *Neuroimage* 2017; **146**: 1128-1141 [PMID: 27720819 DOI: 10.1016/j.neuroimage.2016.10.005]

30 **Sun Y**, Kong Z, Song Y, Liu J, Wang X. The validity and reliability of the PHQ-9 on screening of depression in neurology: a cross sectional study. *BMC Psychiatry* 2022; **22**: 98 [PMID: 35139810 DOI: 10.1186/s12888-021-03661-w]

31 **Kroenke K**. PHQ-9: global uptake of a depression scale. *World Psychiatry* 2021; **20**: 135-136 [PMID: 33432739 DOI: 10.1002/wps.20821]

32 **Spitzer RL**, Kroenke K, Williams JB. Validation and utility of a self-report version of PRIME-MD: the PHQ primary care study. Primary Care Evaluation of Mental Disorders. Patient Health Questionnaire. *JAMA* 1999; **282**: 1737-1744 [PMID: 10568646 DOI: 10.1001/jama.282.18.1737]

33 **Katz C**, Roos LE, Wang Y, Bolton J, Hwang SW, Katz LY, Bourque J, Adair CE, Somers JM, Sareen J; At Home/Chez Soi Investigators. Predictive Validity of the MINI Suicidality Subscale for Suicide Attempts in a Homeless Population With Mental Illness. *Suicide Life Threat Behav* 2019; **49**: 1630-1636 [PMID: 30907470 DOI: 10.1111/sltb.12544]

34 **Angst J**, Adolfsson R, Benazzi F, Gamma A, Hantouche E, Meyer TD, Skeppar P, Vieta E, Scott J. The HCL-32: towards a self-assessment tool for hypomanic symptoms in outpatients. *J Affect Disord* 2005; **88**: 217-233 [PMID: 16125784 DOI: 10.1016/j.jad.2005.05.011]

35 **Yan CG**, Wang XD, Zuo XN, Zang YF. DPABI: Data Processing & Analysis for (Resting-State) Brain Imaging. *Neuroinformatics* 2016; **14**: 339-351 [PMID: 27075850 DOI: 10.1007/s12021-016-9299-4]

36 **Ma H**, Xie Z, Huang L, Gao Y, Zhan L, Hu S, Zhang J, Ding Q. The White Matter Functional Abnormalities in Patients with Transient Ischemic Attack: A Reinforcement Learning Approach. *Neural Plast* 2022; **2022**: 1478048 [PMID: 36300173 DOI: 10.1155/2022/1478048]

37 **Beckmann CF**, DeLuca M, Devlin JT, Smith SM. Investigations into resting-state connectivity using independent component analysis. *Philos Trans R Soc Lond B Biol Sci* 2005; **360**: 1001-1013 [PMID: 16087444 DOI: 10.1098/rstb.2005.1634]

38 **Himberg J**, Hyvärinen A, Esposito F. Validating the independent components of neuroimaging time series *via* clustering and visualization. *Neuroimage* 2004; **22**: 1214-1222 [PMID: 15219593 DOI: 10.1016/j.neuroimage.2004.03.027]

39 **Wakana S**, Caprihan A, Panzenboeck MM, Fallon JH, Perry M, Gollub RL, Hua K, Zhang J, Jiang H, Dubey P, Blitz A, van Zijl P, Mori S. Reproducibility of quantitative tractography methods applied to cerebral white matter. *Neuroimage* 2007; **36**: 630-644 [PMID: 17481925 DOI: 10.1016/j.neuroimage.2007.02.049]

40 **Hua K**, Zhang J, Wakana S, Jiang H, Li X, Reich DS, Calabresi PA, Pekar JJ, van Zijl PC, Mori S. Tract probability maps in stereotaxic spaces: analyses of white matter anatomy and tract-specific quantification. *Neuroimage* 2008; **39**: 336-347 [PMID: 17931890 DOI: 10.1016/j.neuroimage.2007.07.053]

41 **Gazzaniga MS**. Cerebral specialization and interhemispheric communication: does the corpus callosum enable the human condition? *Brain* 2000; **123**: 1293-1326 [PMID: 10869045 DOI: 10.1093/brain/123.7.1293]

42 **Tamietto M**, Adenzato M, Geminiani G, de Gelder B. Fast recognition of social emotions takes the whole brain: interhemispheric cooperation in the absence of cerebral asymmetry. *Neuropsychologia* 2007; **45**: 836-843 [PMID: 16996092 DOI: 10.1016/j.neuropsychologia.2006.08.012]

43 **Seltzer B**, Pandya DN. Posterior parietal projections to the intraparietal sulcus of the rhesus monkey. *Exp Brain Res* 1986; **62**: 459-469 [PMID: 3720878 DOI: 10.1007/BF00236024]

44 **Mayberg HS**. Modulating dysfunctional limbic-cortical circuits in depression: towards development of brain-based algorithms for diagnosis and optimised treatment. *Br Med Bull* 2003; **65**: 193-207 [PMID: 12697626 DOI: 10.1093/bmb/65.1.193]

45 **Price JL**, Drevets WC. Neurocircuitry of mood disorders. *Neuropsychopharmacology* 2010; **35**: 192-216 [PMID: 19693001 DOI: 10.1038/npp.2009.104]

46 **Caetano SC**, Fonseca M, Hatch JP, Olvera RL, Nicoletti M, Hunter K, Lafer B, Pliszka SR, Soares JC. Medial temporal lobe abnormalities in pediatric unipolar depression. *Neurosci Lett* 2007; **427**: 142-147 [PMID: 17949901 DOI: 10.1016/j.neulet.2007.06.014]

47 **Zhang X**, Yao S, Zhu X, Wang X, Zhong M. Gray matter volume abnormalities in individuals with cognitive vulnerability to depression: a voxel-based morphometry study. *J Affect Disord* 2012; **136**: 443-452 [PMID: 22129771 DOI: 10.1016/j.jad.2011.11.005]

48 **Friedman A**, Homma D, Gibb LG, Amemori K, Rubin SJ, Hood AS, Riad MH, Graybiel AM. A Corticostriatal Path Targeting Striosomes Controls Decision-Making under Conflict. *Cell* 2015; **161**: 1320-1333 [PMID: 26027737 DOI: 10.1016/j.cell.2015.04.049]

49 **Sisti HM**, Geurts M, Gooijers J, Heitger MH, Caeyenberghs K, Beets IA, Serbruyns L, Leemans A, Swinnen SP. Microstructural organization of corpus callosum projections to prefrontal cortex predicts bimanual motor learning. *Learn Mem* 2012; **19**: 351-357 [PMID: 22837217 DOI: 10.1101/Lm.026534.112]

50 **Stave EA**, De Bellis MD, Hooper SR, Woolley DP, Chang SK, Chen SD. Dimensions of Attention Associated With the Microstructure of Corona Radiata White Matter. *J Child Neurol* 2017; **32**: 458-466 [PMID: 28090797 DOI: 10.1177/0883073816685652]

51 **Karababa IF**, Bayazıt H, Kılıçaslan N, Celik M, Cece H, Karakas E, Selek S. Microstructural Changes of Anterior Corona Radiata in Bipolar Depression. *Psychiatry Investig* 2015; **12**: 367-371 [PMID: 26207131 DOI: 10.4306/pi.2015.12.3.367]

52 **Fernández-Sevillano J**, Alberich S, Zorrilla I, González-Ortega I, López MP, Pérez V, Vieta E, González-Pinto A, Saíz P. Cognition in Recent Suicide Attempts: Altered Executive Function. *Front Psychiatry* 2021; **12**: 701140 [PMID: 34366931 DOI: 10.3389/fpsyt.2021.701140]

53 **Schmahmann JD**, Pandya DN, Wang R, Dai G, D'Arceuil HE, de Crespigny AJ, Wedeen VJ. Association fibre pathways of the brain: parallel observations from diffusion spectrum imaging and autoradiography. *Brain* 2007; **130**: 630-653 [PMID: 17293361 DOI: 10.1093/brain/awl359]

54 **Caspers S**, Zilles K. Microarchitecture and connectivity of the parietal lobe. *Handb Clin Neurol* 2018; **151**: 53-72 [PMID: 29519479 DOI: 10.1016/B978-0-444-63622-5.00003-6]

55 **Biesbroek JM**, Kuijf HJ, van der Graaf Y, Vincken KL, Postma A, Mali WP, Biessels GJ, Geerlings MI; SMART Study Group. Association between subcortical vascular lesion location and cognition: a voxel-based and tract-based lesion-symptom mapping study. The SMART-MR study. *PLoS One* 2013; **8**: e60541 [PMID: 23593238 DOI: 10.1371/journal.pone.0060541]

56 **Xia W**, Zhou R, Zhao G, Wang F, Mao R, Peng D, Yang T, Wang Z, Chen J, Fang Y. Abnormal white matter integrity in Chinese young adults

with first-episode medication-free anxious depression: a possible neurological biomarker of subtype major depressive disorder. *Neuropsychiatr Dis Treat* 2018; **14**: 2017-2026 [PMID: 30127612 DOI: 10.2147/NDT.S169583]

57 **Zhuang L**, Wen W, Zhu W, Trollor J, Kochan N, Crawford J, Reppermund S, Brodaty H, Sachdev P. White matter integrity in mild cognitive impairment: a tract-based spatial statistics study. *Neuroimage* 2010; **53**: 16-25 [PMID: 20595067 DOI: 10.1016/j.neuroimage.2010.05.068]

58 **Zou Q**, Wu CW, Stein EA, Zang Y, Yang Y. Static and dynamic characteristics of cerebral blood flow during the resting state. *Neuroimage* 2009; **48**: 515-524 [PMID: 19607928 DOI: 10.1016/j.neuroimage.2009.07.006]

59 **Li C**, Dang C, Liu G, Chen L, Zhang J, Li J, Ou Z, Zhang Y, Xu A. Secondary damage in left-sided frontal white matter detected by diffusion tensor imaging is correlated with executive dysfunction in patients with acute infarction at the ipsilateral posterior corona radiata. *Eur J Med Res* 2014; **19**: 44 [PMID: 25135459 DOI: 10.1186/s40001-014-0044-x]

60 **Poletti S**, Mazza E, Bollettini I, Falini A, Smeraldi E, Cavallaro R, Benedetti F. The COMT Val158Met polymorphism moderates the association between cognitive functions and white matter microstructure in schizophrenia. *Psychiatr Genet* 2016; **26**: 193-202 [PMID: 26999687 DOI: 10.1097/YPG.0000000000000130]

61 **Kodl CT**, Franc DT, Rao JP, Anderson FS, Thomas W, Mueller BA, Lim KO, Seaquist ER. Diffusion tensor imaging identifies deficits in white matter microstructure in subjects with type 1 diabetes that correlate with reduced neurocognitive function. *Diabetes* 2008; **57**: 3083-3089 [PMID: 18694971 DOI: 10.2337/db08-0724]

62 **Barrett EA**, Sundet K, Simonsen C, Agartz I, Lorentzen S, Mehlum L, Mork E, Andreassen OA, Melle I. Neurocognitive functioning and suicidality in schizophrenia spectrum disorders. *Compr Psychiatry* 2011; **52**: 156-163 [PMID: 21295222 DOI: 10.1016/j.comppsych.2010.06.001]

63 **Davey DK**, Jurick SM, Crocker LD, Hoffman SN, Sanderson-Cimino M, Tate DF, Velez CS, Delano-Wood L, Jak AJ. White matter integrity, suicidal ideation, and cognitive dysfunction in combat-exposed Iraq and Afghanistan Veterans. *Psychiatry Res Neuroimaging* 2021; **317**: 111389 [PMID: 34563989 DOI: 10.1016/j.pscychresns.2021.111389]

64 **Long Y**, Ouyang X, Liu Z, Chen X, Hu X, Lee E, Chen EYH, Pu W, Shan B, Rohrbaugh RM. Associations Among Suicidal Ideation, White Matter Integrity and Cognitive Deficit in First-Episode Schizophrenia. *Front Psychiatry* 2018; **9**: 391 [PMID: 30210372 DOI: 10.3389/fpsyt.2018.00391]

65 **Goh S**, Bansal R, Xu D, Hao X, Liu J, Peterson BS. Neuroanatomical correlates of intellectual ability across the life span. *Dev Cogn Neurosci* 2011; **1**: 305-312 [PMID: 22436512 DOI: 10.1016/j.dcn.2011.03.001]

66 **Pessoa L**. A Network Model of the Emotional Brain. *Trends Cogn Sci* 2017; **21**: 357-371 [PMID: 28363681 DOI: 10.1016/j.tics.2017.03.002]

67 **Gawryluk JR**, Mazerolle EL, D'Arcy RC. Does functional MRI detect activation in white matter? A review of emerging evidence, issues, and future directions. *Front Neurosci* 2014; **8**: 239 [PMID: 25152709 DOI: 10.3389/fnins.2014.00239]

World Journal of Psychiatry

Submit a Manuscript: https://www.f6publishing.com

World J Psychiatry 2024 February 19; 14(2): 287-295

DOI: 10.5498/wjp.v14.i2.287

ISSN 2220-3206 (online)

ORIGINAL ARTICLE

Observational Study

Depression and anxiety among cancer patients visiting a tertiary care cancer hospital

Maheshor Kaphle, Diya Bajracharya, Nirmala Regmi, Dipsikha Aryal, Rajesh Karki

Specialty type: Psychiatry

Provenance and peer review: Invited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

Grade A (Excellent): 0
Grade B (Very good): 0
Grade C (Good): C, C
Grade D (Fair): 0
Grade E (Poor): 0

P-Reviewer: Majid A, Pakistan; Mammadzada G, Italy

Received: September 29, 2023
Peer-review started: September 29, 2023
First decision: December 6, 2023
Revised: December 25, 2023
Accepted: January 19, 2024
Article in press: January 19, 2024
Published online: February 19, 2024

Maheshor Kaphle, Dipsikha Aryal, Department of Public Health, Peoples Dental College and Hospital, Tribhuvan University, Kathmandu 44600, Bagmati, Nepal

Diya Bajracharya, Department of Public Health, CiST College, Pokhara University, Kathmandu 44600, Bagmati, Nepal

Nirmala Regmi, Department of Oncology, Kanti Hospital, Maharajgunj, Kathmandu 44600, Nepal

Rajesh Karki, Central Department of Public Health, Institute of Medicine, Tribhuvan University, Maharajgunj, Kathmandu 44600, Bagmati, Nepal

Corresponding author: Maheshor Kaphle, MHsc, Reader (Associate Professor), Department of Public Health, Peoples Dental College and Hospital, Nayabazar, Kathmandu 44600, Bagmati, Nepal. kafmahesh@gmail.com

Abstract

BACKGROUND

Cancer patients frequently experience psychological problems related to reactions to cancer diagnosis, cancer type and stage, treatment effects, recurrence, fear of end-of-life, survivorship, and financial burden. Depression and anxiety are both psychological and physiological disturbances among cancer patients.

AIM

To assess the prevalence of depression and anxiety among cancer patients attending a tertiary care cancer hospital.

METHODS

A cross-sectional study was conducted at Bhaktapur Cancer Hospital in Kathmandu Valley among 220 cancer patients aged from 18 years to 70 years. Ethical approval was taken from the Institutional Review Committee of CiST College. Convenient sampling was used to interview patients with the standardized Patient-Health Questionnaire (PHQ-9) for Depression and Hospital Anxiety and Depression sub-scale (HADS-A) for anxiety. Epi-Data was used for data entry and transferred to SPSS Version 25 for analysis.

RESULTS

The study revealed that of 220 patients, most of the respondents belonged to the

age group 51-60 years. More than half 131 (59.6%) of the respondents were female, most of them had depression, and one-third had anxiety. Among the respondents, 124 (56.4%) had mild depression, 70 (31.8%) had moderate depression, and 3 (1.3%) had severe depression; 79 (35.9%) had mild anxiety, 64 (29.1%) had moderate anxiety, and 4 (1.8%) had severe anxiety.

CONCLUSION

Most respondents were depressed and one-third had anxiety. More than half and nearly one-third had mild and moderate depression, respectively, and nearly one-third had mild and moderate anxiety, which is higher than other studies.

Key Words: Anxiety; Cancer patients; Depression; Nepal; Prevalence

Core Tip: A cancer diagnosis sparks fear, and those with this condition commonly exhibit greater psychological and emotional stress levels than the general population. Most cancer patients may face psychological problems due to the unavailability of appropriate services in middle and low-income countries like Nepal. We conducted a cross-sectional study among 220 cancer patients to assess the prevalence of depression and anxiety through standard tools. This study found a high prevalence of depression and some anxiety among the patients and suggested that physicians organize counseling services and cancer therapy in hospitals.

Citation: Kaphle M, Bajracharya D, Regmi N, Aryal D, Karki R. Depression and anxiety among cancer patients visiting a tertiary care cancer hospital. *World J Psychiatry* 2024; 14(2): 287-295
URL: https://www.wjgnet.com/2220-3206/full/v14/i2/287.htm
DOI: https://dx.doi.org/10.5498/wjp.v14.i2.287

INTRODUCTION

Cancer is a feared diagnosis, and cancer patients demonstrate a higher tendency for psychological and emotional stress compared to the general population[1]. Cancer patients are more likely to experience adverse mental health outcomes such as depression and anxiety, both psychological and physiological disturbances characterized by a set of physical, emotional, and behavioral elements[2,3]. Depression is a common mental disorder. Globally, it is estimated that 5% of adults suffer from the disorder. It is characterized by persistent sadness and a lack of interest or pleasure in previously rewarding or enjoyable activities[4]. Patients who are depressed have been shown to have worse treatment compliance rates. Patients with anxiety symptoms are more likely to be readmitted, whereas patients with mental distress and depressive symptoms have been linked to extended hospital stays. Additionally, survival seems to be impacted since cancer patients with mental health disorders have higher mortality rates[5]. The primary cancer site also affects the prevalence of depression, with pancreatic and lung cancers having the highest rates and invasive skin cancer having the lowest. Age also affects prevalence. While several cancers in adults were found to be inversely correlated with age and depression, data suggests that children and adolescents with cancer are less depressed than healthy controls. Another important consideration is sex. Researchers discovered that female cancer patients were two to three times as likely than male patients to experience depression[6]. Patients with cancer are more likely than the general population to have psychological discomfort at any point after diagnosis, including long after finishing treatment. Psychological discomfort is linked to reduced life satisfaction and a reduction in daily activities, as well as lower treatment compliance and efficacy, increased mortality, and a higher risk of suicidal thoughts. As a result, treating the symptoms of anxiety and sadness can help these people live better in the 1st year after being diagnosed with cancer. Anxiety and despair may also be exacerbated by the outward signs of some tumors[7].

Cancer is far more than a physical illness. The psychosocial impact of cancer and cancer treatment, because it is multifaceted and potentially long-lasting, often extends into the disease-free survival period. The nature and intensity of this impact varies widely, depending on tumor sites, disease staging, nature of the treatment, patient's life circumstances, personal resources, and resilience[8]. According to Literature, Germany had a lifetime prevalence of anxiety disorders of 30.5% (95%CI: 28.0-33.0) based on 2 studies and a pooled adjusted 4-wk prevalence of 13.5% (95%CI: 7.1-24.3) based on 10 studies[9,10]. It is estimated that cancer patients experience depression at a rate that is up to three times higher than that of the general population. While palliative care wards have reported depression rates as high as 49.0%, studies utilizing the Diagnostic and Statistical Manual of Mental Disorders criteria for major depressive disorder have found prevalence rates ranging from 2.0%-43.5%[1]. The prevalence of depression and anxiety was found to be higher in Nepal for breast cancer patients and may trigger other psychological morbidities[11]. High levels of signs and symptoms can persist for a long time in some patients, interfering with their daily activities and bringing on perceived threats such as disruption of family and life plans, a decline in quality of life, recurrence or progression of disease, and even death[12]. More attention has recently been given to the cancer population's rapidly rising prevalence of psychological issues. Cancer diagnosis and

treatment can be an extremely stressful situation during and after the therapy. Despite the increasing evidence that cancer patients are more likely to experience psychological distress, research has shown that in 40%–90% of cases, medical professionals fail to recognize cancer patients who are depressed and anxious, which results in inadequate treatment[13]. Depression in cancer patients should be identified since it may lower survival rates and indicate early death. When anxiety and depression are present, treatment for depression and cancer might become more difficult and treatment compliance issues can make matters worse. The aim of this study is to assess the prevalence of depression and anxiety among cancer patients attending Bhaktapur Cancer Hospital in Nepal.

MATERIALS AND METHODS

Design and study duration

A cross-sectional and descriptive study was conducted among cancer patients attending Bhaktapur Cancer Hospital, Nepal. The total study duration was from April to September 2022.

Data source and sampling method

Cancer patients 18 years or older who gave consent to participate in the study and were undergoing chemotherapy treatment and follow-up during the study period were included in the study. However, patients who were critically ill at the time of the interview and those with a history of diagnosed mental disorders were excluded from the study. Convenient sampling methods were used for data collection. The Patient-Health Questionnaire (PHQ-9) was used to assess for depression and the Hospital Anxiety and Depression Sub-Scale (HADS-A) was used to assess for anxiety during interviews.

The sample size for this study was calculated using a single population proportion formula, with the proportion of cancer patients with depression (24%)[14], 95% confidence interval, 6% margin of error, and adding a 10% non-response rate by using the following formula:

$n = Z^2 pq/e^2$.

$n = 1.96^2 \times 0.24 \times (1\text{-}0.24)/0.06^2 = 195.5$.

Where n = sample size; Z = 1.96 at 95%CI; P = prevalence of depression 24% taken from previous study[14].

The sample size needed for this study was 196 participants. By adding 10% non-response, the sample size was increased to 215 participants. A sample of 220 participants were used for the analysis.

Tools and techniques

Data was collected from July 1, 2022 to July 15, 2022 by in-person interviews. Two standardized questionnaires were used for data collection. We used the Nepali version of the Patient Health Questionnaire (PHQ-9) for depression[15] and the Hospital Anxiety and Depression Scale (HADS-A) for anxiety[16].

The HADS-A consists of 14 items. Seven of the items indicate anxiety and those seven items were used to measure anxiety. PHQ-9 consists of nine ordinal scale questions ranging from '0' for 'Not at all' to '3' for 'Nearly every day'. Seven anxiety ordinal questions also consist of ordinal scale questions ranging from '0' for 'Not at all' and 3 for 'Most of the time'. Scores from both scales were summed separately. To assess depression, scores were categorized as no depression (0-4), mild depression (5-9), moderate depression (10-19), and severe depression (≥ 20)[17] on the PHQ-9. To assess anxiety, scores were categorized as no anxiety (0-7), mild anxiety (8-10), moderate anxiety (11-15), and severe anxiety (16-21) on the HADS-A scale[18,19].

Statistical analysis

Data were entered into Epi-Data v.3.1 and exported to SPSS Version 25 for analysis. Variables were recoded and transformed before the final analysis. Descriptive statistics such as mean, standard deviation, frequency, and percentage were calculated to present the sociodemographic characteristics of study participants. The prevalence of anxiety and depression symptoms were calculated by summing the PHQ-9 and HADS-A scores and categorizing them.

Ethical approval

Permission was obtained from the hospital and ethical clearance was obtained from the Institutional Review Committee of CiST College (Ref. No.152/077/078) before the study. Written consent was taken from the patients before interviewing them. The names of the participants were not used in any documents, instead, identification codes were used. Voluntarism and the freedom to withdraw from the study at any time were maintained.

RESULTS

Sociodemographic characteristics and level of depression and anxiety

Among 220 cancer patients attending Bhaktapur Hospital, 131 (59.5%) were female. The mean age of the patient was 50.38 (± 12.63) years with a minimum of 18 and a maximum of 79 years. Most of the patients 161 (73.2%) were married and had more than secondary-level education 137 (62.3%; Table 1). Most of the patients were involved in business 72 (32.7%), followed by being a homemaker 62 (28.2%), and service industry 41 (18.6%). It is noteworthy that 77 (43.8%) of the

Table 1 Sociodemographic characteristic and level of depression and anxiety, *n* (%)

Characteristic	Attributes	Not depressed	Depression	Total	Not anxious	Anxious
Age	18-59	34 (20.2)	134 (79.8)	168 (76.4)	57 (33.9)	111 (66.1)
	60-80	10 (19.2)	42 (80.8)	52 (23.6)	16 (30.8)	36 (69.2)
Sex	Male	17 (19.1)	72 (80.9)	89 (40.5)	35 (39.3)	54 (60.7)
	Female	27 (20.6)	104 (79.4)	131 (59.5)	38 (29.0)	93 (71.0)
Marital status	Married	37 (23.0)	124 (77.0)	161 (73.2)	58 (36.0)	103 (64.0)
	Single	7 (11.9)	52 (88.1)	59 (26.8)	15 (25.4)	44 (74.6)
Education	Up to secondary level	19 (22.9)	64 (77.1)	83 (37.7)	26 (31.3)	57 (68.7)
	More than secondary level	25 (18.2)	112 (81.8)	137 (62.3)	47 (34.3)	90 (65.7)
Stage of cancer	First stage	2 (4.5)	14 (8.0)	16 (7.3)	7 (9.6)	9 (6.1)
	Second stage	22 (50.0)	58 (33.0)	80 (36.4)	27 (37.0)	53 (36.1)
	Third stage	17 (38.6)	77 (43.8)	94 (42.7)	30 (41.1)	64 (43.5)
	Fourth stage	3 (6.8)	27 (15.3)	30 (13.6)	9 (12.3)	21 (14.3)

depressed patients were diagnosed with third-stage cancer, followed by 58 (33.0%) with second-stage cancer. Among those suffering from third-stage cancer, 64 (43.5%) patients were identified as anxious (Table 1).

Of the patients, 124 (56.4%) respondents were identified as mildly depressed, 70 (31.8%) as moderately depressed, and 3 (1.4%) as severely depressed. Meanwhile, 23 (10.5%) respondents were categorized as having no depression. Additionally, 73 (33.2%) respondents exhibited no anxiety, while 79 (35.9%) showed mild anxiety. Among the patients, 64 (29.1%) had moderate anxiety, and only 4 (1.8%) were found to have severe anxiety (Table 2).

Most of the patients have breast cancer 50 (22.7%) followed by lung cancer 25 (11.4%), stomach cancer 22 (10.0%), ovarian cancer 18 (8.2%), gall bladder cancer 15(6.8%), and other different types of cancer as shown in Figure 1A.

Most of the respondents were treated for third-stage cancer 94 (42.7%), followed by second-stage cancer 80 (36.4%), and fourth-stage cancer 30 (13.6%) as presented in Figure 1B.

DISCUSSION

The study findings revealed that 56.4% of the respondents were found to be mildly depressed, 31.8% were moderately depressed, and only 1.4% as severely depressed, while 10.5% of the respondents were found to be not depressed. These findings are similar to a study conducted in Germany where 49.8% were not depressed, 35.1% were mildly depressed, 11.3% were moderately depressed, and 3.7% developed severe depression[20].

Similarly, 33.2% of the respondents were found to be not anxious, 35.9% had mild anxiety, 29.1% had moderate anxiety, and only 1.8% had severe anxiety. This finding is similar to the study conducted in Iran where 54.0% of patients had no clinical symptoms of anxiety, 29.3% had mild anxiety, and 16.7% with moderate anxiety, respectively[21].

Anxiety and depression are common complications of cancer that are often neglected. Cancer is a feared diagnosis, and cancer patients demonstrate a higher tendency for psychological and emotional stress compared to the general population[22]. In a sample of 220 participants, 80.0% exceeded clinical cut-off scores on standardized depression. This finding is similar to a study conducted through the National Cancer Institute, where 46.7% of the study exceeded the clinical cut-off score on the PHQ-9 standardized measure[23]. In this study, the prevalence of depression was remarkably higher. In the sample of the study, the depression status of the patients was measured for a short time. In addition, most of the cancer patients were in their second and third stages (36.4% and 42.7%), which may be one of the reasons for the higher prevalence of depression. Advanced stages of cancer might lead to increased psychological distress due to factors like increased symptom burden, more aggressive treatments, or decreased prognosis.

The study findings also revealed that a higher proportion of anxiety was observed in females. Of the 220 respondents, 71.0% were female. This finding is similar to the study conducted by Imtiaz Ahmad Dogar (2009) in Pakistan which concluded that 70% of the female population met the criteria for major depression, anxiety disorder, or both[24]. Similarly, young women diagnosed with any type of advanced cancer are particularly vulnerable to distress disorders as they see their expected life roles and responsibilities changed, generally with respect to their family and work environment[25]. However, a higher proportion of depression was seen in males (80.9%) which is similar to a study conducted in India where a higher proportion of depression was observed in men compared to women[26].

The study findings also showed that anxiety and depression levels were found to be higher in the 45 years and older age group, which is similar to a study in Ethiopian patients with cancer. The finding of this study showed that older age groups were more prone to depression. Older patients experience longer disease duration, a higher risk of cancer metastases, and more disabilities, all of which contribute to depression[2]. Another reason could be that older patients have difficulty seeking assistance and communicating with others. Furthermore, worrying about excessive treatment

Table 2 Distribution of respondents according to depression and anxiety level, *n* (%)

Level	Normal	Mild	Moderate	Severe
Depression	23 (10.5)	124 (56.4)	70 (31.8)	3 (1.4)
Anxiety	73 (33.2)	79 (35.9)	64 (29.1)	4 (1.8)

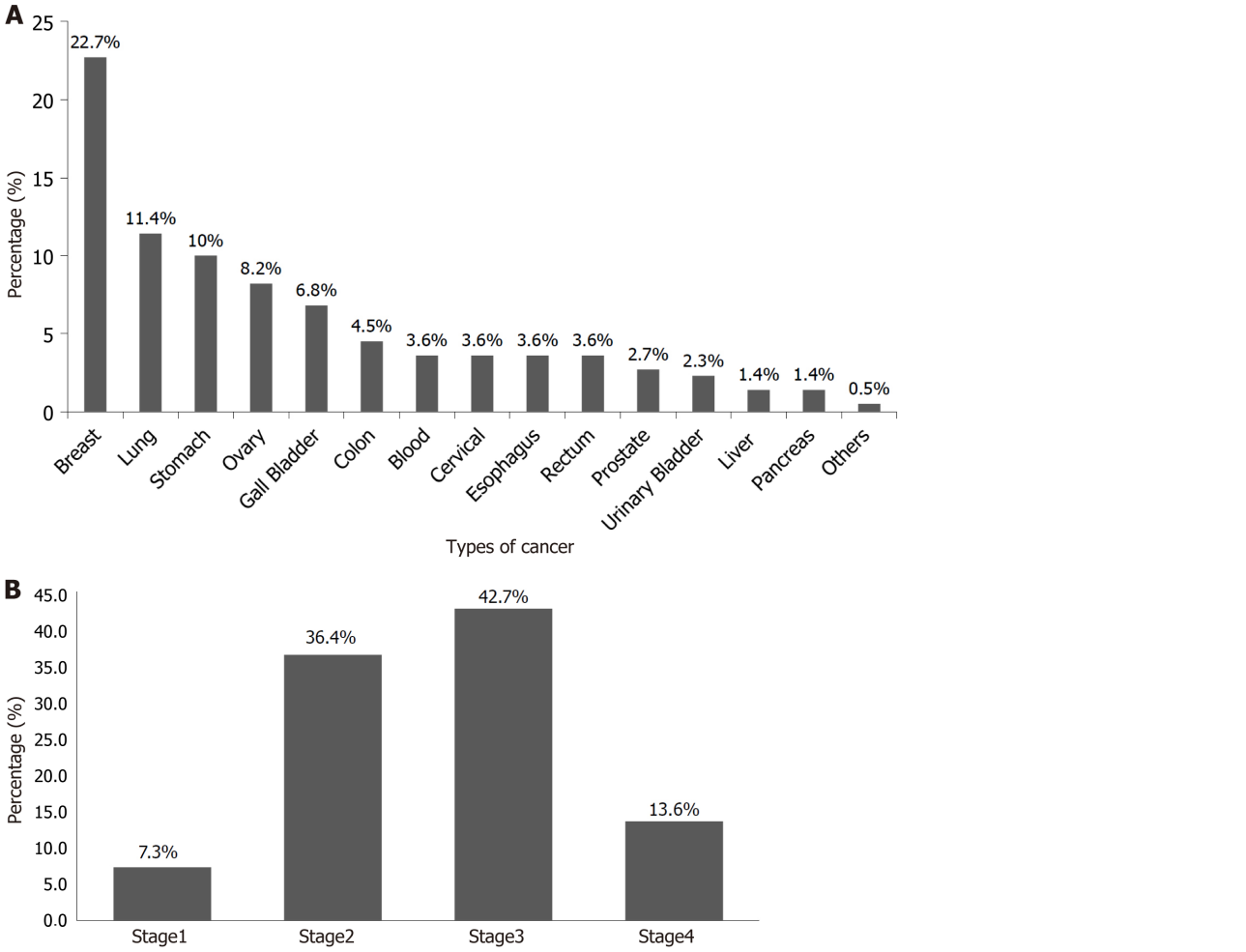

Figure 1 Different cancer among patients. A: Type of cancer among patients; B: Stage of cancer in patients.

costs and family financial difficulties may be causes of psychological distress.

The study findings revealed that a higher proportion of depression and anxiety was observed in illiterate patients. This finding is supported by a study from Nepal where the education category was most affected. For illiterate respondents with lower levels of education, challenges increase as it becomes difficult for them to get enough information or understand the disease processes and its management, which results in cognitive and emotional difficulty in understanding complex information and decision-making[27]. Similar findings were seen in a study conducted by the *Department of Psychology* among Ethiopian cancer patients, where illiterate patients were more anxious and depressed than literate ones[28]. Likewise, the finding is similar to the study conducted by Khalil *et al*[26] in 2016 which showed that out of 143 (47.7%) uneducated patients, 85 (59.4%) were depressed and the educational category was most affected[29].

The interesting finding in this research is about marital status, where depression (88.1%) and anxiety (74.6%) were present in higher proportions compared to single patients. It was found that single patients faced more depression than married patients. This study's findings matched with previous research conducted by Lavdaniti *et al*[30] in 2012 which found that unmarried and divorced individuals showed higher levels of depression compared to married persons. A possible explanation for this is that divorced/single patients did not have moral support from their family members compared to married patients. Similar to another study, Pasquini and Biondi[31] mentioned in 2007 that social support also played an important role in alleviating depression among cancer patients, and family counselling should be implemented to educate the family members.

In this study, the prevalence of depression (80.4%) and anxiety (66.9%) was seen more in unemployed respondents. This finding is supported by previous studies where unemployed patients with cancer are more likely to be affected by depression. Hence, unemployment in combination with cancer exerts overwhelming physical and psychological strain,

such as depression and anxiety in an individual[2]. Employment was found to have a significant impact on depression in those suffering from cancer. Similarly, Rwandan patients showed a higher prevalence of anxiety (52.1%) and depression (67.1%)[22].

The prevalence of psychiatric disorders mostly varies at different stages of cancer. Despite the fact that adjustment disorders with depressed or anxious moods are more frequent at the early stage of the disease, severe psychiatric complications are more common in the late stages of cancer[32]. The study also shows that most of the patients had second or third-stage cancer (36.4% and 42.7%) in our study, which may be one of the reasons for the higher prevalence of depression, which is similar to a study conducted by Hong and Tian[33] which shows that 34.5% had third-stage cancer. The most common cancer found was breast cancer (22.7%). This is consistent with other studies finding breast cancer to be the most common cancer in Sudan[34]. The prevalence of depression and anxiety in breast cancer patients was found to be 54.5% and 46.8%, respectively[35].

Limitation

Despite recent advancements in cancer treatment, Nepal is still struggling to improve and manage conventional modalities for cancer treatment because of many socioeconomic and political conditions. This scenario makes people believe cancer treatment is a dead-end which leads to higher levels of anxiety and depression among cancer patients. A major number of cancer patients die due to a lack of treatment facilities in Nepal. The limitation of the study was that the study was conducted in only one tertiary hospital.

CONCLUSION

The burden of depression and anxiety among cancer patients in this study was relatively higher. Since depression and anxiety disorders are common psychiatric disorders among oncology patients and can have a significant impact on the functioning of patients, it is important to screen them regularly and to provide necessary clinical interventions, treatment, and support. This is even more important in oncology patients in developing countries with limited resources. Priority should be given to screening and counseling cancer patients for anxiety and depression to help them cope with cancer as a disease and its impact on their mental health. The authors are encouraged to provide opportunities for potential avenues of future research within this field.

ARTICLE HIGHLIGHTS

Research background

Depression in cancer patients should be identified since it may lower survival rates and indicate early death. When anxiety and depression are present, treatment for depression and cancer might become more difficult and treatment compliance issues can make matters worse.

Research motivation

Cancer patients are more likely to experience psychological distress, and medical professionals fail to recognize cancer patients who are depressed and anxious, which results in inadequate treatment.

Research objectives

To assess the prevalence of depression and anxiety among cancer patients in a tertiary cancer center.

Research methods

A cross-sectional study was conducted among 220 cancer patients by convenience sampling of patients attending a tertiary cancer hospital. We used a face-to-face interview technique to collect the data by using the standard tool Patient Health Questionnaire (PHQ-9) for depression and the Hospital Anxiety and Depression sub-scale for anxiety. Simple descriptive analysis was performed by categorizing the depression and anxiety according to the score.

Research results

Most of the cancer patients had depression and one-third had anxiety. Among the respondents, 124 (56.4%) had mild depression, 70 (31.8%) had moderate depression, and 3 (1.3%) had severe depression; 79 (35.9%) had mild anxiety, 64 (29.1%) had moderate anxiety, and 4 (1.8%) had severe anxiety. It is noteworthy that 77 (43.8%) of the depressed patients were diagnosed with third-stage, followed by 58 (33.0%) with second-stage cancer, and 64 (43.5%) anxious patients with third-stage cancer.

Research conclusions

Most of the cancer patients had depression and about one-third had anxiety which was high in third-stage cancer.

Research perspectives

The prevalence of depression and anxiety was higher than in other studies. Our findings highlighted the necessity of counseling services parallel to cancer therapy.

ACKNOWLEDGEMENTS

The authors are obliged to Bhaktapur Cancer Hospital for providing permission to conduct this study. Also, we extend our humble gratitude to all the patients who gave their valuable time for the study in the hospital. Furthermore, we would like to thank Julius Tonzel (Public Health Researcher) from Louisiana State University Health Sciences Center LA, US who edited the language throughout the article.

FOOTNOTES

Co-first authors: Maheshor Kaphle and Diya Bajracharya.

Author contributions: Kaphle M and Bajracharya D (equal contributors) conceptualized the study and prepared the proposal, data collection, data analysis, and preliminary preparation of the manuscript; Regmi N was involved in data curation and review of the manuscript; Aryal D was involved in writing and editing the manuscript; Karki R was involved in investigating, editing, and critically reviewing the manuscript; Kaphle M had the final authority to submit for publication; all authors have read and agreed to the published final version of the manuscript. Kaphle M and Bajracharya D have been designated co-first authors in recognition of their distinct yet complementary contributions throughout the research. Kaphle M excelled in data management, analysis, and bringing expertise in the critical review of the manuscript, while Bajracharya D played a key role in data collection, entry, preliminary analysis and contributed significantly to manuscript writing. Both authors demonstrated equal dedication and effort from project inception to completion, particularly during concept development, design, and critical writing and response to the reviewer. The collaborative nature of the research team was essential, with each member contributing unique skills and acknowledging it. It's important to note that while Kaphle M and Bajracharya D are co-first authors, appreciation extends to the entire team for their valuable contributions. The decision for co-first authorship reflects a transparent and inclusive process, honoring the collaborative spirit that propelled the success of the research.

Institutional review board statement: Permission was obtained from the hospital and ethical clearance was obtained from the Institutional Review Committee of CiST College (Ref. No.152/077/078) before the study.

Informed consent statement: Written consent was taken from the patients before interviewing them. The names of the participants were not used in any documents, instead, identification codes were used. Voluntarism and the freedom to withdraw from the study at any time were maintained.

Conflict-of-interest statement: The authors declare that they have no conflicts of interest.

Data sharing statement: The data related to this research can be found from correspondence author with reasonable demand.

STROBE statement: The authors have read the STROBE Statement—checklist of items, and the manuscript was prepared and revised according to the STROBE Statement—checklist of items.

Country/Territory of origin: Nepal

ORCID number: Maheshor Kaphle 0000-0001-8121-6206; Dipsikha Aryal 0000-0002-1219-6982; Rajesh Karki 0000-0002-8431-2890.

S-Editor: Lin C
L-Editor: Filipodia
P-Editor: Zhang YL

REFERENCES

1 **Smith HR**. Depression in cancer patients: Pathogenesis, implications and treatment (Review). *Oncol Lett* 2015; **9**: 1509-1514 [PMID: 25788991 DOI: 10.3892/ol.2015.2944]
2 **Ayalew M**, Deribe B, Duko B, Geleta D, Bogale N, Gemechu L, Gebretsadik A, Bedaso A. Prevalence of depression and anxiety symptoms and their determinant factors among patients with cancer in southern Ethiopia: a cross-sectional study. *BMJ Open* 2022; **12**: e051317 [PMID: 35063957 DOI: 10.1136/bmjopen-2021-051317]
3 **Wondie Y**, Mehnert A, Hinz A. The Hospital Anxiety and Depression Scale (HADS) applied to Ethiopian cancer patients. *PLoS One* 2020; **15**:

e0243357 [PMID: 33270779 DOI: 10.1371/journal.pone.0243357]
4 **World Health Organization**. Depression. 2023 [cited 11 September 2023]. Available from: https://www.who.int/health-topics/depression
5 **Heathcote LC**, Cunningham SJ, Webster SN, Tanna V, Mattke E, Loecher N, Spunt SL, Simon P, Dahl G, Walentynowicz M, Murnane E, Tutelman PR, Schapira L, Simons LE, Mueller C. Smartphone-based Ecological Momentary Assessment to study "scanxiety" among Adolescent and Young Adult survivors of childhood cancer: A feasibility study. *Psychooncology* 2022; **31**: 1322-1330 [PMID: 35411626 DOI: 10.1002/pon.5935]
6 **Laccourreye O**, Maisonneuve H. French scientific medical journals confronted by developments in medical writing and the transformation of the medical press. *Eur Ann Otorhinolaryngol Head Neck Dis* 2019; **136**: 475-480 [PMID: 31540851 DOI: 10.1016/j.anorl.2019.09.002]
7 **Wynn Mon S**, Myint Zu WW, Myint Maw M, Win H, Zin Thant K, Yang G, Malhotra C, Teo I, Finkelstein E, Ozdemir S. Awareness of and preference for disease prognosis and participation in treatment decisions among advanced cancer patients in Myanmar: Results from the APPROACH study. *Asia Pac J Clin Oncol* 2021; **17**: 149-158 [PMID: 32921003 DOI: 10.1111/ajco.13430]
8 **El-Saharty S**, Ahsan KZ, Koehlmoos TL, Engelgau MM. Tackling Noncommunicable Diseases in Bangladesh. NW Washington: World Bank Group, 2013 [DOI: 10.1596/978-0-8213-9920-0]
9 **Goerling U**, Hinz A, Koch-Gromus U, Hufeld JM, Esser P, Mehnert-Theuerkauf A. Prevalence and severity of anxiety in cancer patients: results from a multi-center cohort study in Germany. *J Cancer Res Clin Oncol* 2023; **149**: 6371-6379 [PMID: 36757620 DOI: 10.1007/s00432-023-04600-w]
10 **Vehling S**, Koch U, Ladehoff N, Schön G, Wegscheider K, Heckl U, Weis J, Mehnert A. [Prevalence of affective and anxiety disorders in cancer: systematic literature review and meta-analysis]. *Psychother Psychosom Med Psychol* 2012; **62**: 249-258 [PMID: 22585582 DOI: 10.1055/s-0032-1309032]
11 **Sharma A**, Zhang J. Predictors of post traumatic growth among breast cancer patients in Nepal. *Asian Pac J Health Sci* 2017; **4**: 9-17 [DOI: 10.21276/apjhs.2017.4.2.3]
12 **Yang YL**, Liu L, Wang Y, Wu H, Yang XS, Wang JN, Wang L. The prevalence of depression and anxiety among Chinese adults with cancer: a systematic review and meta-analysis. *BMC Cancer* 2013; **13**: 393 [PMID: 23967823 DOI: 10.1186/1471-2407-13-393]
13 **Jadoon NA**, Munir W, Shahzad MA, Choudhry ZS. Assessment of depression and anxiety in adult cancer outpatients: a cross-sectional study. *BMC Cancer* 2010; **10**: 594 [PMID: 21034465 DOI: 10.1186/1471-2407-10-594]
14 **Hartung TJ**, Brähler E, Faller H, Härter M, Hinz A, Johansen C, Keller M, Koch U, Schulz H, Weis J, Mehnert A. The risk of being depressed is significantly higher in cancer patients than in the general population: Prevalence and severity of depressive symptoms across major cancer types. *Eur J Cancer* 2017; **72**: 46-53 [PMID: 28024266 DOI: 10.1016/j.ejca.2016.11.017]
15 **Kohrt BA**, Luitel NP, Acharya P, Jordans MJ. Detection of depression in low resource settings: validation of the Patient Health Questionnaire (PHQ-9) and cultural concepts of distress in Nepal. *BMC Psychiatry* 2016; **16**: 58 [PMID: 26951403 DOI: 10.1186/s12888-016-0768-y]
16 **Risal A**, Manandhar K, Linde M, Koju R, Steiner TJ, Holen A. Reliability and Validity of a Nepali-language Version of the Hospital Anxiety and Depression Scale (HADS). *Kathmandu Univ Med J (KUMJ)* 2015; **13**: 115-124 [PMID: 26657079 DOI: 10.3126/kumj.v13i2.16783]
17 **Moriarty AS**, Gilbody S, McMillan D, Manea L. Screening and case finding for major depressive disorder using the Patient Health Questionnaire (PHQ-9): a meta-analysis. *Gen Hosp Psychiatry* 2015; **37**: 567-576 [PMID: 26195347 DOI: 10.1016/j.genhosppsych.2015.06.012]
18 **Lopes C**, Lopes-Conceição L, Fontes F, Ferreira A, Pereira S, Lunet N, Araújo N. Prevalence and Persistence of Anxiety and Depression over Five Years since Breast Cancer Diagnosis-The NEON-BC Prospective Study. *Curr Oncol* 2022; **29**: 2141-2153 [PMID: 35323373 DOI: 10.3390/curroncol29030173]
19 **Rishi P**, Rishi E, Maitray A, Agarwal A, Nair S, Gopalakrishnan S. Hospital anxiety and depression scale assessment of 100 patients before and after using low vision care: A prospective study in a tertiary eye-care setting. *Indian J Ophthalmol* 2017; **65**: 1203-1208 [PMID: 29133652 DOI: 10.4103/ijo.IJO_436_17]
20 **Hinz A**, Mehnert A, Kocalevent RD, Brähler E, Forkmann T, Singer S, Schulte T. Assessment of depression severity with the PHQ-9 in cancer patients and in the general population. *BMC Psychiatry* 2016; **16**: 22 [PMID: 26831145 DOI: 10.1186/s12888-016-0728-6]
21 **Nikbakhsh N**, Moudi S, Abbasian S, Khafri S. Prevalence of depression and anxiety among cancer patients. *Caspian J Intern Med* 2014; **5**: 167-170 [PMID: 25202445]
22 **Uwayezu MG**, Gishoma D, Sego R, Mukeshimana M, Collins A. Anxiety and depression among cancer patients: prevalence and associated factors at a Rwandan referral hospital. *Rwanda Med Health Sci* 2019; **2**: 118-125 [DOI: 10.4314/rjmhs.v2i2.7]
23 **Wagner LI**, Pugh SL, Small W Jr, Kirshner J, Sidhu K, Bury MJ, DeNittis AS, Alpert TE, Tran B, Bloom BF, Mai J, Yeh A, Sarma K, Becker M, James J, Bruner DW. Screening for depression in cancer patients receiving radiotherapy: Feasibility and identification of effective tools in the NRG Oncology RTOG 0841 trial. *Cancer* 2017; **123**: 485-493 [PMID: 27861753 DOI: 10.1002/cncr.29969]
24 **Dogar IA**, Azeem MW, Kiran M, Hussain I, Mehmood K, Hina I. Depression and anxiety in cancer patients in outpatient department of a tertiary care hospital in Pakistan. survival. *Pak J Med Sci* 2009; **25**: 734-737
25 **Obispo-Portero B**, Cruz-Castellanos P, Jiménez-Fonseca P, Rogado J, Hernandez R, Castillo-Trujillo OA, Asensio-Martínez E, González-Moya M, Carmona-Bayonas A, Calderon C. Anxiety and depression in patients with advanced cancer during the COVID-19 pandemic. *Support Care Cancer* 2022; **30**: 3363-3370 [PMID: 34993652 DOI: 10.1007/s00520-021-06789-3]
26 **Pandey M**, Devi N, Thomas BC, Kumar SV, Krishnan R, Ramdas K. Distress overlaps with anxiety and depression in patients with head and neck cancer. *Psychooncology* 2007; **16**: 582-586 [PMID: 17109494 DOI: 10.1002/pon.1123]
27 **Sharma A**, Zhang J. Depression and its predictors among breast cancer patients in Nepal. *ASEAN J Psychiatr* 2014; **16**: 106-115
28 **Wong CW**, Schumm MA, Zhu CY, Tseng CH, Arasu A, Han J, Livhits MJ. Quality of Life Following Molecular Marker Testing for Indeterminate Thyroid Nodules. *Endocr Pract* 2020; **26**: 960-966 [PMID: 33471700 DOI: 10.4158/EP-2020-0101]
29 **Khalil A**, Faheem M, Fahim A, Innocent H, Mansoor Z, Rizvi S, Farrukh H. Prevalence of Depression and Anxiety amongst Cancer Patients in a Hospital Setting: A Cross-Sectional Study. *Psychiatry J* 2016; **2016**: 3964806 [PMID: 27752508 DOI: 10.1155/2016/3964806]
30 **Lavdaniti M**, Barbas G, Fratzana A, Zyga S. Evaluation of depression in colon cancer patients. *Health Sci J* 2012; **6**: 681-692
31 **Pasquini M**, Biondi M. Depression in cancer patients: a critical review. *Clin Pract Epidemiol Ment Health* 2007; **3**: 2 [PMID: 17288583 DOI: 10.1186/1745-0179-3-2]
32 **Villoria E**, Lara L, Salcedo R. [Frequency of depression and anxiety in a group of 623 patients with cancer]. *Rev Med Chil* 2021; **149**: 708-715 [PMID: 34751323 DOI: 10.4067/s0034-98872021000500708]
33 **Hong JS**, Tian J. Prevalence of anxiety and depression and their risk factors in Chinese cancer patients. *Support Care Cancer* 2014; **22**: 453-

459 [PMID: 24091720 DOI: 10.1007/s00520-013-1997-y]

34 **Bakhiet TE**, Ali SM, Bakhiet AM. Prevalence of depression and anxiety among adult patients undergoing chemotherapy in Khartoum, Sudan: A cross-sectional study. *J Affect Disord Rep* 2021; **6**: 100218 [DOI: 10.1016/j.jadr.2021.100218]

35 **Tsaras K**, Papathanasiou IV, Mitsi D, Veneti A, Kelesi M, Zyga S, Fradelos EC. Assessment of Depression and Anxiety in Breast Cancer Patients: Prevalence and Associated Factors. *Asian Pac J Cancer Prev* 2018; **19**: 1661-1669 [PMID: 29938451 DOI: 10.22034/APJCP.2018.19.6.1661]

World Journal of Psychiatry

Submit a Manuscript: https://www.f6publishing.com

World J Psychiatry 2024 February 19; 14(2): 296-307

DOI: 10.5498/wjp.v14.i2.296

ISSN 2220-3206 (online)

ORIGINAL ARTICLE

Observational Study

Disparities in the impact of economic well-being on self-esteem in adulthood: Race and ethnicity

Jaewon Lee

Specialty type: Psychology and social

Provenance and peer review: Unsolicited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

Grade A (Excellent): 0
Grade B (Very good): 0
Grade C (Good): C
Grade D (Fair): 0
Grade E (Poor): 0

P-Reviewer: Zhou B, China

Received: October 19, 2023
Peer-review started: October 19, 2023
First decision: December 11, 2023
Revised: December 15, 2023
Accepted: January 18, 2024
Article in press: January 18, 2024
Published online: February 19, 2024

Jaewon Lee, School of Social Work, Inha University, Incheon 22212, South Korea

Corresponding author: Jaewon Lee, PhD, Assistant Professor, School of Social Work, Inha University, 100 Inha-ro, Incheon 22212, South Korea. j343@inha.ac.kr

Abstract

BACKGROUND

Most studies have defined economic well-being as socioeconomic status, with little attention given to whether other indicators influence self-esteem. Little is known about racial/ethnic disparities in the relationship between economic well-being and self-esteem during adulthood.

AIM

To explore the impact of economic well-being on self-esteem in adulthood and differences in the association across race/ethnicity.

METHODS

The current study used data from the National Longitudinal Survey of Youth 1979. The final sample consisted of 2267 African Americans, 1425 Hispanics, and 3678 non-Hispanic Whites. Ordinary linear regression analyses and logistic regression analyses were conducted.

RESULTS

African Americans and Hispanics were more likely to be in poverty in comparison with non-Hispanic Whites. More African Americans were unemployed than Whites. Those who received fringe benefits, were more satisfied with jobs, and were employed were more likely to have higher levels of self-esteem. Poverty was negatively associated with self-esteem. Interaction effects were found between African Americans and job satisfaction predicting self-esteem.

CONCLUSION

The role of employers is important in cultivating employees' self-esteem. Satisfactory outcomes or feelings of happiness from the workplace may be more important to non-Hispanic Whites compared to African Americans and Hispanics.

Key Words: Economic well-being; Self-esteem; Racial/Ethnic disparities; Adulthood

Core Tip: Little is known about racial/ethnic disparities in the relationship between economic well-being and self-esteem during adulthood. Findings from this study expand on prior research in several ways: Focusing on adults' self-esteem rather than adolescents, looking at racial/ethnic disparities in self-esteem among adults, better understanding of economic well-being by including factors that have not been addressed in previous studies, and examining racial/ethnic disparities in the relationship between economic well-being and self-esteem.

Citation: Lee J. Disparities in the impact of economic well-being on self-esteem in adulthood: Race and ethnicity. *World J Psychiatry* 2024; 14(2): 296-307
URL: https://www.wjgnet.com/2220-3206/full/v14/i2/296.htm
DOI: https://dx.doi.org/10.5498/wjp.v14.i2.296

INTRODUCTION

Self-esteem is an important factor for achievement in the workplace[1,2]. Specifically, individuals with higher self-esteem were more likely to have characteristics that directly contribute to successful performance in the labor market[2-4]. Levels of self-esteem were documented as changing over the life course[5], with the highest levels of self-esteem reported just before entering into older adulthood, followed by a rapid decrease in later years[1,6]. The reasons for these changes can be attributed partially to the level of economic well-being[7]. For instance, individuals with low socioeconomic status (SES) backgrounds reported lower levels of self-esteem during childhood[8]. However, little attention has been given to examining whether other aspects of economic well-being, aside from SES, may impact self-esteem during adulthood. Furthermore, little is known about how aspects of economic well-being beyond standard measures of SES (*e.g.*, poverty and employment), such as job satisfaction and fringe benefits, influence self-esteem; the majority of this work has focused primarily on the influence of economic well-being on self-esteem in adolescence or childhood rather than adulthood[3,5].

Racial/ethnic disparities in the association between economic well-being and self-esteem also exist. Research has shown that African Americans are more likely to have greater self-esteem than Whites and Hispanics[9], while Hispanics were less likely to have higher levels of self-esteem in comparison with Whites[10]. In terms of economic well-being, African Americans were less likely to be employed[11] and more likely to be exposed to disadvantages in income and assets[12]. For instance, rates of unemployment among African Americans were approximately twice those of Whites[13]. Given differences in levels of self-esteem and economic well-being across racial/ethnic groups, it is necessary to identify how race/ethnicity may moderate the relationship between economic well-being and self-esteem. Thus, the present study explores whether other aspects of economic well-being, aside from SES, influence self-esteem among adults and investigates whether any racial/ethnic disparities exist in this relationship.

Self-esteem

Self-esteem refers to values and beliefs about oneself, as well as individual self-assessment[5,14]. Levels of self-esteem have a direct association with physical and mental health outcomes. For instance, individuals with low levels of self-esteem were more likely to experience poor physical and mental health[2-4,15].

When it comes to factors that affect self-esteem, race/ethnicity has been shown to have a greater effect than other demographic characteristics[5], making race/ethnicity an important factor in understanding racial/ethnic differences in self-esteem[16]. For example, Hispanics showed lower levels of self-esteem in comparison with non-Hispanic Whites[10,17]. Conversely, African Americans in the United States reported higher self-esteem when compared to non-Hispanic Whites[5,18]. While the gap between these different levels of self-esteem across racial/ethnic groups is not large in childhood, it increases, based on racial/ethnic disparities, with age[10].

Individuals with higher self-esteem tend to be proud of themselves regardless of their performance feedback and tend not to be ashamed of poor performance[18]. As such, they are more likely to adapt to a workplace even if they make mistakes while working, leading them to have better resilience and productivity. On the other hand, people with low self-esteem were likely to suffer from work-related problems[2]. In other words, higher self-esteem in adulthood is critical to adjust workplace and produce better performance and productivity in society. Given that previous research has mainly addressed self-esteem before adulthood, the current study expands on the range of age in its investigation on self-esteem by focusing on adults.

Economic well-being and self-esteem

Economic well-being is a broad concept and can roughly be defined as economic hardship; difficulties, or challenges, such as trouble paying bills, dissatisfaction with individual economic resources; and an inability to meet basic household needs such as clothing, food, housing, and health services[19]. Economic strains greatly increase levels of stress and can pose threats to daily life and basic needs[20]. Individuals who have unsatisfied needs regarding their economic resources are more likely to suffer from stresses due to their poor economic well-being, leading them to feel a sense of uncertainty and unhappiness. Thus, individuals with poor economic well-being often experience difficulties in developing higher self-esteem due to feelings of hopelessness or desperation.

Racial/ethnic disparities have a close relationship with socioeconomic inequalities[21]. Hispanics are exposed to higher risks of chronic financial hardship due to accumulated limitations in education, employment, and access to resources[22]. Hispanics also experienced higher rates of poverty than non-Hispanic Whites[23]. African Americans tended to have lower levels of economic well-being due to racial discrimination compared to non-Hispanic Whites[24] and other factors which can lead to fewer opportunities for employment[11]. Conversely, non-Hispanic White men and women were less likely to live in poverty in comparison with African American, Hispanic, and Asian men and women[25].

As a result of economic disparities, racial/ethnic minorities with low levels of economic well-being may be more at risk for low self-esteem[7] due to limited resources, higher rates of unemployment, and lower economic status in comparison with non-Hispanic Whites. Thus, it is necessary to examine racial/ethnic disparities in economic well-being and whether these disparities negatively influence self-esteem.

Given that previous research regarding economic well-being has mainly addressed income-related factors such as poverty and employment, which are considered objective factors[26], it is necessary to shift the perspective from objective economic well-being to subjective economic well-being because well-being should be measured by self-evaluation of one's economic status. Subjective well-being refers to a broad concept of life satisfaction[27], with subjective factors influencing quality of life and mental health[28]. Therefore, the current study seeks to expand the concept of economic well-being to include objective factors such as employment status, poverty level, and presence of work-related fringe benefits (such as employment-based benefits including health insurance, life insurance, and paid vacation), as well as the subjective factor of job satisfaction.

In terms of objective factors, unemployment has been linked to a sense of helplessness and mental illnesses, both of which discourage individuals from engaging in productive activities[29]. Research has shown that joblessness is associated with decreased personal efficacy and lower levels of self-esteem[30]. Furthermore, individuals who are unemployed for extended periods of time are at an even greater risk for low self-esteem[31]. Unemployment can lead to a sense of losing control of one's life due to concerns about potential unemployment and the uncertainty of one's living and financial situation[32]. In addition to unemployment, as poverty has an impact on lives across the life course[33], people who had often been exposed to poverty showed a higher prevalence of depression or suffer from poorer mental health [34]. As a result of mental health problems, individuals in poverty may be more likely to have poor self-esteem.

Given workers' well-being has become critical in achieving economic development and improving individuals' satisfaction with their lives[35], fringe benefits enhancing individuals' satisfaction with their jobs should be considered in relation to their well-being. In the workplace, individuals with better financial planning may be more likely to have higher levels of self-esteem. For example, individuals with a retirement plan as part of their fringe benefits were likely to develop greater self-esteem due to financial assistance in later life[36]. While previous research has mainly addressed the effects of unemployment or poverty as predictors of self-esteem, less is known about the relationship between subjective factors of economic well-being and self-esteem in adulthood.

As a subjective factor, levels of job satisfaction can also influence self-esteem. Psychological stressors from the workplace arise from a lack of support from supervisors, job strain, or job insecurity[37]. As some of these stressors are attributed to individuals' differing perceptions of their jobs, levels of job satisfaction may either positively or negatively influence their mental health. Research has identified relationships between mental health and job satisfaction[38,39]. For example, employees who consider themselves unemployed are more likely to have poor physical and mental health[40], while those who are employed and suffer less from work-related stresses may be satisfied with their work situation. In addition, job strains, which result from subjective perceptions of one's workload and workplace support, can also impact psychiatric morbidity negatively[41].

Racial and ethnic disparities

African Americans may be more likely to have lower self-esteem in comparison with Whites. This disparity can be explained by the influence of negative perceptions of minority groups by the majority culture. In other words, because African Americans in the United States are stigmatized as a minority group, they tend to have poor self-esteem compared with Whites[42]. Furthermore, racial majority, referring to non-Hispanic Whites, are less likely to report poor self-esteem than minority groups[18]. When African Americans compare their poor resources and lower SES to their non-Hispanic White counterparts, this can lead to a negative self-perception as disadvantaged and inferior in comparison to Whites[5]. However, racial/ethnic disparities in self-esteem have not been consistent[9]. Little empirical evidence exists to support the inconsistent findings during adulthood. Therefore, further exploration is needed to determine whether risk factors that lead to low self-esteem differ across racial/ethnic groups.

The current study

Given that different levels of self-esteem across individuals and racial/ethnic groups may lead to disparities in quality of life, exploring which factors contribute to unequal levels of self-esteem should be investigated. The research questions in this study are as follows: (1) Are there racial/ethnic disparities in economic well-being after controlling for individual characteristics? (2) How does economic well-being influence self-esteem? and (3) Does this association differ across race/ethnicity? We hypothesize that: (1) There are racial/ethnic disparities in poverty, employment, fringe benefits, and job satisfaction; (2) Economic well-being (employment, poverty, fringe benefits, and job satisfaction) influences self-esteem; and (3) Race/ethnicity moderates the relationship between economic well-being and self-esteem. Findings from this study expand on prior research in several ways: Focusing on adults' self-esteem rather than adolescents, looking at racial/ethnic disparities in self-esteem among adults, better understanding of economic well-being by including factors that have not been addressed in previous studies, and examining racial/ethnic disparities in the relationship between economic well-being and self-esteem.

MATERIALS AND METHODS

Target sample

The primary data source for the proposed study is the National Longitudinal Survey of Youth 1979 (NLSY79), which was conducted by the United States Department of Labor. The NLSY79 is a nationwide representative data set of 12686 participants living in the United States whose ages ranged from 14 to 22 years back in 1979, when the survey was first conducted. The NLSY79 participants have been re-interviewed annually from 1979 through 1994 and biennially since then. The initial response rate was approximately 90% with retention rates over 90% in the first 16 waves, and the rates in subsequent waves were over 80%. The NLSY79 measured self-esteem in 1980, 1987, and 2006. The current study uses data from the NLSY79 for the year 2006, which is the latest wave of the NLSY79 available, to access findings related to self-esteem in order to explore the effect of economic well-being on self-esteem. The final sample from the 2006 wave consists of 2267 African Americans, 1425 Hispanics, and 3678 non-Hispanic Whites, and those who were not interviewed (non-interview) or refused to be interviewed were excluded from the study. Of the 7370 participants, males made up 48.7% (3589) while females accounted for 51.3% (3781).

Measures

Self-esteem: The Rosenberg Self-Esteem Scale was used to measure respondents' self-esteem. The scale illustrates a level of approval or disapproval toward oneself[43]. The Rosenberg Self-Esteem Scale consists of 10 items with a four-point Likert-type scale ranging from 0 (strongly disagree) to 3 (strongly agree). Five items were reversed prior to using the scale for analysis. All items were summed with higher scores indicating higher self-esteem (range 5-30; mean ± SD = 23.48 ± 4.45).

Poverty: Poverty indicates whether individuals' total family income was above or below the poverty level. The poverty variable was classified into two groups: Those who were above the poverty level (coded = 0) and those who were below the poverty level (coded = 1).

Job satisfaction: Respondents were queried about their levels of job satisfaction regarding up to five jobs. Respondents were asked how they felt about current/recent jobs with a four-point scale ranging from 1 (very like) to 4 (very dislike). All items concerning jobs were reverse-scored prior to conducting the analysis, with a higher score indicating higher satisfaction with their jobs. Total job satisfaction scores were computed by calculating the mean of individual items (range 1-4; mean ± SD = 3.36 ± 0.65).

Employment: Respondents reported their employment status by answering one of the following conditions: Employed, unemployed, out of labor force, or in active forces. The respondents were classified into two groups: Those who were employed (coded = 1) and those who were not (coded = 0).

Fringe benefits

Respondents answered yes/no about whether they received any of nine fringe benefits from up to five of their jobs: Hospital and life insurance, paid vacation and sick days, dental benefits, maternity/paternity leave, retirement plans, profit sharing, training, childcare, and flexible work schedule hours. The respondents answered either yes (coded = 1) if they had ever received the benefits or no (coded = 0) if they had not. Total fringe benefits were computed by adding all answers (range 0-35; mean ± SD = 6.18 ± 3.76).

Baseline variables

Demographics variables were included as covariates in this study as follows: Age, gender, education, urban/rural residence, and marital status.

Analysis strategies

Ordinary linear regression analyses and logistic regression analyses were conducted to examine whether there are racial/ethnic disparities in economic well-being after controlling for individual characteristics. Ordinary linear regression analyses tested whether economic well-being influences self-esteem and if this association differs across race/ethnicity.

RESULTS

Table 1 indicates racial/ethnic differences in variables used in the current study. Hispanics reported lower levels of self-esteem than African Americans and non-Hispanic Whites. With respect to economic well-being, African Americans were more likely to receive fringe benefits than Hispanics. On the other hand, Hispanics indicated higher job satisfaction compared with African Americans and non-Hispanic Whites. Both African Americans and Hispanics were vulnerable to low levels of income: They were more likely to be in poverty and unemployed and received less education than non-Hispanic Whites. In addition, both African Americans and Hispanics were less likely to be currently married in comparison with non-Hispanic Whites.

Findings for research question 1: Are there racial/ethnic disparities in economic well-being after controlling for individual characteristics?

Table 1 Sample characteristics by race/ethnicity (mean ± SD)

Variables	African American (*n* = 2267), %	Hispanic (*n* = 1425), %	Non-Hispanic White (*n* = 3678), %	Total (*n* = 7370)	*P* value
Self-esteem	23.66 (4.48)	22.91 (4.48)	23.59 (4.41)	23.48 (4.45)	[a,c]
Economic well-being					
Fringe benefits	6.40 (4.06)	5.95 (3.82)	6.12 (3.55)	6.18 (3.76)	[a]
Job satisfaction	3.32 (0.67)	3.41 (0.63)	3.36 (0.65)	3.36 (0.65)	[a,c]
Poverty	24.1	17.1	7.7	14.5	[a,b,c]
Employment	74.7	78.0	83.4	79.7	[a,b,c]
Demographics					
Age (yr)	44.57 (2.22)	44.50 (2.25)	44.58 (2.27)	44.56 (2.25)	
Gender (male)	49.0	49.5	48.2	48.7	
Education (non-higher education)	73.1	74.6	56.8	65.2	[b,c]
Urban resident	85.7	89.1	67.6	77.3	[a,b,c]
Marital status (marriage)	35.5	54.3	67.4	55.1	[a,b,c]

[a]Significant difference between African American and Hispanic at 0.05.
[b]Significant difference between African American and non-Hispanic White at 0.05.
[c]Significant difference between Hispanic and non-Hispanic White at 0.05.

As shown in Model 1 of Table 2, African Americans were more likely to receive fringe benefits than non-Hispanic Whites (β = 0.33, t = 2.70, P < 0.01). There were no significant disparities between Hispanics and non-Hispanic Whites. Model 2 of Table 2 indicated that the racial/ethnic disparities in fringe benefits between African Americans and non-Hispanic Whites remained significant (β = 0.52, t = 0.06, P < 0.001) after controlling for demographics. Individuals with higher education (β = -1.12, t = -10.09, P < 0.001, living in urban areas (β = 0.52, t = 3.97, P < 0.001), and who were married (β = 0.42, t = 3.81, P < 0.001) were more likely to receive the fringe benefits. On the other hand, Hispanics had higher levels of job satisfaction in comparison with non-Hispanic Whites (β = 0.05, t = 2.27, P < 0.05). When demographic variables were entered into the model, Hispanics remained significant, indicating greater job satisfaction compared with non-Hispanic Whites (β = 0.07, t = 2.98, P < 0.01). Respondents who had higher education and were married were more satisfied with their jobs (β = -0.06, t = -3.15, P < 0.01; β = 0.09, t = 4.65, P < 0.001).

Table 3 indicates racial/ethnic disparities in poverty and employment. Both African Americans [β = 1.40, Wald = 242.12, odds ratio (OR) = 4.05, P < 0.001] and Hispanics (β = 0.84, Wald = 57.94, OR = 2.30, P < 0.001) were more likely to be in poverty in comparison with non-Hispanic Whites (Model 1). The significant differences remained after controlling for demographics (Model 2). More African Americans (β = -0.56, Wald = 60.81, OR = 0.57, P < 0.001) and Hispanics (β = -0.30, Wald = 11.73, OR = 0.74, P < 0.01) were unemployed than non-Hispanic Whites (Model 1). As demographics were entered into the model, these disparities remained significant between African Americans and non-Hispanic Whites (β = -0.27, Wald = 11.38, OR = 0.77, P < 0.01) while there was no significant association between Hispanics and non-Hispanic Whites. Females were more likely to be in a low-income family (β = -0.53, Wald = 39.12, OR = 0.59, P < 0.001) and be unemployed compared to males (β = 0.53, Wald= 62.83, OR = 1.70, P < 0.001). In addition, individuals with low levels of education were significantly associated with poverty (β = 1.34, Wald = 126.70, OR = 3.82, P < 0.001) and unemployment (β = -0.76, Wald = 92.81, OR = 0.47, P < 0.001). Lastly, married individuals were less likely to end up in poverty (β = -2.01, Wald = 348.81, OR = 0.13, P < 0.001) or be unemployed (β = 0.58, Wald = 70.44, OR = 1.79, P < 0.001).

Findings for research question 2: How does economic well-being influence self-esteem and does this association differ across race/ethnicity?

As shown in the Table 4, there were significant racial/ethnic differences in self-esteem. Model 1 indicated that African Americans were more likely to have greater levels of self-esteem compared with non-Hispanic Whites (β = 0.26, t =1.85, P < 0.1). Model 2 showed that the racial/ethnic disparities between African Americans' and non-Hispanic Whites' self-esteem remained significant (β = 0.67, t = 4.53, P < 0.001) after controlling for demographics. Model 3 indicated that African Americans' elevated levels of self-esteem significantly persisted even after controlling for economic well-being (β = 0.70, t = 4.72, P < 0.001). Males were more likely to have greater self-esteem (β = 0.27, t = 2.21, P < 0.05). Having less education (β = -1.21, t = -9.34, P < 0.001) was negatively associated with self-esteem, while being married (β = 0.45, t = 3.42, P < 0.01) was positively associated with self-esteem.

With respect to economic well-being, those who received fringe benefits (β = 0.07, t = 3.90, P < 0.001) were more satisfied with their jobs (β = 0.77, t = 8.28, P < 0.001), and those who were employed (β = 0.56, t = 2.46, P < 0.05) were more likely to have higher levels of self-esteem. Poverty was negatively associated with self-esteem (β = -1.25, t = -5.23, P < 0.001). Interaction effects were found between African Americans and fringe benefits predicting self-esteem (β = 0.13, t =

Table 2 Regression results of unstandardized coefficients (standard error) and (standardized coefficients) predicting economic well-being

Variables	Economic well-being			
	Fringe benefits		Job satisfaction	
	Model 1	Model 2	Model 1	Model 2
(Constant)	6.12 (0.07)	6.06 (1.05)	3.35 (0.01)	3.24 (0.18)
Ethnicity				
African American	0.33	0.52	-0.03	0.00
	(0.12)	(0.13)	(0.02)	(0.02)
	[0.04][b]	[0.06][c]	[-0.02]	[0.00]
Hispanic	-0.06	0.08	0.05	0.07
	(0.14)	(0.15)	(0.02)	(0.03)
	[-0.01]	[0.01]	[0.03][a]	[0.04][b]
Ages		0.00		0.00
		(0.02)		(0.00)
		[0.00]		[0.01]
Gender (male)		-0.02		-0.02
		(0.11)		(0.02)
		[-0.00]		[-0.02]
Education (non-higher education)		-1.12		-0.06
		(0.11)		(0.02)
		[-0.15][c]		[-0.04][b]
Residence (urban)		0.52		0.01
		(0.13)		(0.02)
		[0.06][c]		[0.01]
Marital status (marriage)		0.42		0.09
		(0.11)		(0.02)
		[0.06][c]		[0.07][c]

[a]$P < 0.05$.
[b]$P < 0.01$.
[c]$P < 0.001$.

1.78, $P < 0.10$) and African Americans and job satisfaction predicting self-esteem (β = -0.81, t = -3.86, $P < 0.001$). As shown in Figure 1, self-esteem among African Americans was less influenced by job satisfaction than it was among non-Hispanic Whites and Hispanics. The gap between those who were less satisfied with jobs and those who more satisfied with jobs among African Americans (0.56) was smaller than that among non-Hispanic Whites (1.43) and Hispanics (1.36).

DISCUSSION

The findings of this study suggest evidence of important racial/ethnic disparities both in economic well-being and self-esteem for adults. In terms of economic well-being, African Americans were more likely to be in poverty and be unemployed in comparison with non-Hispanic Whites and received significantly greater fringe benefits than their counterparts. Hispanics were at greater risk of unemployment compared with non-Hispanic Whites; however, they were more satisfied with their jobs than non-Hispanic Whites. Also, African Americans reported higher self-esteem compared with non-Hispanic Whites. With regard to the relationship between economic well-being and mental health, those who received fringe benefits were more satisfied with jobs, and those who were employed reported higher levels of self-esteem. Furthermore, poverty was negatively associated with self-esteem. Interaction effects were found: African American ethnicity moderates the relationship between fringe benefits and self-esteem, as well as the relationship

Table 3 Logistic regression coefficients (Wald) [odds ratio] of predicting economic well-being

Variables	Economic well-being							
	Poverty		95%CI		Employment		95%CI	
	Model 1	Model 2			Model 1	Model 2		
(Constant)	-2.56 (0.07)	-3.10 (0.85)	Lower	Upper	-3.45 (2.35)	1.96 (0.66)	Lower	Upper
Ethnicity								
African American	1.40	0.83	1.89	2.80	-0.56	-0.27	0.66	0.89
	(242.12)	(69.73)			(60.81)	(11.48)		
	[4.05][c]	[2.30][c]			[0.57][c]	[0.77][b]		
Hispanic	0.84	0.54	1.36	2.18	-0.30	-0.90	0.76	1.09
	(57.94)	(20.22)			(11.73)	(1.03)		
	[2.30][c]	[1.72][c]			[0.74][b]	[0.91]		
Ages		0.02	0.99	1.06		-0.01	0.96	1.02
		(1.49)				(0.37)		
		[1.02]				[0.99]		
Gender (male)		-0.53	0.50	0.70		0.53	1.19	1.94
		(39.12)				(62.83)		
		[0.59][c]				[1.70][c]		
Education (non-higher education)		1.34	3.02	4.82		-0.76	0.40	0.55
		(126.70)				(92.81)		
		[3.82][c]				[0.47][c]		
Residence (urban)		-0.35	0.57	0.87		-0.02	0.83	1.15
		(10.62)				(0.07)		
		[0.71][b]				[0.98]		
Marital status (marriage)		-2.01	0.11	0.17		0.58	1.56	2.05
		(348.81)				(70.44)		
		[0.13][c]				[1.79][c]		

[a]$P < 0.05$.
[b]$P < 0.01$.
[c]$P < 0.001$.
CI: Confidence intervals.

between job satisfaction and self-esteem.

In terms of income-related factors, findings among African Americans and Hispanics are consistent with previous research indicating lower levels of economic well-being across racial/ethnic minority populations[23,24], with results showing higher rates of unemployment and poverty in these groups. However, although they are less likely to be employed compared to non-Hispanic Whites, the findings from this study provide evidence that African Americans are more protected by fringe benefits compared to non-Hispanic Whites once they are employed.

While there are no studies that focus specifically on racial/ethnic disparities using a comprehensive measure of fringe benefits, previous work has shown that minorities are less likely to have employer-sponsored health plans[44], a form of fringe benefits. In addition, African Americans and Hispanics are less likely than non-Hispanic Whites to have health insurance, and uninsured minorities tend not to buy private insurance compared with uninsured non-Hispanic Whites. Our study adds to this literature by showing that, with a more comprehensive measure of fringe benefits, African Americans report higher fringe benefits than non-Hispanic Whites. As African Americans are more likely to have lower SES compared with non-Hispanic Whites, they may actively seek out jobs that provide employer-based benefits in order to supplement a lack of access to health insurance. These efforts may be related to the findings that they received more fringe benefits than non-Hispanic Whites, who may seek fringe benefits less often due to higher income. In other words, fringe benefits may play a role as an alternative to social insurance or social safety nets by covering some parts of social benefits.

Table 4 Regression results of unstandardized coefficients, (standard error), and [standardized coefficients] predicting self-esteem

Variables	Self-esteem			
	Model 1	Model 2	Model 3	Model 4
(Constant)	23.78 (0.09)	24.54 (1.23)	21.37 (1.26)	20.16 (1.30)
Ethnicity				
African American	0.27	0.67	0.70	3.02
	(0.14)	(0.15)	(0.15)	(0.74)
	[0.03][a]	[0.07][d]	[0.08][d]	[0.33][d]
Hispanic	-0.35	-0.05	-0.10	1.70
	(0.17)	(0.17)	(0.17)	(0.92)
	[-0.03][b]	[-0.01]	[-0.01]	[0.16][a]
Ages		-0.02	-0.02	-0.02
		(0.03)	(0.03)	(0.03)
		[-0.01]	[-0.01]	[-0.01]
Gender (male)		0.26	0.27	0.29
		(0.12)	(0.12)	(0.12)
		[0.03][b]	[0.03][b]	[0.04][b]
Education (non-higher education)		-1.43	-1.21	-1.19
		(0.13)	(0.13)	(0.13)
		[-0.16][d]	[-0.14][d]	[-0.14][d]
Residence (urban)		0.10	0.05	0.02
		(0.15)	(0.15)	(0.15)
		[0.01]	[0.00]	[0.00]
Marital status (marriage)		0.72	0.45	0.42
		(0.13)	(0.13)	(0.14)
		[0.08][d]	[0.05][c]	[0.05][c]
Economic well-being				
Fringe benefits			0.07	0.07
			(0.02)	(0.02)
			[0.06][d]	[0.06][d]
Job satisfaction			0.77	1.10
			(0.09)	(0.13)
			[0.12][d]	[0.17][d]
Poverty			-1.25	-1.23
			(0.24)	(0.24)
			[-0.08][d]	[-0.08][d]
Employment			0.56	0.57
			(0.23)	(0.23)
			[0.04][b]	[0.04][b]
Fringe benefits X, African American				0.13
				(0.07)
				[0.05][a]
Fringe benefits X, Hispanic				-0.14

	(0.09)
	[-0.05]
Job satisfaction X, African American	-0.81
	(0.21)
	[-0.30][d]
Job satisfaction X, Hispanic	-0.40
	(0.26)
	[-0.13]

[a]$P < 0.10$.
[b]$P < 0.05$.
[c]$P < 0.01$.
[d]$P < 0.001$.

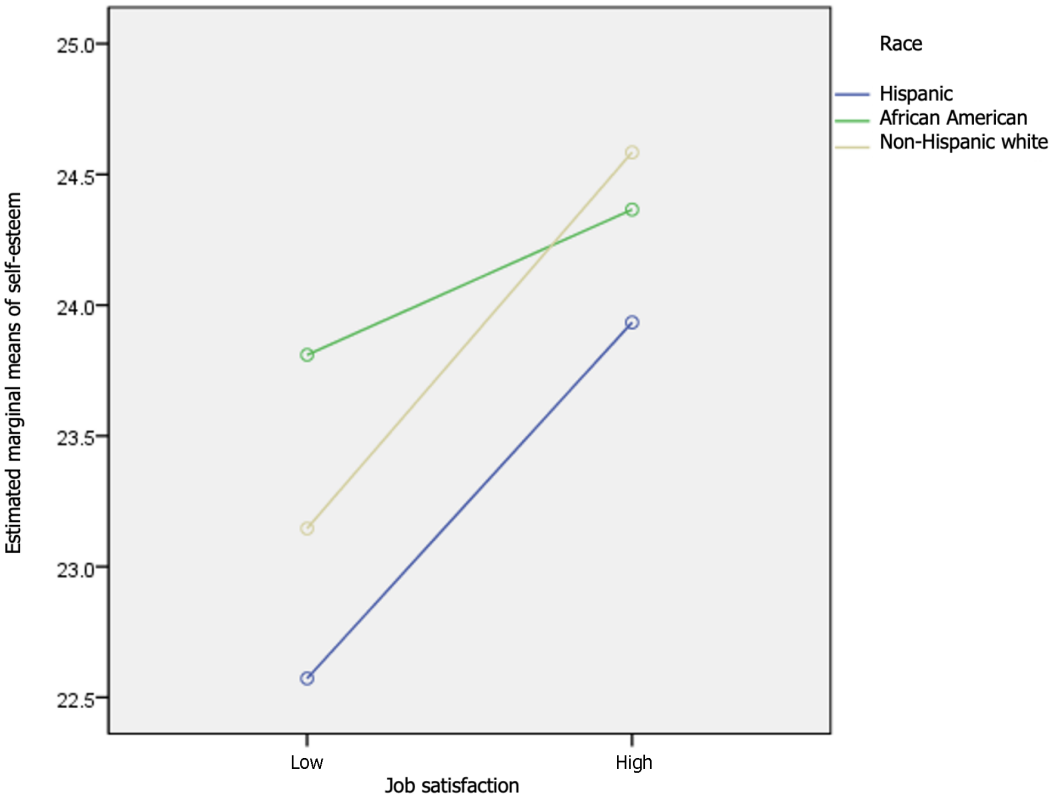

Figure 1 Effects of job satisfaction and race/ethnicity on self-esteem.

Hispanics may be likely to commit to their workplace compared to their counterparts due to greater levels of job satisfaction. Furthermore, as minorities with greater job satisfaction may be more productive in the workplace, their work may result in greater performance and contribute to a more productive society. In other words, impacts of employment may be much more extensive in Hispanics. As such, increasing levels of job satisfaction is important to improve the quality of minorities' lives while also building a productive workplace.

In terms of self-esteem, consistent with prior studies that African Americans reported greater levels of self-esteem[5,10], this study also shows African Americans reporting higher self-esteem. This result provides further evidence that racial/ethnic differences in self-esteem have continued from adolescence to adulthood. Previous research has mainly addressed self-esteem among adolescents rather than adults[2,3,5]. However, given that adulthood is another stage of life entering into new environments and tasks, self-esteem is still important in understanding adulthood as self-esteem influences individuals' success or performance[2]. In particular, as most individuals are employed when they become adults, it is necessary to examine how economic factors influence their self-esteem. On the other hand, this study demonstrates the associations between economic factors and self-esteem among adults. Consistent with previous studies [30,31], findings indicate that unemployed individuals and those in poverty are more likely to have poor self-esteem. In addition, those who received more fringe benefits and are more satisfied with their jobs are more likely to develop greater

levels of self-esteem. Given that little is known about the relationship between economic well-being, which is affected by factors such as job satisfaction and fringe benefits, and self-esteem, findings of the current study shed light on the importance of examining economic factors other than just poverty or employment, which were the primary focus of earlier research. In particular, because we found that individuals with higher job satisfaction and greater support from their workplace have better self-esteem, and workers with greater self-esteem are more likely to perform better work, employers should be encouraged to create a positive environment in the workplace and expand the benefits they offer to employees.

CONCLUSION

Findings from this study reveal that African Americans moderate the relationships between job satisfaction and self-esteem. Job satisfaction among African Americans had less of an effect on increasing self-esteem, whereas job satisfaction had a great impact on increasing levels of self-esteem among non-Hispanic Whites. Generally, greater numbers of non-Hispanic Whites already meet their basic needs through sufficient income than African Americans, and, as such, they do not need to receive benefits to maintain their daily lives because their physiological needs are more satisfied than those of African Americans. Consequently, satisfactory outcomes or feelings of happiness from the workplace may be more important to them, while African Americans may seek out tangible benefits rather than personal satisfaction with their jobs. For these reasons, fringe benefits have a greater effect on the self-esteem of African Americans, while job satisfaction has a greater effect on the self-esteem of non-Hispanic Whites. These findings offer further evidence that employment-based benefits are critical to increase levels of self-esteem for African Americans who have entered into labor markets and job satisfaction is more important for non-Hispanic Whites' self-esteem in adulthood.

Although the current study provides important information on the relationships between economic well-being and self-esteem in the context of race/ethnicity, the findings from this study should be interpreted in the context of limitations. The proposed study was conducted by ordinary linear regression and logistic regression even though the NLSY79 measured self-esteem throughout three separate waves for a longitudinal study: 1980, 1987, and 2006. Given that few respondents might be employed in the labor market before their early 20s, it is not reasonable to consider economic well-being factors in 1980 and 1987. However, given that it is limited to capturing the complexity of the relationship between economic well-being and self-esteem, further study should use longitudinal data set to identify the cumulative effects of economic well-being on self-esteem during adulthood as well as to examine the causal relationships. While the current study includes new factors of economic well-being, such as job satisfaction and fringe benefits, it is necessary to include additional factors, such as welfare benefits, in order to explore different effects of employment-based benefits and government support. Furthermore, the current study indicated that other socio-demographics were related to self-esteem. Although the main focus of this study identified racial and ethnic disparities in the association between economic well-being and self-esteem, we suggest that future studies may show a benefit from a deeper exploration of how other factors interact with economic well-being and self-esteem.

ARTICLE HIGHLIGHTS

Research background

Little attention has been given to examining whether other aspects of economic well-being may impact self-esteem during adulthood. Given differences in levels of self-esteem and economic well-being across racial/ethnic groups, it is necessary to identify how race/ethnicity may moderate the relationship between economic well-being and self-esteem.

Research motivation

Little is known about how aspects of economic well-being beyond standard measures of socioeconomic status (*e.g.*, poverty and employment), such as job satisfaction and fringe benefits, influence self-esteem; the majority of this work has focused primarily on the influence of economic well-being on self-esteem in adolescence or childhood rather than adulthood.

Research objectives

This study aims to explore the relationships between economic well-being (employment, poverty, fringe benefits, and job satisfaction) and self-esteem, and investigate the moderating effects of race/ethnicity on the association between economic well-being and self-esteem.

Research methods

Using secondary data, ordinary linear regression analyses and logistic regression analyses were conducted.

Research results

African Americans and Hispanics were more likely to be in poverty in comparison with non-Hispanic Whites. More African Americans were unemployed than Whites. Those who received fringe benefits, were more satisfied with jobs, and those who were employed were more likely to have higher levels of self-esteem. Poverty was negatively associated with

self-esteem. Interaction effects were found between African Americans and job satisfaction predicting self-esteem.

Research conclusions

Satisfactory outcomes or feelings of happiness from the workplace may be more important to Non-Hispanic Whites, while African Americans may seek out tangible benefits rather than personal satisfaction with their jobs. Employment-based benefits are critical to increase levels of self-esteem for African Americans who have entered into labor markets and job satisfaction is more important for non-Hispanic Whites' self-esteem in adulthood.

Research perspectives

We suggest that future studies may show a benefit from a deeper exploration of how other factors interact with economic well-being and self-esteem, and that the use of a longitudinal data set could identify the cumulative effects of economic well-being on self-esteem during adulthood as well as the causal relationships.

FOOTNOTES

Author contributions: Author has read and approved the final manuscript.

Institutional review board statement: This is not applicable as this study used secondary data which are publicly accessible.

Informed consent statement: Not applicable in this study.

Conflict-of-interest statement: The author declares that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Data sharing statement: Data has been made publicly available *via* National Longitudinal Surveys and can be accessed at https://www.nlsinfo.org/content/cohorts/nlsy79.

STROBE statement: The authors have read the STROBE Statement—checklist of items, and the manuscript was prepared and revised according to the STROBE Statement—checklist of items.

Country/Territory of origin: South Korea

ORCID number: Jaewon Lee 0000-0002-8479-4586.

S-Editor: Fan JR
L-Editor: Webster JR
P-Editor: Zhang XD

REFERENCES

1 **Orth U**, Robins RW. The development of self-esteem. *Curr Dir Psychol Sci* 2014; **23**: 381-387 [DOI: 10.1177/09637214145474]
2 **Trzesniewski KH**, Donnellan MB, Moffitt TE, Robins RW, Poulton R, Caspi A. Low self-esteem during adolescence predicts poor health, criminal behavior, and limited economic prospects during adulthood. *Dev Psychol* 2006; **42**: 381-390 [PMID: 16569175 DOI: 10.1037/0012-1649.42.2.381]
3 **Donnellan MB**, Trzesniewski KH, Robins RW, Moffitt TE, Caspi A. Low self-esteem is related to aggression, antisocial behavior, and delinquency. *Psychol Sci* 2005; **16**: 328-335 [PMID: 15828981 DOI: 10.1111/j.0956-7976.2005.01535.x]
4 **John OP**, Robins RW. Handbook of personality: Theory and research. 4th ed. London, England: Guilford Press, 2021
5 **Bachman JG**, O'Malley PM, Freedman-Doan P, Trzesniewski KH, Donnellan MB. Adolescent Self-Esteem: Differences by Race/Ethnicity, Gender, and Age. *Self Identity* 2011; **10**: 445-473 [PMID: 22279425 DOI: 10.1080/15298861003794538]
6 **Robins RW**, Trzesniewski KH. Self-esteem development across the lifespan. *Curr Dir Psychol Sci* 2005; **14**: 158-162 [DOI: 10.1111/j.0963-7214.2005.00353]
7 **Chen W**, Niu G, Zhang D, Fan C, Tian Y, Zhou Z. Socioeconomic status and life satisfaction in Chinese adolescents: Analysis of self-esteem as a mediator and optimism as a moderator. *Pers Individ Dif* 2016; **95**: 105-109 [DOI: 10.1016/j.paid.2016.01.036]
8 **McLoyd VC**. Socioeconomic disadvantage and child development. *Am Psychol* 1998; **53**: 185-204 [PMID: 9491747 DOI: 10.1037//0003-066x.53.2.185]
9 **Sprecher S**, Brooks JE, Avogo W. Self-esteem among young adults: Differences and similarities based on gender, race, and cohort (1990–2012). *Sex Roles* 2013; **69**: 264-275 [DOI: 10.1007/s11199-013-0295-y]
10 **Twenge JM**, Crocker J. Race and self-esteem: meta-analyses comparing whites, blacks, Hispanics, Asians, and American Indians and comment on Gray-Little and Hafdahl (2000). *Psychol Bull* 2002; **128**: 371-408; discussion 409 [PMID: 12002695 DOI:

10.1037/0033-2909.128.3.371]
11 **Western B**, Bloome D, Sosnaud B, Tach L. Economic insecurity and social stratification. *Annu Rev Sociol* 2012; **38**: 341-359 [DOI: 10.1146/annurev-soc-071811-145434]
12 **Thomas ME**, Hughes M. The continuing significance of race: a study of race, class, and quality of life in America, 1972-1985. *Am Sociol Rev* 1986; **51**: 830-841 [PMID: 11613887]
13 **Unemployment rates by age**, sex, race, and Hispanic or Latino ethnicity. Bls.gov. 2022. [cited 1 October 2023]. Available from: http://www.bls.gov/web/empsit/cpsee_e16.htm
14 **Mann M**, Hosman CM, Schaalma HP, de Vries NK. Self-esteem in a broad-spectrum approach for mental health promotion. *Health Educ Res* 2004; **19**: 357-372 [PMID: 15199011 DOI: 10.1093/her/cyg041]
15 **Flory K**, Lynam D, Milich R, Leukefeld C, Clayton R. Early adolescent through young adult alcohol and marijuana use trajectories: early predictors, young adult outcomes, and predictive utility. *Dev Psychopathol* 2004; **16**: 193-213 [PMID: 15115071 DOI: 10.1017/s0954579404044475]
16 **Wantchekon KA**, McDermott ER, Jones SM, Satterthwaite-Freiman M, Baldeh M, Rivas-Drake D, Umaña-Taylor AJ. The Role of Ethnic-Racial Identity and Self-Esteem in Intergroup Contact Attitudes. *J Youth Adolesc* 2023; **52**: 2243-2260 [PMID: 37528244 DOI: 10.1007/s10964-023-01819-1]
17 **Carlson C**, Uppal S, Prosser EC. Ethnic differences in processes contributing to the self-esteem of early adolescent girls. *J Early Adolesc* 2000; **20**: 44-67
18 **Gray-Little B**, Hafdahl AR. Factors influencing racial comparisons of self-esteem: a quantitative review. *Psychol Bull* 2000; **126**: 26-54 [PMID: 10668349 DOI: 10.1037/0033-2909.126.1.26]
19 **Kernis MH**. Self-esteem issues and answers: A sourcebook of current perspectives. London, England: Psychology Press, 2013
20 **Mirowsky J**, Ross CE. Economic hardship across the life course. *Am Sociol Rev* 1999; **64**: 548-569 [DOI: 10.2307/2657255]
21 **Kahn JR**, Pearlin LI. Financial strain over the life course and health among older adults. *J Health Soc Behav* 2006; **47**: 17-31 [PMID: 16583773 DOI: 10.1177/002214650604700102]
22 **Kahn JR**, Fazio EM. Economic status over the life course and racial disparities in health. *J Gerontol B Psychol Sci Soc Sci* 2005; **60** Spec No 2: 76-84 [PMID: 16251596 DOI: 10.1093/geronb/60.special_issue_2.s76]
23 **Berkman B**. Handbook of social work in health and aging. Cary, NC: Oxford University Press, 2010
24 **Menselson T**, Rehkopf DH, Kubzansky LD. Depression among Latinos in the United States: a meta-analytic review. *J Consult Clin Psychol* 2008; **76**: 355-366 [PMID: 18540730 DOI: 10.1037/0022-006X.76.3.355]
25 **Hughes M**, Kiecolt KJ, Keith VM. How racial identity moderates the impact of financial stress on mental health among African Americans. *Soc Ment Health* 2014; **4**: 38-54 [DOI: 10.1177/2156869313509635]
26 **Federal Interagency Forum on Aging-Related Statistics**. Older Americans 2012: Key indicators of well-being. [cited 1 October 2023]. Available from: https://nepis.epa.gov/Exe/ZyPDF.cgi?Dockey=P100FDNP.PDF
27 **Ahnquist J**, Wamala SP. Economic hardships in adulthood and mental health in Sweden. The Swedish National Public Health Survey 2009. *BMC Public Health* 2011; **11**: 788 [PMID: 21989478 DOI: 10.1186/1471-2458-11-788]
28 **Stam K**, Sieben I, Verbakel E, de Graaf PM. Employment status and subjective well-being: the role of the social norm to work. *Work Employ Soc* 2016; **30**: 309-333
29 **Keyes CLM**. Subjective well-being in mental health and human development research worldwide: An introduction. *Soc Indic Res* 2006; **77**: 1-10 [DOI: 10.1007/s11205-005-5550-3]
30 **Goldsmith AH**, Darity W. Social psychology, unemployment exposure and equilibrium unemployment. *J Econ Psychol* 1992; **13**: 449-471 [DOI: 10.1016/0167-4870(92)90004-Q]
31 **Goldsmith AH**, Veum JR, William D. The impact of labor force history on self-esteem and its component parts, anxiety, alienation and depression. *J Econ Psychol* 1996; **17**: 183-220 [DOI: 10.1016/0167-4870(96)00003-7]
32 **Goldsmith AH**, Veum JR, Darity W. Unemployment, joblessness, psychological well-being and self-esteem: Theory and evidence. *J Socio Econ* 1997; **26**: 133-158 [DOI: 10.1016/S1053-5357(97)90030-5]
33 **Kalil A**, Ziol-Guest KM, Hawkley LC, Cacioppo JT. Job insecurity and change over time in health among older men and women. *J Gerontol B Psychol Sci Soc Sci* 2010; **65B**: 81-90 [PMID: 19934165 DOI: 10.1093/geronb/gbp100]
34 **Yoshikawa H**, Aber JL, Beardslee WR. The effects of poverty on the mental, emotional, and behavioral health of children and youth: implications for prevention. *Am Psychol* 2012; **67**: 272-284 [PMID: 22583341 DOI: 10.1037/a0028015]
35 **Andersen I**, Thielen K, Nygaard E, Diderichsen F. Social inequality in the prevalence of depressive disorders. *J Epidemiol Community Health* 2009; **63**: 575-581 [PMID: 19293167 DOI: 10.1136/jech.2008.082719]
36 **New economics foundation**. Well being in four policy area report. [cited 1 October 2023]. Available from: http://b.3cdn.net/nefoundation/ccdf9782b6d8700f7c_lcm6i2ed7.pdf
37 **Neymotin F**. Linking self-esteem with the tendency to engage in financial planning. *J Econ Psychol* 2010; **31**: 996-1007 [DOI: 10.1016/j.joep.2010.08.006]
38 **Burgard SA**, Lin KY. Bad Jobs, Bad Health? How Work and Working Conditions Contribute to Health Disparities. *Am Behav Sci* 2013; **57** [PMID: 24187340 DOI: 10.1177/0002764213487347]
39 **Moksnes UK**, Espnes GA. Self-esteem and life satisfaction in adolescents-gender and age as potential moderators. *Qual Life Res* 2013; **22**: 2921-2928 [PMID: 23661225 DOI: 10.1007/s11136-013-0427-4]
40 **Sowislo JF**, Orth U. Does low self-esteem predict depression and anxiety? A meta-analysis of longitudinal studies. *Psychol Bull* 2013; **139**: 213-240 [PMID: 22730921 DOI: 10.1037/a0028931]
41 **Geuskens GA**, Koppes LLJ, van den Bossche SNJ, Joling CI. Enterprise restructuring and the health of employees: a cohort study: A cohort study. *J Occup Environ Med* 2012; **54**: 4-9 [DOI: 10.1097/JOM.0b013e31823c766e]
42 **Stansfeld S**, Candy B. Psychosocial work environment and mental health--a meta-analytic review. *Scand J Work Environ Health* 2006; **32**: 443-462 [PMID: 17173201 DOI: 10.5271/sjweh.1050]
43 **Crocker J**, Major B. Social stigma and self-esteem: The self-protective properties of stigma. *Psychol Rev* 1989; **96**: 608-630 [DOI: 10.1037/0033-295X.96.4.608]
44 **Rosenberg M**. Society and the adolescent self-image. Princeton, NJ: Princeton University Press, 2016

World Journal of Psychiatry

Submit a Manuscript: https://www.f6publishing.com

World J Psychiatry 2024 February 19; 14(2): 308-314

DOI: 10.5498/wjp.v14.i2.308

ISSN 2220-3206 (online)

ORIGINAL ARTICLE

Prospective Study

Risk factors for cognitive impairment in patients with chronic kidney disease

Xiao-Hui Wang, Yong He, Huan Zhou, Ting Xiao, Ran Du, Xin Zhang

Specialty type: Psychiatry

Provenance and peer review: Unsolicited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

Grade A (Excellent): 0
Grade B (Very good): B
Grade C (Good): C
Grade D (Fair): 0
Grade E (Poor): 0

P-Reviewer: Reid RD, Canada; Susen Y, Turkey

Received: October 30, 2023
Peer-review started: October 30, 2023
First decision: November 8, 2023
Revised: December 1, 2023
Accepted: January 5, 2024
Article in press: January 5, 2024
Published online: February 19, 2024

Xiao-Hui Wang, Yong He, Huan Zhou, Ting Xiao, Xin Zhang, Department of Nephrology, The Fifth Hospital of Wuhan, Wuhan 430050, Hubei Province, China

Ran Du, Department of Nephrology, The Central Hospital of Enshi Tujia and Miao Autonomous Prefecture, Enshi 445000, Hubei Province, China

Corresponding author: Xin Zhang, MMed, Associate Chief Physician, Department of Nephrology, The Fifth Hospital of Wuhan, No. 122 Xianzheng Street, Hanyang District, Wuhan 430050, Hubei Province, China. 13437187830@163.com

Abstract

BACKGROUND

Chronic kidney disease (CKD) patients have been found to be at risk of concurrent cognitive dysfunction in previous studies, which has now become an important public health issue of widespread concern.

AIM

To investigate the risk factors for concurrent cognitive dysfunction in patients with CKD.

METHODS

This is a prospective cohort study conducted among patients with CKD between October 2021 and March 2023. A questionnaire was formulated by literature review and expert consultation and included questions about age, sex, education level, per capita monthly household income, marital status, living condition, payment method, and hypertension.

RESULTS

Logistic regression analysis showed that patients aged 60-79 years [odds ratio (OR) = 1.561, P = 0.015] and ≥ 80 years (OR = 1.760, P = 0.013), participants with middle to high school education (OR = 0.820, P = 0.027), divorced or widowed individuals (OR = 1.37, P = 0.032), self-funded patients (OR = 2.368, P = 0.008), and patients with hypertension (OR = 2.011, P = 0.041) had a higher risk of cognitive impairment. The risk of cognitive impairment was lower for those with a college degree (OR = 0.435, P = 0.034) and married individuals.

CONCLUSION

The risk factors affecting cognitive dysfunction are age, 60-79 years and ≥ 80

years; education, primary school education or less; marital status, divorced or widowed; payment method, self-funded; hypertension; and CKD.

Key Words: Cognitive impairment; Cognitive dysfunction; Chronic kidney disease

Core Tip: The prevalence of cognitive impairment in patients with chronic kidney disease (CKD) ranges from 10% to 40% depending on the method of cognitive impairment assessment and CKD stage. The risk factors affecting cognitive dysfunction were age, 60-79 years and ≥ 80 years; education, primary school education or less; marital status, divorced or widowed; payment method, self-funded; hypertension; and CKD.

Citation: Wang XH, He Y, Zhou H, Xiao T, Du R, Zhang X. Risk factors for cognitive impairment in patients with chronic kidney disease. *World J Psychiatry* 2024; 14(2): 308-314
URL: https://www.wjgnet.com/2220-3206/full/v14/i2/308.htm
DOI: https://dx.doi.org/10.5498/wjp.v14.i2.308

INTRODUCTION

Chronic kidney disease (CKD) is defined as chronic impairment of renal structure and function resulting from a variety of factors that have altered the structure and function of the kidneys for more than 3 mo. It is clinically manifested by an abnormal glomerular filtration rate (GFR) caused by abnormal case injury, abnormal blood or urine composition, or unexplained reduction in GFR (< 60 mL/min/1.73 m^2) for more than 3 mo[1,2]. CKD has a large number of clinical causative factors, which are mainly divided into two categories: Primary and secondary. Secondary CKD commonly includes glomerulonephritis, tubular injury, hypertensive renal arteriosclerosis, chronic pyelonephritis, and so on, which can be divided into five stages according to GFR[3,4]. The clinical manifestations of CKD differ at different stages. Prior to CKD stage 3, the patient's clinical symptoms are not significant or are accompanied only by mild discomfort, such as fatigue, lumbar acid, or increased nocturnal urination. After CKD3, the clinical symptoms become more obvious, and renal function declines further, accompanied by hypertension, heart failure, hyperkalaemia, acid-base balance disorders, gastrointestinal disturbances, and impaired consciousness, *etc*. Some patients may develop anorexia, metabolic acidosis, or mild anaemia. And clinical studies have found that CKD stage 3 can be life-threatening in severe cases[5,6].

Cognitive impairment affects multiple cognitive domains, including orientation, attention, memory, calculation, analysis, comprehensive understanding, judgment, structural ability, and executive ability[7,8]. If a disorder occurs in one of the cognitive domains, it is named after the cognitive domain, such as memory, computing, or orientation disorders. If a disorder occurs in multiple cognitive domains, it is called an impairment. Cognitive impairment can range from mild to severe; severe impairment that impairs daily living and independence is typically referred to as dementia[9,10].

Previous studies have found a 10%-40% prevalence of concomitant cognitive dysfunction in patients with CKD by scoring cognitive function in patients with different CKD stages[11]. Studies have shown that cognitive impairment in CKD patients may be caused by different dialysis methods, GFRs, and other factors[12,13]. This study aimed to explore the risk factors for cognitive impairment in patients with CKD.

MATERIALS AND METHODS

Research contents

This is a prospective cohort study conducted among patients with CKD between October 2021 and March 2023. A questionnaire was formulated using literature review and expert consultation. The integrity of all returned questionnaires was checked before input and invalid questionnaires with logical contradictions or too many missing items were eliminated. Two hundred patients completed the questionnaire. The questionnaire included questions about age, sex, educational level, per capita monthly household income, marital status, living conditions, payment method, and hypertension.

Patient selection

The inclusion criteria were age > 18 years and willingness to cooperate with the investigation of dialysis for more than 3 mo. During the study period, patients were on good dialysis. No complications of heart failure, serious infections, malignancies, or other diseases, and no depression, other mental disorders, or long history of substance abuse, alcohol abuse, dementia, Parkinson's disease, or other neurodegenerative diseases were noted. During the external monitoring of peritoneal dialysis, patients did not take nervous system drugs or nutrition. All participants signed informed consent forms. The study was approved by the Medical Ethics Committee of our hospital. Patients who did not wish to continue

treatment at the hospital were excluded.

Materials

The Montreal Cognitive Assessment Scale is an effective and rapid screening tool for mild cognitive impairment. It targets seven cognitive domains including visuospatial and executive function, naming, attention, language, abstraction, delayed recall, and orientation[14,15]. It consists of 12 questions and 30 items. Each correct answer is worth 1 point, and an incorrect or skipped answer is worth 0 points. It takes approximately 10 min to complete the test. The total score on this scale is 30. A score of 26 points or more indicates normal cognitive function. A higher score indicates better cognitive function, and an additional point was added to the test results to correct for literacy bias.

Statistical analysis

All data were processed and analysed using R studio (4.1.0). Quantitative data are expressed as the mean ± SD. The risk factors for cognitive impairment were analysed using binary logistic regression. $P > 0.05$ was considered statistically significant.

RESULTS

Based on the inclusion and exclusion criteria, 200 patients with CKD who underwent peritoneal dialysis in our hospital were included in the study.

Univariate analysis of CKD and cognitive dysfunction in patients undergoing peritoneal dialysis

Eighty-five (42.5%) out of 200 patients had cognitive impairment. Eighty-six patients who had CKD and were undergoing peritoneal dialysis were 60-79 years old. Among them, 40.70% had cognitive impairment. There were no statistically significant differences in the incidence of cognitive dysfunction among patients according to their marital status, residence status, payment methods, and hypertension ($P < 0.05$). Table 1 presents the detailed results.

Cognitive dysfunction in patients with CKD undergoing peritoneal dialysis: Multivariate logistic regression analysis

Cognitive impairment in patients with CKD undergoing peritoneal dialysis was used as the dependent variable, and age, education level, per capita monthly family income, marital status, residence status, payment method, and hypertension were used as the independent variables. Logistic regression analysis showed that patients with CKD undergoing peritoneal dialysis aged 60-79 years [odds ratio (OR) = 1.561, $P = 0.015$] and ≥ 80 years (OR = 1.760, $P = 0.013$) had a higher risk of cognitive impairment. Participants with middle and high school education (OR = 0.820, $P = 0.027$) had a higher risk as well. The risk of cognitive impairment was lower for those with a college degree or above (OR = 0.435, $P = 0.034$) than for those with primary school education or less. The risk of cognitive impairment was lower in married than in unmarried individuals (OR = 0.817, $P = 0.046$). The risk of cognitive impairment was higher in divorced and widowed individuals than in unmarried individuals (OR = 1.37, $P = 0.032$). Self-funded patients had a higher risk as well (OR = 2.368 $P = 0.008$). Patients with hypertension had a higher risk of cognitive impairment (OR = 2.011, $P = 0.041$). Table 2 presents the detailed results.

DISCUSSION

This study found that 42.50% of patients with CKD undergoing peritoneal dialysis had cognitive impairment, which was higher than the results of a previous study[16]. This may be due to the decrease in the incidence of cognitive impairment in 26.00% of participants who were < 60 years old. Patients with normal cognitive function can better fulfill doctors' orders. During peritoneal dialysis, patients can be asked about their medication status and feelings, which is conducive to its safety. Patients with cognitive impairments may be confused about their medication status. Caregivers must confirm that patients have a reasonable understanding of the treatment, which seriously affects their quality of life.

This study suggests that the age of incidence for cognitive impairment in patients with chronic renal disease and undergoing peritoneal dialysis was 60-79 years (OR = 1.561, $P = 0.015$). Patients aged ≥ 80 years (OR = 1.760, $P = 0.013$) had a higher risk of developing cognitive impairment than patients aged < 60 years. The incidence of cognitive impairment increased with age. Studies have shown that the prevalence of cognitive impairment increases by a factor of one per five years of age[17,18]. The effectiveness of dopamine neurotransmission is reduced and the number of circulating endothelial progenitor cells decreases, which affects patients' cognitive function[19,20].

The results of this study showed that educational level is one of the factors affecting cognitive dysfunction in patients with CKD undergoing peritoneal dialysis. The risk of cognitive impairment was lower in those with primary school education or less, which is consistent with the results of previous studies indicating that the level of education has a positive effect on cognitive function[21].

The risk of cognitive impairment in married patients was lower than that in unmarried patients (OR = 0.817, $P = 0.046$), while the risk of cognitive impairment in divorced or widowed patients was higher than that in unmarried patients (OR = 1.137, $P = 0.032$), possibly because married patients receive better care and social support during peritoneal dialysis and studies have shown that social support is positively correlated with cognitive function[22].

Table 1 Univariate analysis of cognitive dysfunction in chronic kidney disease patients undergoing peritoneal dialysis

		Number	Patients with cognitive impairment	χ^2 value	*P* value
Age (yr)	< 60	50	13 (26.00%)	11.825	0.03
	60-79	86	35 (40.70%)		
	≥ 80	64	37 (57.81%)		
Sex	Female	97	46 (47.42%)	1.868	0.172
	Male	103	39 (37.86%)		
Education level	Primary school or less	60	36 (60.00%)	13.816	0.001
	Junior and senior high schools	98	39 (39.80%)		
	Junior college or above	42	10 (23.81%)		
Per capita monthly household income	Less than 3000 yuan	37	23 (62.16%)	11.543	0.003
	3000-6000 yuan	96	43 (44.79%)		
	> 6000 yuan	67	19 (28.36%)		
Marital status	Unmarried	27	11 (40.74%)	23.747	< 0.001
	Married	132	43 (32.58%)		
	Divorced or widowed	41	31 (75.61%)		
Living condition	Living alone	57	33 (57.89%)	8.757	0.013
	Living with children	42	18 (42.86%)		
	Conjugal residence	101	34 (33.66%)		
Payment method	Insurance	143	36 (25.17%)	61.63	< 0.001
	Self-funded	57	49 (85.96%)		
Hypertension	Yes	68	37 (45.41%)	5.982	0.014
	No	132	48 (36.36%)		

Table 2 Multivariate regression analysis of cognitive dysfunction in patient with chronic kidney disease undergoing peritoneal dialysis by logistic

	Reference group	Comparative group	Regression coefficient	Standard error	Wald χ^2 value	*P* value	OR	95%CI
Age	< 60	60-79	1.185	0.821	4.741	0.015	1.561	1.518-4.182
		≥ 80	1.235	0.764	4.886	0.013	1.76	1.218-2.881
Educational level	Primary school or below	Junior and senior high schools	0.735	0.855	4.842	0.027	0.82	0.218-0.881
		Junior college or above	0.403	0.236	5.636	0.034	0.435	0.273-0.764
Marital status	Unmarried	Married	0.845	0.214	1.241	0.046	0.817	0.423-0.985
		Divorced or widowed	1.134	0.138	4.312	0.032	1.137	1.001-6.013
	Payment method	Self-funded	1.185	0.31	8.864	0.008	2.368	1.608-4.486
		Insurance	1.621	0.288	27.572	0.001	2.011	1.211-5.432

OR: Odds ratio; CI: Confidence interval.

The high burden of cognitive impairment in hemodialysis and CKD patients has only recently been recognized. Recent studies have described a strong grading relationship between GFR and cognitive function in patients with CKD[23-25]. Elias *et al*[26] believed that the mechanism of association between CKD and cognition may be similar to that of hypertension or diabetes. We believe that there is a need for more research, including multiple cognitive tests, measures of everyday cognitive ability related to patients' understanding of the disease and treatment, and more research on epidemic and episodic dementia outcomes.

This study also found that hypertensive patients had a higher risk of cognitive dysfunction (OR = 2.011, P = 0.041). Peritoneal dialysis patients may experience vasculopathy during treatment, and hypertensive patients may experience altered cerebral blood flow and cerebrovascular changes, and ischemia and hypoxia may damage brain cells, leading to cognitive dysfunction[27].

CONCLUSION

By analyzing 200 patients with CKD undergoing peritoneal dialysis, we found that the risk factors affecting cognitive dysfunction include age, 60-79 years and ≥ 80 years; education, primary school education or less; marital status, divorced or widowed; payment method, self-funded; hypertension; and CKD. Medical staff should assess the cognitive function of patients at the right time and pay regular attention to changes in the patients' cognitive function.

ARTICLE HIGHLIGHTS

Research background

Chronic kidney disease (CKD) patients have been found to be at risk of concurrent cognitive dysfunction in previous studies, which has now become an important public health issue of widespread concern.

Research motivation

Studies have shown that cognitive impairment in CKD patients may be caused by different dialysis methods and glomerular filtration rates.

Research objectives

This object of this study is to explore the risk factors for cognitive impairment in patients with CKD.

Research methods

We conducted the prospective cohort study between October 2021 and March 2023 in renal internal medicine. A questionnaire was formulated by the method of literature and expert consultation. The questionnaire included questions about age, sex, education level, per capita monthly household income, marital status, living condition, payment method, and hypertension.

Research results

Two hundred patients with CKD undergoing peritoneal dialysis at the hospital were included in this study. Logistic regression analysis showed that patients with CKD undergoing peritoneal dialysis aged 60-79 years [odds ratio (OR) = 1.561, P = 0.015] and ≥ 80 years (OR = 1.760, P = 0.013) had a higher risk of cognitive impairment. Participants with middle and high school education (OR = 0.820, P = 0.027) had a higher risk of cognitive impairment. However, the risk of cognitive impairment was lower for those with a college degree or more (OR = 0.435, P = 0.034) than for those with primary school education or less. The risk of cognitive impairment was lower in married than in unmarried individuals (OR = 0.817, P = 0.046). The risk of cognitive impairment was higher in divorced and widowed individuals than in unmarried individuals (OR = 1.37, P = 0.032). Self-funded patients a higher risk of cognitive impairment (OR = 2.368 P = 0.008). Individuals with hypertension had a higher risk of cognitive impairment (OR = 2.011, P = 0.041).

Research conclusions

The risk factors affecting cognitive dysfunction include age, 60-79 years and ≥ 80 years; education, primary school education or less; marital status, divorced or widowed; payment method, self-funded; hypertension; and CKD, which gradually decreases with continuous peritoneal dialysis.

Research perspectives

Medical staff should assess the cognitive function of patients at the right time and pay regular attention to changes in the patients' cognitive function.

FOOTNOTES

Co-first authors: Xiao-Hui Wang and Ran Du.

Author contributions: Wang XH, Zhang X, and Du R contributed equally to this work; Wang XH, He Y, Zhou H, Xiao T, Du R, and Zhang X designed the research study, and performed the research; Wang XH and Zhang X contributed new reagents and analytic tools; Wang XH, Zhou H, and Zhang X analyzed the data and wrote the manuscript; and all authors have read and approved the final manuscript.

Institutional review board statement: The study was reviewed and approved by the Fifth Hospital of Wuhan Institutional Review Board.

Clinical trial registration statement: The study was registered at the Clinical Trial Center (www.researchregistry.com) with registration number (researchregistry10159).

Informed consent statement: All study participants, or their legal guardian, provided informed written consent prior to study enrollment.

Conflict-of-interest statement: All the authors report no relevant conflicts of interest for this article.

Data sharing statement: No additional data are available.

CONSORT 2010 statement: The authors have read the CONSORT 2010 Statement, and the manuscript was prepared and revised according to the CONSORT 2010 Statement.

Country/Territory of origin: China

ORCID number: Xiao-Hui Wang 0009-0008-1420-2662; Yong He 0009-0009-7802-3070; Huan Zhou 0000-0002-5185-313X; Xin Zhang 0009-0000-9687-4375.

S-Editor: Wang JJ
L-Editor: Wang TQ
P-Editor: Zhang YL

REFERENCES

1 **Olsen E**, van Galen G. Chronic Renal Failure-Causes, Clinical Findings, Treatments and Prognosis. *Vet Clin North Am Equine Pract* 2022; **38**: 25-46 [PMID: 35365250 DOI: 10.1016/j.cveq.2021.11.003]
2 **Ellis P**. An overview of haemodialysis. *Br J Nurs* 2023; **32**: 356-360 [PMID: 37083382 DOI: 10.12968/bjon.2023.32.8.356]
3 **Zhang W**, Li P, Zhou H. Mid-short-term risk factors for chronic renal failure in children with posterior urethral valve. *Pediatr Surg Int* 2022; **38**: 1321-1326 [PMID: 35779105 DOI: 10.1007/s00383-022-05154-7]
4 **Flagg AJ**. Chronic Renal Therapy. *Nurs Clin North Am* 2018; **53**: 511-519 [PMID: 30388977 DOI: 10.1016/j.cnur.2018.07.002]
5 **Kanda H**, Hirasaki Y, Iida T, Kanao-Kanda M, Toyama Y, Chiba T, Kunisawa T. Perioperative Management of Patients With End-Stage Renal Disease. *J Cardiothorac Vasc Anesth* 2017; **31**: 2251-2267 [PMID: 28803771 DOI: 10.1053/j.jvca.2017.04.019]
6 **Price IN**, Wood AF. Chronic kidney disease and renal replacement therapy: an overview for the advanced clinical practitioner. *Br J Nurs* 2022; **31**: 124-134 [PMID: 35152740 DOI: 10.12968/bjon.2022.31.3.124]
7 **Jongsiriyanyong S**, Limpawattana P. Mild Cognitive Impairment in Clinical Practice: A Review Article. *Am J Alzheimers Dis Other Demen* 2018; **33**: 500-507 [PMID: 30068225 DOI: 10.1177/1533317518791401]
8 **Sanford AM**. Mild Cognitive Impairment. *Clin Geriatr Med* 2017; **33**: 325-337 [PMID: 28689566 DOI: 10.1016/j.cger.2017.02.005]
9 **Morley JE**. An Overview of Cognitive Impairment. *Clin Geriatr Med* 2018; **34**: 505-513 [PMID: 30336985 DOI: 10.1016/j.cger.2018.06.003]
10 **Campbell NL**, Unverzagt F, LaMantia MA, Khan BA, Boustani MA. Risk factors for the progression of mild cognitive impairment to dementia. *Clin Geriatr Med* 2013; **29**: 873-893 [PMID: 24094301 DOI: 10.1016/j.cger.2013.07.009]
11 **Drew DA**, Weiner DE, Sarnak MJ. Cognitive Impairment in CKD: Pathophysiology, Management, and Prevention. *Am J Kidney Dis* 2019; **74**: 782-790 [PMID: 31378643 DOI: 10.1053/j.ajkd.2019.05.017]
12 **Harhay MN**, Xie D, Zhang X, Hsu CY, Vittinghoff E, Go AS, Sozio SM, Blumenthal J, Seliger S, Chen J, Deo R, Dobre M, Akkina S, Reese PP, Lash JP, Yaffe K, Kurella Tamura M; CRIC Study Investigators. Cognitive Impairment in Non-Dialysis-Dependent CKD and the Transition to Dialysis: Findings From the Chronic Renal Insufficiency Cohort (CRIC) Study. *Am J Kidney Dis* 2018; **72**: 499-508 [PMID: 29728316 DOI: 10.1053/j.ajkd.2018.02.361]
13 **Zhang YH**, Yang ZK, Wang JW, Xiong ZY, Liao JL, Hao L, Liu GL, Ren YP, Wang Q, Duan LP, Zheng ZX, Dong J. Cognitive Changes in Peritoneal Dialysis Patients: A Multicenter Prospective Cohort Study. *Am J Kidney Dis* 2018; **72**: 691-700 [PMID: 30007504 DOI: 10.1053/j.ajkd.2018.04.020]
14 **Ciesielska N**, Sokołowski R, Mazur E, Podhorecka M, Polak-Szabela A, Kędziora-Kornatowska K. Is the Montreal Cognitive Assessment

(MoCA) test better suited than the Mini-Mental State Examination (MMSE) in mild cognitive impairment (MCI) detection among people aged over 60? Meta-analysis. *Psychiatr Pol* 2016; **50**: 1039-1052 [PMID: 27992895 DOI: 10.12740/PP/45368]

15 **Davis DH**, Creavin ST, Yip JL, Noel-Storr AH, Brayne C, Cullum S. Montreal Cognitive Assessment for the detection of dementia. *Cochrane Database Syst Rev* 2021; **7**: CD010775 [PMID: 34255351 DOI: 10.1002/14651858.CD010775.pub3]

16 **Golenia A**, Zolek N, Olejnik P, Wojtaszek E, Glogowski T, Malyszko J. Prevalence of Cognitive Impairment in Peritoneal Dialysis Patients and Associated Factors. *Kidney Blood Press Res* 2023; **48**: 202-208 [PMID: 36940679 DOI: 10.1159/000530168]

17 **Zhao Y**, Zhang Y, Yang Z, Wang J, Xiong Z, Liao J, Hao L, Liu G, Ren Y, Wang Q, Duan L, Zheng Z, Dong J. Sleep Disorders and Cognitive Impairment in Peritoneal Dialysis: A Multicenter Prospective Cohort Study. *Kidney Blood Press Res* 2019; **44**: 1115-1127 [PMID: 31537006 DOI: 10.1159/000502355]

18 **Kalirao P**, Pederson S, Foley RN, Kolste A, Tupper D, Zaun D, Buot V, Murray AM. Cognitive impairment in peritoneal dialysis patients. *Am J Kidney Dis* 2011; **57**: 612-620 [PMID: 21295896 DOI: 10.1053/j.ajkd.2010.11.026]

19 **Liao JL**, Zhang YH, Xiong ZB, Hao L, Liu GL, Ren YP, Wang Q, Duan LP, Zheng ZX, Xiong ZY, Dong J. The Association of Cognitive Impairment with Peritoneal Dialysis-Related Peritonitis. *Perit Dial Int* 2019; **39**: 229-235 [PMID: 30852523 DOI: 10.3747/pdi.2018.00180]

20 **Huang X**, Yi C, Wu M, Qiu Y, Wu H, Ye H, Peng Y, Xiao X, Lin J, Yu X, Yang X. Risk Factors and Clinical Outcomes of Cognitive Impairment in Diabetic Patients Undergoing Peritoneal Dialysis. *Kidney Blood Press Res* 2021; **46**: 531-540 [PMID: 34229326 DOI: 10.1159/000514172]

21 **Madero M**, Gul A, Sarnak MJ. Cognitive function in chronic kidney disease. *Semin Dial* 2008; **21**: 29-37 [PMID: 18251955 DOI: 10.1111/j.1525-139X.2007.00384.x]

22 **Griva K**, Stygall J, Hankins M, Davenport A, Harrison M, Newman SP. Cognitive impairment and 7-year mortality in dialysis patients. *Am J Kidney Dis* 2010; **56**: 693-703 [PMID: 20800327 DOI: 10.1053/j.ajkd.2010.07.003]

23 **Murray AM**. Cognitive impairment in the aging dialysis and chronic kidney disease populations: an occult burden. *Adv Chronic Kidney Dis* 2008; **15**: 123-132 [PMID: 18334236 DOI: 10.1053/j.ackd.2008.01.010]

24 **Seliger SL**, Wendell CR, Waldstein SR, Ferrucci L, Zonderman AB. Renal function and long-term decline in cognitive function: the Baltimore Longitudinal Study of Aging. *Am J Nephrol* 2015; **41**: 305-312 [PMID: 26201453 DOI: 10.1159/000430922]

25 **Romijn MD**, van Marum RJ, Emmelot-Vonk MH, Verhaar HJ, Koek HL. Mild chronic kidney disease is associated with cognitive function in patients presenting at a memory clinic. *Int J Geriatr Psychiatry* 2015; **30**: 758-765 [PMID: 25366465 DOI: 10.1002/gps.4226]

26 **Elias MF**, Dore GA, Davey A. Kidney disease and cognitive function. *Contrib Nephrol* 2013; **179**: 42-57 [PMID: 23652448 DOI: 10.1159/000346722]

27 **Cheng BC**, Chen PC, Lu CH, Huang YC, Chou KH, Li SH, Lin AN, Lin WC. Decreased cerebral blood flow and improved cognitive function in patients with end-stage renal disease after peritoneal dialysis: An arterial spin-labelling study. *Eur Radiol* 2019; **29**: 1415-1424 [PMID: 30105409 DOI: 10.1007/s00330-018-5675-9]

World Journal of Psychiatry

Submit a Manuscript: https://www.f6publishing.com

World J Psychiatry 2024 February 19; 14(2): 315-329

DOI: 10.5498/wjp.v14.i2.315

ISSN 2220-3206 (online)

META-ANALYSIS

Alterations of sleep deprivation on brain function: A coordinate-based resting-state functional magnetic resonance imaging meta-analysis

Qin Zhang, Yong-Zhe Hou, Hui Ding, Yan-Ping Shu, Jing Li, Xi-Zhao Chen, Jia-Lin Li, Qin Lou, Dai-Xing Wang

Specialty type: Neuroimaging

Provenance and peer review: Unsolicited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

Grade A (Excellent): 0
Grade B (Very good): B
Grade C (Good): 0
Grade D (Fair): 0
Grade E (Poor): 0

P-Reviewer: Sawadogo W, United States

Received: November 29, 2023
Peer-review started: November 30, 2023
First decision: December 11, 2023
Revised: December 21, 2023
Accepted: January 3, 2024
Article in press: January 3, 2024
Published online: February 19, 2024

Qin Zhang, Hui Ding, Jing Li, Xi-Zhao Chen, Qin Lou, Dai-Xing Wang, Department of Radiology, The Second People's Hospital of Guizhou Province, Guiyang 550000, Guizhou Province, China

Qin Zhang, Department of Radiology, Guizhou Provincial People's Hospital, Guiyang 550000, Guizhou Province, China

Yong-Zhe Hou, Yan-Ping Shu, Department of Psychiatry of Women and Children, The Second People's Hospital of Guizhou Province, Guiyang 550000, Guizhou Province, China

Jia-Lin Li, Medical Humanities College, Guizhou Medical University, Guiyang 550000, Guizhou Province, China

Corresponding author: Hui Ding, Doctor, Professor, Department of Radiology, The Second People's Hospital of Guizhou Province, No. 206 South Section of Xintian Avenue, Yunyan District, Guiyang 550000, Guizhou Province, China. 857747438@qq.com

Abstract

BACKGROUND

Sleep deprivation is a prevalent issue that impacts cognitive function. Although numerous neuroimaging studies have explored the neural correlates of sleep loss, inconsistencies persist in the reported results, necessitating an investigation into the consistent brain functional changes resulting from sleep loss.

AIM

To establish the consistency of brain functional alterations associated with sleep deprivation through systematic searches of neuroimaging databases. Two meta-analytic methods, signed differential mapping (SDM) and activation likelihood estimation (ALE), were employed to analyze functional magnetic resonance imaging (fMRI) data.

METHODS

A systematic search performed according to PRISMA guidelines was conducted across multiple databases through July 29, 2023. Studies that met specific inclusion criteria, focused on healthy subjects with acute sleep deprivation and reported whole-brain functional data in English were considered. A total of 21 studies were selected for SDM and ALE meta-analyses.

RESULTS

Twenty-one studies, including 23 experiments and 498 subjects, were included. Compared to pre-sleep deprivation, post-sleep deprivation brain function was associated with increased gray matter in the right corpus callosum and decreased activity in the left medial frontal gyrus and left inferior parietal lobule. SDM revealed increased brain functional activity in the left striatum and right central posterior gyrus and decreased activity in the right cerebellar gyrus, left middle frontal gyrus, corpus callosum, and right cuneus.

CONCLUSION

This meta-analysis consistently identified brain regions affected by sleep deprivation, notably the left medial frontal gyrus and corpus callosum, shedding light on the neuropathology of sleep deprivation and offering insights into its neurological impact.

Key Words: Sleep deprivation; Resting-state-functional magnetic resonance imaging; Activation likelihood estimation-meta; Signed differential mapping-meta

Core Tip: This meta-analysis revealed consistent brain functional changes resulting from sleep deprivation, revealing notable alterations in the left medial frontal gyrus and corpus callosum. These findings offer crucial insights into the neurological impact of sleep loss and highlight specific brain regions affected by sleep deprivation, which may aid in understanding its neuropathological implications.

Citation: Zhang Q, Hou YZ, Ding H, Shu YP, Li J, Chen XZ, Li JL, Lou Q, Wang DX. Alterations of sleep deprivation on brain function: A coordinate-based resting-state functional magnetic resonance imaging meta-analysis. *World J Psychiatry* 2024; 14(2): 315-329

URL: https://www.wjgnet.com/2220-3206/full/v14/i2/315.htm

DOI: https://dx.doi.org/10.5498/wjp.v14.i2.315

INTRODUCTION

Sleep deprivation refers to insufficient or severe lack of sleep caused by various factors. With the acceleration of the pace of societal life and the escalation of individual pressures, sleep deprivation has evolved into a widespread public health concern[1]. The significance of high-quality sleep for maintaining one's well-being cannot be overlooked. Reports indicate that approximately one-third or more of adults in the Americas, Europe, and Asia consistently fall short of the 7 h of nightly sleep recommended by public health authorities[2-5]. Furthermore, the ceaseless 24-h nature of modern society readily disrupts the human body's circadian rhythms. Both insufficient sleep and disturbances in the sleep-wake cycle exert substantial stress on physical health, including an increased risk of obesity[6,7]. Research has revealed that the risk of obesity increases by 38% when comparing individuals with a short sleep duration (typically defined as less than 5 h or 6 h per day) to those with a normal sleep pattern[8]. Additionally, adverse metabolic health outcomes, such as type 2 diabetes, cardiovascular disease, hypertension, and lipid abnormalities, are frequently associated with sleep deprivation and/or circadian rhythm disruptions[9,10]. Prolonged sleep deprivation has been unequivocally linked to diminished cognitive abilities, altered emotional states, and the onset of inflammation and hormonal imbalances[11,12]. However, our current understanding of how sleep deprivation precipitates changes in brain function is incomplete.

Neuroimaging analysis methods offer potent tools for investigating the neurobiological mechanisms of neuropsychiatric disorders. However, despite the promising prospects of neuroimaging, recent research reports have cast doubts upon the reliability of studies in this domain, raising concerns regarding issues such as small sample sizes, clinical heterogeneity, and the correction of multiple comparisons. These collective concerns have contributed to an increase in false-positive rates[13]. Notwithstanding these limitations, neuroimaging techniques continue to provide valuable insights into the effects of sleep deprivation on the brain. It is essential to employ neuroimaging to detect and elucidate neurobiological alterations in specific regions associated with sleep deprivation. Meta-analytic approaches surmount the challenges of methodological diversity and outcome heterogeneity, aiding in the identification of trustworthy, practically significant research findings. In pursuit of comprehensive and persuasive outcomes, this study simultaneously employed both signed differential mapping (SDM) and activation likelihood estimation (ALE) meta-analytic methods.

While ALE-meta analysis has been conducted previously to investigate sleep deprivation, this study not only incorporated resting-state data but also task-related and positron emission tomography (PET) data[14]. The question of whether the integration of results varies due to the inclusion of different data types, such as functional connectivity (FC), independent component analysis (ICA), and cerebral perfusion data, as well as whether different analytical methods impact the distribution of neurobiological biomarkers in sleep-deprived patients warrants further exploration. For example, some scholars argue that FC and ICA methods primarily involve examining functional correlations between seed points and the surrounding brain regions; however, these correlations may not align with the spontaneous neural

brain function activity reflected by regional homogeneity (ReHo), amplitude of low-frequency fluctuation (ALFF), fraction ALFF (fALFF), or dynamic ALFF (dALFF) unless the emphasis is placed on studies of analogous networks[15]. Furthermore, cerebral perfusion delineates the metabolic status and neural activity of corresponding brain regions by measuring local cerebral blood flow but may not comprehensively encapsulate the spontaneous functional activity of neurons in the brain[16]. Despite notable success in transdiagnostic meta-analyses, the absence of crucial single-diagnosis findings underscores the ongoing importance of disease-specific methods as a critical research area.

Through functional neuroimaging SDM and ALE meta-analyses, we endeavored to elucidate the primary cerebral regions underlying alterations in brain function within the context of sleep deprivation. Our fundamental hypothesis posits that post-sleep deprivation imaging will reveal distinct cerebral functional patterns compared to pre-sleep deprivation imaging, potentially revealing the neurotraumatic mechanisms associated with sleep deprivation. This investigation exclusively encompasses studies concerning the reactivity of localized brain functional activities to comprehensively explore the localized activity patterns within sleep-deprived brain regions. With this approach, we aspire to delve deeper into the repercussions of sleep deprivation on the brain, furnishing novel insights into the neurobiological changes intertwined with its effects.

MATERIALS AND METHODS

Literature search

Study selection was conducted in accordance with the PRISMA guidelines[17]. This review was registered with PROSPERO (ID: CRD42023451942). A systematic search was conducted for relevant studies in the PubMed, Web of Science, Google Scholar, Embase, and CNKI databases up to July 29, 2023. The following keywords were used to identify candidate resting-state functional magnetic resonance imaging (rs-fMRI) studies: ("sleep deprivation" OR "sleep loss" OR "sleep restriction") AND ("amplitude of low-frequency fluctuation" OR "ALFF" OR "fALFF" OR "regional homogeneity" OR "ReHo") AND ("magnetic resonance" OR "MRI" OR "functional MRI" OR "fMRI" OR "neuroimaging"). Manual searches in the bibliographies of the retrieved studies and suitable reviews were also conducted.

Studies were considered eligible if they met the following criteria: (1) Original studies investigating the neural correlates of sleep deprivation in healthy subjects without any psychiatric or medical conditions; (2) studies that used a before-after sleep deprivation protocol or compared two groups of subjects with and without sleep deprivation; (3) studies focused on acute sleep deprivation (between 22 h and 48 h at once); (4) studies that reported whole-brain results in the stereotactic space [Montreal Neurological Institute (MNI)] or Talairach coordinates for ALFF, fALFF, dALFF, PerAF, and ReHo; and (5) studies published in English with peer review. Our exclusion criteria were as follows: (1) Editorial letters, case reports, systematic reviews, meta-analyses, or methodological studies; (2) intervention studies; (3) studies with fewer than seven subjects; and (4) studies that did not perform whole-brain analysis. For a study containing multiple independent patient samples, group coordinates were treated as separate datasets. The corresponding authors were asked *via* email for any additional data not included in the original publications. Two researchers (Zhang Q and Hou YZ) independently evaluated the studies, and the inclusion and exclusion criteria were evaluated by consensus (Table 1).

The included studies were primarily assessed for greater activation in sleep deprivation conditions than in non-sleep deprivation conditions (SD > NS) or for lower activation in sleep deprivation conditions than in non-sleep-deprivation conditions (SD < NS). We identified several studies with the same or overlapping samples. ALE meta-analysis was utilized to integrate reported coordinates from different experiments. If publications used the same or an overlapping group of subjects and reported several experiments, those data were combined. Accordingly, we merged experiments from various publications.

Quality assessment

The quality of the included studies was assessed using the Newcastle-Ottawa Scale (NOS), a well-established tool for retrospective studies. The NOS comprises three levels with a total of eight items: (1) Four items for subject selection; (2) one item for comparability between groups; and (3) three items for outcome measurement. The total possible score is 9 points. Studies with a score ≥ 5 were eligible for data analysis. Each study was reviewed and rated by two authors (Zhang Q and Hou YZ) independently. If rating disagreements arose, the papers were discussed by the authors' group to determine a consensus score.

ALE

ALE is a quantitative voxel-based meta-analysis method used in neuroimaging studies to estimate consistent changes in gray matter or functional images across multiple studies reporting peak activation coordinates of statistical significance. ALE models each alteration focus as the center of a spherical Gaussian probability distribution. This approach is employed to create spatial probability maps that highlight consistent brain region involvement in specific tasks or conditions. We set the parameters as cluster-level FWE $P < 0.05$, threshold permutations 1000, and $P < 0.001$, resulting in the generation of the ALE-image threshold map. Finally, the ALE analysis results were visualized using Mango software (http://rii.uthscsa.edu/mango/). Furthermore, to assess the stability (sensitivity) of the ALE meta-analysis results, this study employed the jackknife sensitivity analysis method. Specifically, the ALE meta-analysis was repeated 21 times, with each iteration excluding one of the 21 selected articles (in a nonrepetitive manner) before conducting the meta-analysis.

Table 1 Characteristics of the included studies

Ref.	Sample size	Age (mean ± SD)	rs-fMRI scan	Field strength	Method	Differential brain region	Coordinate	Sample size	Quality
			Before	After					
Dai *et al*[19], 2012	16	21.00	SW	SD 14 h	3.0 T	ReHo	7	MNI	4/1/1
Dai *et al*[20], 2012	15	22.00 ± 1.40	SW	SD 24 h	3.0 T	ReHo	8	MNI	4/1/1
Gao *et al*[21], 2015	16	22.10 ± 0.80	SW	SD	3.0 T	ALFF	9	MNI	4/1/1
Dai *et al*[22], 2015	12	24.83 ± 2.88	SW	SD 72 h	3.0 T	ALFF	1	MNI	4/1/1
Wang *et al*[23], 2016	16	24.51 ± 2.75	SW	SD	3.0 T	ALFF	5	MNI	4/1/1
Li *et al*[24], 2017	16	20.94 ± 1.73	SW	SD 24 h	3.0 T	ReHo	15	MNI	4/1/1
Li *et al*[25], 2017	28	23.94 ± 1.73	SW	SD 24 h	3.0 T	ReHo	13	MNI	4/1/1
Zhou *et al*[26], 2017	16	16.10 ± 0.90	SW	SD 24 h	3.0 T	ALFF	5	MNI	4/1/1
Robinson *et al*[27], 2018	18	14.40 ± 1.94	SW	SD	7.0 T	ReHo	10	MNI	4/1/1
Chen *et al*[28], 2018	22	26.901 ± 6.05	SW	SD	3.0 T	ALFF	7	MNI	4/1/1
Feng *et al*[29,30], 2018	35	21.89 ± 1.97	SW	SD 24 h	3.0 T	zALFF & zReHo & fALFF[1]	2 & 2 & 3	MNI	4/1/1
Guo *et al*[31], 2019	17	23.00 ± 1.37	SW	SD	-	ALFF	19	MNI	4/1/1
Nechifor *et al*[32], 2020	7	31.4 0 ± 5.70	SW	SD 36 h	3.0 T	fALFF	4	MNI	4/1/1
Qiu *et al*[33], 2021	13	28.32 ± 3.71	Control	SD	3.0 T	ReHo	8	MNI	4/1/1
Xu *et al*[34], 2021	54	22.46 ± 1.81	Control	SD	3.0 T	fALFF	13	MNI	4/1/1
Zeng *et al*[35], 2020	20	22.25 ± 1.12	SW	SD	3.0 T	perAF	5	MNI	4/1/1
Cai *et al*[36], 2021	42	21.57 ± 2.25	SW	SD 24 h	3.0 T	ALFF	7	MNI	4/1/1
Nechifor *et al*[37], 2022	7	34.40 ± 5.70	SW	SD 36 h	3.0 T	ReHo	1	MNI	4/1/1
Xin *et al*[38], 2022	54	22.46 ± 1.81	SW	SD	3.0 T	PerAF	5	MNI	4/1/1
Yan *et al*[39], 2023	20	20.00 ± 0.80	SW	SD	3.0 T	dALFF	30	MNI	4/1/1
Chen *et al*[40], 2023	19	21.79 ± 2.37	SW	SD	3.0 T	ReHo	1	MNI	4/1/1

[1]The study of Feng *et al*[29,30] explored the same dataset using distinct methodologies.

ReHo: Regional homogeneity; ALFF: Amplitude of low-frequency fluctuation; fALFF: Fractional amplitude of low-frequency fluctuation; MNI: Montreal Neurological Institute; SW: Sleep-wake; SD: Sleep deprivation.

SDM

In this study, an SDM meta-analysis was conducted using AES-SDM v5.141 software (http://www.sdmproject.com) to identify significantly positive and negative activation peak coordinates at the whole-brain level related to sleep deprivation. Default parameters were utilized, including a full width at half maximum (FWHM) of 20 mm, an uncorrected voxel threshold of $P < 0.005$, a peak height SDM-Z > 1, and a minimum cluster extent of ≥ 10 voxels. The resulting images were visualized on the standardized anatomical template in MNI space. Furthermore, to assess the stability (sensitivity) of the SDM meta-analysis results, this study employed the jackknife sensitivity analysis method, also known as "leave one out" analysis[18]. This method is commonly used for hypothesis testing, confidence interval

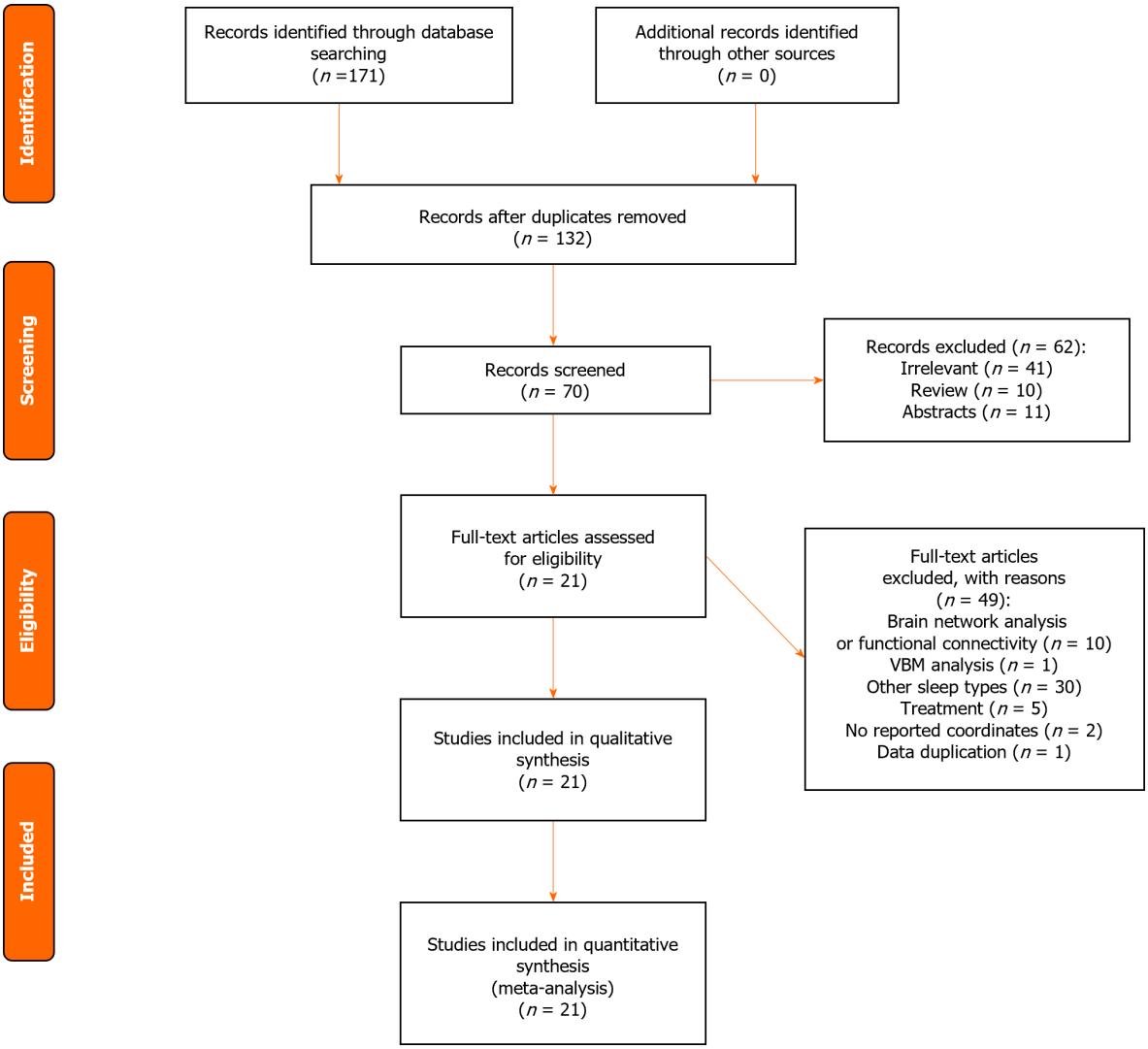

Figure 1 Flow chart of the study selection strategy. VBM: Voxel-based morphometry.

calculations, and assessment of the stability of results in SDM meta-analyses. Specifically, AES-SDM was used to repeat the meta-analysis 21 times, with each iteration excluding one of the 21 selected articles (in a nonrepetitive manner) before conducting the meta-analysis.

RESULTS

General information of the included studies

The search strategy generated 171 related articles, and a total of 21 articles[19-40] were included in this meta-analysis (Figure 1). One of the studies (Pan)[29] used more than one analytical method to study sleep deprivation, and the different methods were considered three separate studies and were compared based on their individual quantities. Consequently, the effective number of "actual" experiments included in the study increased to a total of 23. Of the 171 retrieved papers in this meta-analysis, 21 studies, including 23 experiments and 498 subjects, were eligible for inclusion (Figure 1 and Table 1). These 21 studies included 8 ReHo, 8 ALFF, 3 fALFF, 2 perAF, 1 zReHo, 1 dALFF, and 1 zALFF.

Changes in brain function during sleep deprivation

The ALE results indicated that there was an increase in gray matter in the right corpus callosum and a decrease in the left medial frontal gyrus and the left inferior parietal lobule in the sleep-deprived state compared to the pre-sleep deprivation state (Figure 2 and Table 2). The SDM results indicated heightened brain functional activity in the left striatum and right posterior cingulate cortex, along with decreased activity in the right cerebellar hemisphere, left medial frontal gyrus, corpus callosum, and right cuneus, compared to those in the pre-sleep deprivation condition (Figure 3 and Table 3). Both neuroimaging meta-analytical methods revealed an overlapping increase in brain functional activity in the left medial frontal gyrus following sleep deprivation. However, the right corpus callosum and right cuneus exhibited elevated activity in the ALE results but reduced activity in the SDM results.

Table 2 Applying the activation likelihood estimation method to study changes in brain function activity after sleep deprivation

Research methods	Anatomical label BA	Peak MNI coordinate			ALE value	Volume (mm³)
		X	Y	Z		
ReHo and ALFF/fALFF decrease						
	Left middle frontal gyrus, BA 6	-34	20	42	0.01572180	1208
	Left inferior parietal lobule, BA 40	-48	-58	40	0.02166488	992
ReHo and ALFF/fALFF increase						
	Subcallosal gyrus, BA 34	26	4	-16	0.015194423	680
ALFF decrease						
	Left inferior parietal lobule, BA 40	-48	-58	40	0.021612160	438
	Left supramarginal gyrus, BA 40	-56	-50	40	0.008252133	263
	Left middle frontal gyrus, BA 6	-34	20	42	0.015355002	744
ALFF increase						
	Right cuneus, BA 18	8	-88	20	0.014324005	704
ReHo decrease						
	Left posterior cingulate, BA 30	-9	-54	15	0.015816410	640
	Right cuneus, BA 7	9	-72	36	0.009564294	448

BA: Brodmann area; MNI: Montreal Neurological Institute; ALE: Activation likelihood estimation.

Table 3 Changes in brain function activity after sleep deprivation using the signed differential mapping method

SDM	Anatomical label BA	Peak MNI coordinate			SDM-Z	*P* value	Voxels
		X	Y	Z			
Increase							
	Corpus callosum	58	-20	2	2.573	0.005037844	227
	Left striatum	-28	-4	-2	2.087	0.018434286	19
	Right postcentral gyrus, BA 3	22	-38	64	2.118	0.017078340	11
Decrease							
	Right cerebellum, crus 1	44	-58	-38	-2.878	0.002000034	548
	Left middle frontal gyrus, BA 9	-38	18	48	-2.508	0.006063104	75
	Right cuneus cortex, BA 19	16	-76	40	-2.141	0.016148150	17

BA: Brodmann area; MNI: Montreal Neurological Institute; ALE: Activation likelihood estimation.

Subgroup analysis

Conducting a subgroup analysis utilizing the ALE method on data analysis approaches such as ALFF and ReHo revealed the following: in the ALFF analysis, when compared to the pre-sleep deprivation state, post-sleep deprivation brain functional activity increased in the right cuneus and decreased in the left inferior parietal lobule, left superior frontal gyrus, left medial frontal gyrus, and right pallidum (Figure 2 and Table 2). In the ReHo analysis, in contrast to the pre-sleep deprivation condition, sleep deprivation led to a decrease in brain functional activity in the left cingulate gyrus and right cuneus, with no regions exhibiting increased activity.

When employing the SDM method for subgroup analysis of the ALFF and ReHo data analysis approaches, no regions demonstrating either increased or decreased activity were discerned. This outcome may be attributed to the inclusion of too few studies when conducting meta-analyses of individual analytical techniques. Consequently, the central coordinates (location information of active brain regions) extracted from the included literature might be overly dispersed or insufficient in quantity to meet the threshold criteria, thus remaining undetectable.

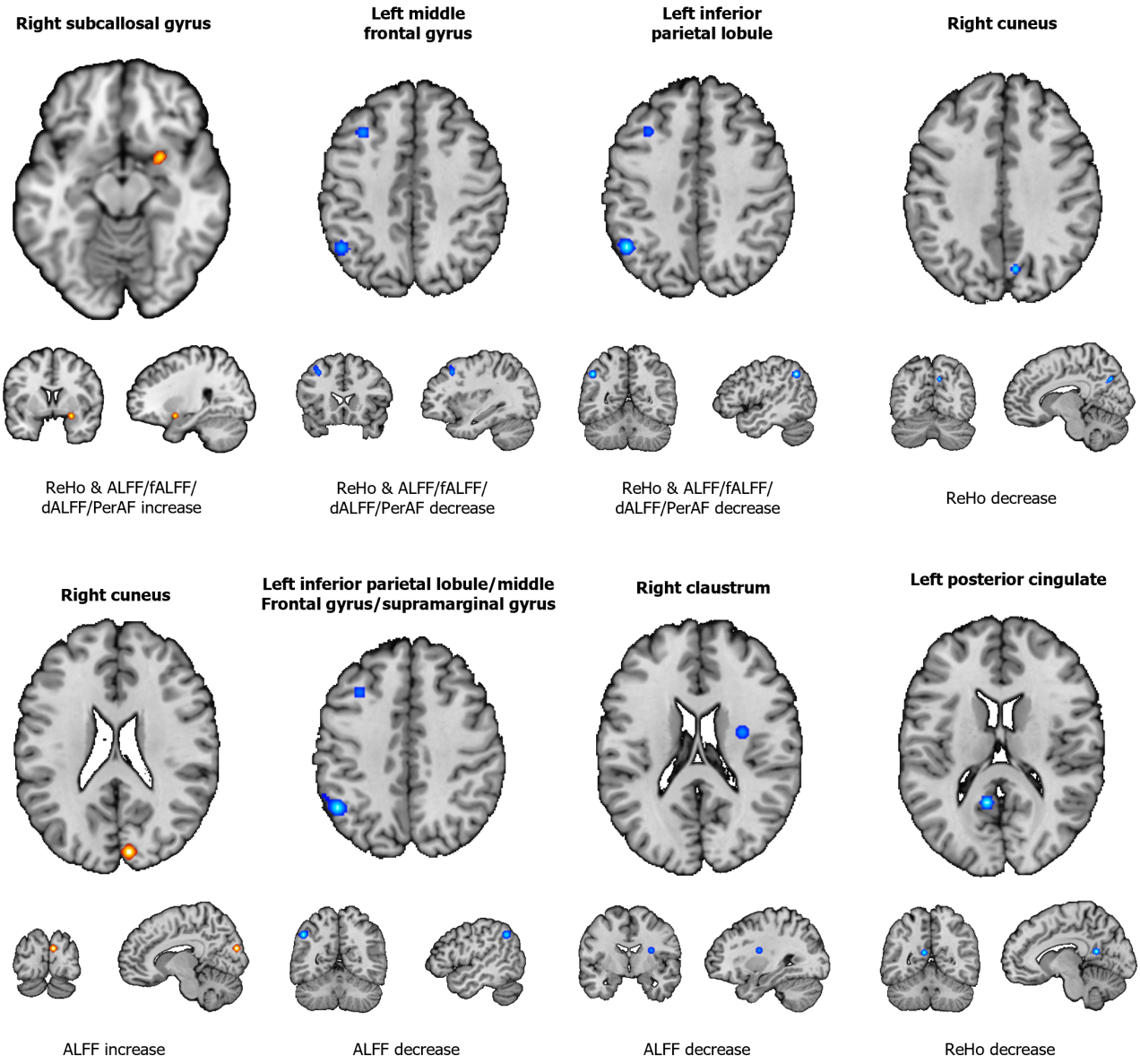

Figure 2 Abnormal regions identified in an activation likelihood estimation meta-analysis of neuroimaging studies in individuals with sleep deprivation. ReHo: Regional homogeneity; ALFF: Amplitude of low-frequency fluctuation; fALFF: Fraction amplitude of low-frequency fluctuation; dALFF: Dynamic amplitude of low-frequency fluctuation.

Sensitivity analysis results

The sensitivity analysis results for the ALE study showed that the left middle frontal gyrus was consistently identified in 17 out of 21 analyses. The left inferior parietal lobule and right subcallosal gyrus were consistently identified in 18 out of 21 analyses (Table 4).

The sensitivity analysis results for the SDM study showed that the right cerebellum crus I was consistently identified in 16 out of 21 analyses. The right cuneus cortex and right postcentral gyrus were consistently identified in 17 out of 21 analyses. The left middle frontal gyrus, left striatum, and corpus callosum were consistently identified in 19 out of 21 analyses. The corpus callosum itself was identified in 18 out of 21 analyses (Table 5).

DISCUSSION

This groundbreaking neuroimaging meta-analysis combined two different meta-analysis methods to explore changes in brain function during sleep deprivation. By integrating these two approaches, we revealed that sleep deprivation induces widespread changes in brain functionality across multiple regions, including the frontal lobe, parietal lobe, sensorimotor areas, temporal lobe, occipital lobe, corpus callosum, striatum, and screenlike nucleus, with the majority of these regions exhibiting downregulation associated with cognitive functions, sensations, motor functions, and pain perception. These findings underscore the critical importance of holistic brain analysis for obtaining a more profound understanding of the neuroactivity alterations underpinning sleep deprivation, with the potential to comprehensively elucidate its impact on

Table 4 Activation likelihood estimation sensitivity analysis results

Discarded article	Decreased		Increased
	Left middle frontal gyrus	Left inferior parietal lobule	Right subcallosal gyrus
Yan *et al*[39], 2023	N	Y	N
Chen *et al*[40], 2023	Y	Y	Y
Nechifor *et al*[37], 2022	Y	Y	Y
Zeng *et al*[35], 2020	Y	Y	Y
Li *et al*[25], 2017	Y	Y	Y
Nechifor *et al*[32], 2020	Y	Y	Y
Guo *et al*[31], 2019	N	N	Y
Robinson *et al*[27], 2018	N	N	N
Chen *et al*[28], 2018	N	N	N
Wang *et al*[23], 2016	Y	Y	Y
Gao *et al*[21], 2015	Y	Y	Y
Dai *et al*[22], 2015	Y	Y	Y
Dai *et al*[19], 2012	Y	Y	Y
Dai *et al*[20], 2012	Y	Y	Y
Xin *et al*[38], 2022	Y	Y	Y
Zhou *et al*[26], 2017	Y	Y	Y
Qiu *et al*[33] 2021	Y	Y	Y
Xu *et al*[34] 2021	Y	Y	Y
Li *et al*[24], 2017	Y	Y	Y
Li *et al*[25], 2017	Y	Y	Y
Feng *et al*[29,30], 2018	Y	Y	Y

Y: Yes; N: No.

brain function. Moreover, both the AES-SDM and ALE methods identified overlapping brain regions, specifically the left middle frontal gyrus and corpus callosum. This provides further evidence that the left medial frontal gyrus and corpus callosum may serve as the neuropathological basis for the brain damage induced by sleep deprivation. The neuropsychiatric damage associated with sleep deprivation may be related to widespread abnormal resting-state brain activity involving the cerebral cortex and subcortical structures. These research findings significantly contribute to broadening our understanding of the neuropathological mechanisms associated with sleep deprivation, helping to elucidate how to treat and prevent related disorders.

The role of the medial frontal gyrus and corpus callosum in sleep deprivation. Adequate sleep forms the bedrock of memory formation, with quality slumber preparing the brain for the establishment of new memories[41]. Despite ongoing debates surrounding the physiological functions of sleep, it is widely acknowledged that sleep is beneficial for neuronal plasticity, which in turn supports brain function and cognition. Correspondingly, research has suggested that sleep deprivation can lead to impaired learning and memory[42], manifesting as memory decline, memory loss, and memory misconstruction, among other issues. As people continue to curtail their sleep duration, the impact of memory deterioration on daily life becomes increasingly pronounced. In a clinical study involving 96 participants, Santisteban *et al*[43] reported that prolonged exposure to mild sleep deprivation negatively affects working memory. In a clinical experiment with 36 subjects, Hennecke *et al*[44] confirmed that sleep deficits impair spatial working memory. Animal research conducted by Scullin *et al*[45] and colleagues affirmed that rapid eye movement sleep deprivation and continuous sleep deprivation for 72 h both detrimentally affect memory capabilities.

The frontal lobe is intricately linked to various aspects of brain function, including cognition, sleep, working memory, short-term memory, sustained attention, planning, and behavioral control[46-50]. Previous research has employed neuroimaging studies to assess the corresponding brain responses and their relationship with behavioral changes in various environments[51]. Sleep deprivation can impair brain function and FC in various regions. Studies have indicated that after sleep deprivation, ReHo is greater in the left medial frontal gyrus, right precentral gyrus, right temporal gyrus, and bilateral posterior central gyrus[20]. One study revealed that sleep deprivation leads to reduced FC between the right prefrontal cortex and the right medial frontal gyrus[52]. Another study revealed that after 36 h of complete sleep

Table 5 Signed differential mapping sensitivity analysis results

Discarded article	Decreased				Increased		
	Right cerebellum, crus	Left middle frontal gyrus	Corpus callosum	Right cuneus cortex	Right postcentral gyrus	Left striatum	Corpus callosum
Yan *et al*[39], 2023	Y	Y	Y	Y	N	Y	Y
Chen *et al*[40], 2023	N	Y	Y	Y	Y	Y	Y
Nechifor *et al*[37], 2022	Y	Y	Y	Y	Y	Y	N
Zeng *et al*[35], 2020	Y	Y	Y	Y	Y	Y	Y
Li *et al*[25], 2017	Y	Y	Y	N	Y	Y	Y
Nechifor *et al*[32], 2020	N	Y	Y	Y	N	N	Y
Guo *et al*[31], 2019	Y	Y	Y	Y	Y	Y	N
Robinson *et al*[27], 2018	Y	Y	Y	Y	Y	Y	Y
Chen *et al*[28], 2018	Y	N	Y	Y	Y	Y	Y
Wang *et al*[23], 2016	Y	Y	Y	Y	Y	Y	Y
Gao *et al*[21], 2015	Y	Y	N	Y	Y	N	Y
Dai *et al*[22], 2015	N	N	Y	Y	N	Y	Y
Dai *et al*[19], 2012	Y	Y	Y	Y	Y	Y	Y
Dai *et al*[20], 2012	Y	Y	Y	Y	Y	Y	Y
Xin *et al*[38], 2022	Y	Y	Y	Y	Y	Y	Y
Zhou *et al*[26], 2017	N	Y	N	Y	Y	Y	Y
Qiu *et al*[33] 2021	Y	Y	Y	Y	Y	Y	Y
Xu *et al*[34] 2021	Y	Y	Y	N	Y	Y	Y
Li *et al*[24], 2017	N	Y	Y	N	Y	Y	N
Li *et al*[25], 2017	Y	Y	N	Y	N	Y	Y
Feng *et al*[29,30], 2018	Y	Y	Y	N	Y	Y	Y

Y: Yes; N: No.

deprivation, with increasing working memory load, there was a decrease in FC between the left hippocampus and the left frontal pole, right superior frontal gyrus, and bilateral anterior cingulate cortex[53]. These findings suggest that sleep deprivation negatively affects brain function and FC in the medial frontal gyrus, leading to impairments in cognitive functions such as attention and working memory. In addition to the frontal lobe, studies using rs-fMRI have shown reduced ALFF in the precuneus[28]. Li *et al*[52] demonstrated that participants experiencing sleep deprivation exhibited decreased alertness and attention, and further investigation revealed reduced FC between the right precuneus and the right medial frontal gyrus after sleep deprivation. However, this finding contrasts with that of a study by Li *et al*[54], which revealed enhanced effective connectivity from the left medial frontal gyrus to the left superior parietal lobule after sleep deprivation. Furthermore, this functional neuroimaging evidence is further supported by a study involving structural imaging and brain metabolism. Sun *et al*[55] used FreeSurfer software to calculate gray matter volume (GMV) and cortical thickness (CT) using volume and surface measurements and found that 24 h after acute sleep deprivation, there was a significant increase in gray matter density in the right frontal pole, right middle frontal gyrus, and right superior frontal gyrus, while the GMV and CT of the right temporal pole significantly decreased. A PET study also revealed a significant decrease in glucose metabolism in particular regions, including the frontal cortex, parietal cortex, and thalamus, following sleep deprivation, which correlated significantly with cognitive performance[56]. In summary, considering the impaired cognitive functions such as attention and working memory in the frontal lobe following sleep deprivation, the reduced activity in the middle frontal gyrus after sleep deprivation observed in this study may reflect a

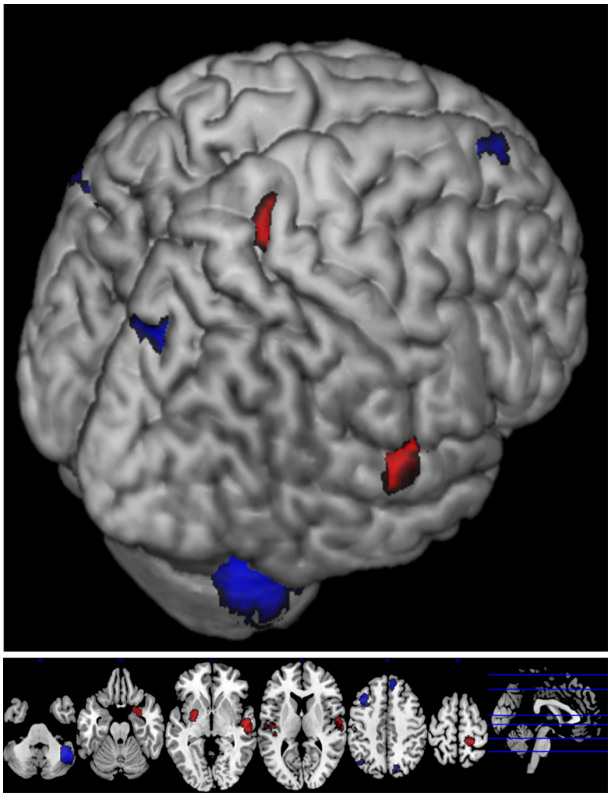

Figure 3 Abnormal regions identified in a signed differential mapping meta-analysis of neuroimaging studies of individuals with sleep deprivation.

compensatory response to reduced attention during sleep deprivation[36].

The corpus callosum, comprising a collection of neural fibers within the brain, serves as a pivotal conduit facilitating information transmission and coordination between the left and right cerebral hemispheres, with alterations in its functionality potentially giving rise to impairments in interhemispheric information exchange and coordination[57]. One study indicated a link between sleep deprivation and functional impairments in the brain cortex, which could be associated with abnormalities in the development of the corpus callosum and visual radiation[58]. Zhu *et al*[59] reported that impaired interhemispheric connections may be a reason for sustained attention deficits following sleep deprivation, offering comprehensive insights into how sleep deprivation modulates interhemispheric connectivity and providing new evidence for the increased relevance of neuroimaging in sleepiness after sleep deprivation. Vargas *et al*[60] reported that young people with symptoms of insomnia are particularly susceptible to sleep deprivation, which can reduce their natural tendency to focus on positive information in the environment due to acute sleep deprivation. In addition to impairing interhemispheric information exchange and coordination, sleep deprivation may also lead to emotional instability and other issues. For instance, Taraku *et al*[61] discovered that individuals with depression exhibit decreased fractional anisotropy (FA) values in multiple white matter tracts, including the corpus callosum and corona radiata, after complete sleep deprivation. Furthermore, changes in FA values within the right superior corona radiata were significantly associated with improvements in rumination after complete sleep deprivation[61]. Li *et al*[62] also found weaker FC between the left corpus callosum/posterior cingulate gyrus and anterior cingulate cortex in patients with comorbid primary insomnia and depression. Additionally, Bellesi *et al*[63] evaluated the ultrastructure of myelin sheaths in two brain regions (the corpus callosum and olfactory lateral bundle) in mice exposed to different durations of sleep deprivation, ranging from several hours to approximately 5 d of chronic sleep restriction. Chronic sleep deprivation led to an increase in the ratio of the axon diameter to the myelinated fiber outer diameter, which was mediated by a reduction in myelin sheath thickness in the corpus callosum and olfactory lateral bundle[63]. Therefore, sleep deprivation can have a significant impact on the structure and function of the corpus callosum, resulting in decreased motor coordination and increased emotional fluctuations, among other issues. Notably, individual responses to sleep deprivation may vary, and many studies on this topic have been conducted using animal models or small sample populations. These studies may not fully represent the diversity of human responses to sleep deprivation.

Further research is needed to determine the precise link between sleep deprivation and brain function and structure. This approach will provide a more comprehensive understanding of the neurobiological mechanisms underlying sleep deprivation and pave the way for the development of more effective strategies to mitigate its adverse consequences.

Reasons for discrepancies with previous meta-analyses

By combining two methods (ALE and SDM) and refining the inclusion criteria (only including literature reflecting changes in spontaneous brain activity), this meta-analysis identified the left medial frontal gyrus, right cuneus, and

corpus callosum as brain regions affected by sleep deprivation. However, in an ALE meta-analysis, Javaheripour *et al*[14] reported reduced activity in the right superior frontal gyrus and superior parietal lobule. Our study did not yield the same results, which could be due to several reasons. First, their study included not only ReHo, ALFF, FC, and ICA but also t-fMRI, VBM, and PET-related data. The differences in experimental design, data preprocessing, and statistical methods used for t-fMRI, PET, and VBM compared to those used for rs-fMRI (ReHo, ALFF, FC, and ICA) might have led to the absence of brain regions showing abnormal activity. Second, different meta-analysis software may have been used. Third, our study included differences in sex, age, educational level, disease severity, and disease duration, which might have contributed to the differences in the results. Finally, the central coordinates (location information of active brain regions) extracted in our study were dispersed or insufficient in quantity to meet the threshold, potentially resulting in a lack of significant findings. This meta-analysis shares similarities with the research of Javaheripour *et al*[14] but also presents differences, enriching our understanding of the mechanisms underlying impaired brain function before and after sleep deprivation.

Limitations

Several limitations should be noted in this meta-analysis. First, the number of included studies was relatively small. Second, while ALE and SDM effectively control false-positive results, avoiding false negatives is a challenge[18]. Finally, it was not possible to completely eliminate heterogeneity among the included studies, such as variations in the demographic characteristics of patients and different imaging modalities representing aspects of resting-state abnormalities. For example, ALFF and ReHo are related to the strength and temporal synchronization of spontaneous neuronal activity, respectively, in various regions of the whole brain[64,65]. Despite these differences, multiple analytical methods can complement each other and provide more comprehensive information. Different analysis modalities can also detect similar patterns of resting-state abnormalities. For instance, in most of the included studies, regardless of the imaging approach, reduced activity in the occipital lobe during the resting state was consistently observed.

CONCLUSION

In summary, this meta-analysis discerned notable and consistent alterations in brain function consequent to sleep deprivation, notably within the left middle frontal gyrus and corpus callosum. These discoveries hold the potential to provide fresh perspectives regarding the neuropathological underpinnings of sleep deprivation. Future investigations must further explore the potential applications of these brain regions, characterized by modified functionality, in the diagnosis and ongoing assessment of sleep deprivation.

ARTICLE HIGHLIGHTS

Research background

Sleep deprivation, a widespread public health concern, is characterized by inadequate or severely reduced sleep. With societal acceleration and increased individual pressures, the prevalence of sleep deprivation has risen, impacting cognitive function and overall well-being. Despite extensive research on its health implications, a comprehensive understanding of how sleep deprivation affects brain function remains incomplete.

Research motivation

Quality sleep is essential for well-being, yet a significant proportion of the global population consistently falls short of recommended sleep durations. Sleep deprivation is associated with various health risks, including obesity, metabolic disorders, and cognitive decline. Understanding the consistent neurobiological alterations resulting from sleep loss is crucial for devising effective preventive and therapeutic strategies.

Research objectives

To address the inconsistencies in existing neuroimaging studies on sleep deprivation by identifying and elucidating the brain functional changes associated with acute sleep loss. Through the integration of signed differential mapping (SDM) and activation likelihood estimation (ALE) meta-analytic methods, the study aims to provide a comprehensive understanding of the neuropathological impact of sleep deprivation.

Research methods

A systematic search following PRISMA guidelines was conducted across multiple databases to identify 21 eligible studies focusing on acute sleep deprivation in healthy subjects. The studies, written in English, reported whole-brain functional data and met specific inclusion criteria. SDM and ALE meta-analyses were employed on functional magnetic resonance imaging (fMRI) data to analyze brain functional changes consistently associated with sleep deprivation.

Research results

The meta-analysis, encompassing 21 studies with 23 experiments and 498 subjects, identified consistent brain functional alterations post-sleep deprivation. Notable changes included increased gray matter in the right corpus callosum and

decreased activity in the left medial frontal gyrus and left inferior parietal lobule. SDM revealed additional alterations in brain functional activity, providing a comprehensive view of the impact of sleep deprivation on neural processes.

Research conclusions

This study consistently identified brain regions affected by sleep deprivation, emphasizing the left medial frontal gyrus and corpus callosum as key areas influenced by acute sleep loss. The findings contribute valuable insights into the neuropathology of sleep deprivation, offering a foundation for further research and potential interventions aimed at mitigating its adverse effects on brain function.

Research perspectives

Future research should explore the clinical implications of the identified brain regions and their functional changes in the context of sleep deprivation. Additionally, investigations into individual variability in response to sleep loss and the potential longitudinal effects on brain function will further enhance our understanding of the complex interplay between sleep, cognition, and neurological health.

FOOTNOTES

Co-first authors: Qin Zhang and Yong-Zhe Hou.

Co-corresponding authors: Hui Ding and Yan-Ping Shu.

Author contributions: Zhang Q, Hou YZ, Chen XZ, Li J, Wang DX, and Lou Q designed the experiment and wrote the manuscript; Zhang Q, Hou YZ, and Li JL analyzed the data; Ding H and Shu YP contributed to the critical revision and editing of the article; Zhang Q and Hou YZ contributed equally to this manuscript and are therefore listed as co-first authors; Ding H and Shu YP contributed equally to this manuscript and are therefore listed as co-corresponding authors; this designation as co-corresponding authors underscores our shared responsibilities in handling correspondence, communicating with peers, and providing essential guidance throughout the research process. Our equal commitment and involvement affirm our joint leadership and contribution to this significant scientific endeavor.

Supported by the Guizhou Province Traditional Chinese Medicine and Ethnic Medicine Science and Technology Research Special Project, No. QZYY-2020-069; Health Commission of Guizhou Province, No. gzwjkj2019-1-203; 2024 Guizhou Provincial Health Commission Science and Technology Fund Project; Guizhou Province Science and Technology Plan Project, No. ZK-2023-195; 2021 Health Commission of Guizhou Province Project, No. gzwkj2021-150; and 2020 National Clinical Key Specialized Projects, No. 2020-128.

Conflict-of-interest statement: The authors declared that they have no conflicts of interest to this work.

PRISMA 2009 Checklist statement: The authors have read the PRISMA 2009 Checklist, and the manuscript was prepared and revised according to the PRISMA 2009 Checklist.

Country/Territory of origin: China

ORCID number: Yong-Zhe Hou 0000-0003-2694-8441; Hui Ding 0000-0003-0753-1341; Yan-Ping Shu 0000-0002-0828-5675.

S-Editor: Chen YL
L-Editor: A
P-Editor: Chen YX

REFERENCES

1 **Griggs S**, Harper A, Hickman RL Jr. A systematic review of sleep deprivation and neurobehavioral function in young adults. *Appl Nurs Res* 2022; **63**: 151552 [PMID: 35034695 DOI: 10.1016/j.apnr.2021.151552]

2 **Denney JT**, Zamora-Kapoor A, Hansen DA, Whitney P. Race/ethnicity, sleep duration, and mortality risk in the United States. *SSM Popul Health* 2023; **21**: 101350 [PMID: 36785549 DOI: 10.1016/j.ssmph.2023.101350]

3 **Gilmour H**, Lu D, Polsky JY. Sleep duration, sleep quality and obesity in the Canadian Armed Forces. *Health Rep* 2023; **34**: 3-14 [PMID: 37219888 DOI: 10.25318/82-003-x202300500001-eng]

4 **Svensson T**, Saito E, Svensson AK, Melander O, Orho-Melander M, Mimura M, Rahman S, Sawada N, Koh WP, Shu XO, Tsuji I, Kanemura S, Park SK, Nagata C, Tsugane S, Cai H, Yuan JM, Matsuyama S, Sugawara Y, Wada K, Yoo KY, Chia KS, Boffetta P, Ahsan H, Zheng W, Kang D, Potter JD, Inoue M. Association of Sleep Duration With All- and Major-Cause Mortality Among Adults in Japan, China, Singapore, and Korea. *JAMA Netw Open* 2021; **4**: e2122837 [PMID: 34477853 DOI: 10.1001/jamanetworkopen.2021.22837]

5 **Chan CMH**, Siau CS, Wong JE, Wee LH, Jamil NA, Hoe VCW. Prevalence of Insufficient Sleep and Its Associated Factors Among Working

Adults in Malaysia. *Nat Sci Sleep* 2021; **13**: 1109-1116 [PMID: 34285616 DOI: 10.2147/NSS.S295537]

6 **Chaput JP**, McHill AW, Cox RC, Broussard JL, Dutil C, da Costa BGG, Sampasa-Kanyinga H, Wright KP Jr. The role of insufficient sleep and circadian misalignment in obesity. *Nat Rev Endocrinol* 2023; **19**: 82-97 [PMID: 36280789 DOI: 10.1038/s41574-022-00747-7]

7 **Boege HL**, Bhatti MZ, St-Onge MP. Circadian rhythms and meal timing: impact on energy balance and body weight. *Curr Opin Biotechnol* 2021; **70**: 1-6 [PMID: 32998085 DOI: 10.1016/j.copbio.2020.08.009]

8 **Chaput JP**, Dutil C, Featherstone R, Ross R, Giangregorio L, Saunders TJ, Janssen I, Poitras VJ, Kho ME, Ross-White A, Carrier J. Sleep duration and health in adults: an overview of systematic reviews. *Appl Physiol Nutr Metab* 2020; **45**: S218-S231 [PMID: 33054337 DOI: 10.1139/apnm-2020-0034]

9 **Evbayekha EO**, Aiwuyo HO, Dilibe A, Nriagu BN, Idowu AB, Eletta RY, Ohikhuai EE. Sleep Deprivation Is Associated With Increased Risk for Hypertensive Heart Disease: A Nationwide Population-Based Cohort Study. *Cureus* 2022; **14**: e33005 [PMID: 36712752 DOI: 10.7759/cureus.33005]

10 **Button KS**, Ioannidis JP, Mokrysz C, Nosek BA, Flint J, Robinson ES, Munafò MR. Power failure: why small sample size undermines the reliability of neuroscience. *Nat Rev Neurosci* 2013; **14**: 365-376 [PMID: 23571845 DOI: 10.1038/nrn3475]

11 **Thompson KI**, Chau M, Lorenzetti MS, Hill LD, Fins AI, Tartar JL. Acute sleep deprivation disrupts emotion, cognition, inflammation, and cortisol in young healthy adults. *Front Behav Neurosci* 2022; **16**: 945661 [PMID: 36212194 DOI: 10.3389/fnbeh.2022.945661]

12 **Garbarino S**, Lanteri P, Bragazzi NL, Magnavita N, Scoditti E. Role of sleep deprivation in immune-related disease risk and outcomes. *Commun Biol* 2021; **4**: 1304 [PMID: 34795404 DOI: 10.1038/s42003-021-02825-4]

13 **Ye H**, Ji M, Wang C, Li Y, Chen Y, Cheng L, Yang JJ. Integrated Functional Neuroimaging, Monoamine Neurotransmitters, and Behavioral Score on Depressive Tendency in Intensive Care Unit Medical Staffs Induced by Sleep Deprivation After Night Shift Work. *Front Psychiatry* 2022; **13**: 848709 [PMID: 35392383 DOI: 10.3389/fpsyt.2022.848709]

14 **Javaheripour N**, Shahdipour N, Noori K, Zarei M, Camilleri JA, Laird AR, Fox PT, Eickhoff SB, Eickhoff CR, Rosenzweig I, Khazaie H, Tahmasian M. Functional brain alterations in acute sleep deprivation: An activation likelihood estimation meta-analysis. *Sleep Med Rev* 2019; **46**: 64-73 [PMID: 31063939 DOI: 10.1016/j.smrv.2019.03.008]

15 **Zang YF**, Zuo XN, Milham M, Hallett M. Toward a Meta-Analytic Synthesis of the Resting-State fMRI Literature for Clinical Populations. *Biomed Res Int* 2015; **2015**: 435265 [PMID: 26171391 DOI: 10.1155/2015/435265]

16 **Zhang DS**, Gao J, Zhe X. Meta-analysis of activation likelihood estimation in resting state function MRI abnormal activity brain region in type 2 diabetes mellitus patients. *Chin J Radiol* 2018; **52**: 241-246 [DOI: 10.3760/cma.j.issn.1005-1201.2018.04.001]

17 **Moher D**, Liberati A, Tetzlaff J, Altman DG; PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med* 2009; **6**: e1000097 [PMID: 19621072 DOI: 10.1371/journal.pmed.1000097]

18 **Radua J**, Mataix-Cols D, Phillips ML, El-Hage W, Kronhaus DM, Cardoner N, Surguladze S. A new meta-analytic method for neuroimaging studies that combines reported peak coordinates and statistical parametric maps. *Eur Psychiatry* 2012; **27**: 605-611 [PMID: 21658917 DOI: 10.1016/j.eurpsy.2011.04.001]

19 **Dai XJ**, Gong HH, Wang YX, Zhou FQ, Min YJ, Zhao F, Wang SY, Liu BX, Xiao XZ. Gender differences in brain regional homogeneity of healthy subjects after normal sleep and after sleep deprivation: a resting-state fMRI study. *Sleep Med* 2012; **13**: 720-727 [PMID: 22503940 DOI: 10.1016/j.sleep.2011.09.019]

20 **Dai XJ**, Gong HH, Min YJ, Wang SY, Liu BX. Resting-state fMRI observation on difference of regional homogeneity in healthy subjects after normal sleep and sleep deprivation. *Zhongguo Yixue Yingxiang Jishu* 2012; **28**: 243-246 [DOI: 10.13929/j.1003-3289.2012.02.002]

21 **Gao L**, Bai L, Zhang Y, Dai XJ, Netra R, Min Y, Zhou F, Niu C, Dun W, Gong H, Zhang M. Frequency-dependent changes of local resting oscillations in sleep-deprived brain. *PLoS One* 2015; **10**: e0120323 [PMID: 25798918 DOI: 10.1371/journal.pone.0120323]

22 **Dai XJ**, Liu CL, Zhou RL, Gong HH, Wu B, Gao L, Wang YX. Long-term total sleep deprivation decreases the default spontaneous activity and connectivity pattern in healthy male subjects: a resting-state fMRI study. *Neuropsychiatr Dis Treat* 2015; **11**: 761-772 [PMID: 25834451 DOI: 10.2147/NDT.S78335]

23 **Wang L**, Chen Y, Yao Y, Pan Y, Sun Y. Sleep deprivation disturbed regional brain activity in healthy subjects: evidence from a functional magnetic resonance-imaging study. *Neuropsychiatr Dis Treat* 2016; **12**: 801-807 [PMID: 27110113 DOI: 10.2147/NDT.S99644]

24 **Li JY**, Song YL, Qi JL, Wu Y, Peng ZB. Observation of local consistency changes in adult brain after long-term sleep deprivation at different times using resting state fMRI. *Cigongzhen Chengxiang* 2017; **8**: 95-99

25 **Li JY**, Cai XP, Zhou L, Shao YC. The fMRI findings of the effect of transcranial electrical stimulation on local brain consistency after sleep deprivation. *Zhongguo Yixue Yingxiangxue Zazhi* 2017; **25**: 335-339, 343

26 **Zhou GL**, Zhou YY, Liu Y, Peng L, Pan SY, Sun YY, Huang CJ, Chen XL, Zhu XH, Hu WM. Functional magnetic resonance imaging study on low-frequency amplitude changes during sleep deprivation in healthy adolescents. *Zhongguo Xinlijiankang Zazhi* 2017; **31**: 170-176

27 **Robinson JL**, Erath SA, Kana RK, El-Sheikh M. Neurophysiological differences in the adolescent brain following a single night of restricted sleep - A 7T fMRI study. *Dev Cogn Neurosci* 2018; **31**: 1-10 [PMID: 29680789 DOI: 10.1016/j.dcn.2018.03.012]

28 **Chen L**, Qi X, Zheng J. Altered Regional Cortical Brain Activity in Healthy Subjects After Sleep Deprivation: A Functional Magnetic Resonance Imaging Study. *Front Neurol* 2018; **9**: 588 [PMID: 30116216 DOI: 10.3389/fneur.2018.00588]

29 **Feng P**, Becker B, Feng T, Zheng Y. Alter spontaneous activity in amygdala and vmPFC during fear consolidation following 24 h sleep deprivation. *Neuroimage* 2018; **172**: 461-469 [PMID: 29378319 DOI: 10.1016/j.neuroimage.2018.01.057]

30 **Feng P**, Jin YL, Zheng Y, Feng TY. Neural mechanisms underlying fear memory consolidation influenced by sleep deprivation using the fraction amplitude of low- frequency fluctuations as marker. *Zhongguo Kexue: Shengming Kexue* 2018; **48**: 1115-1125

31 **Guo Z**, Jiang Z, Jiang B, McClure MA, Mu Q. High-Frequency Repetitive Transcranial Magnetic Stimulation Could Improve Impaired Working Memory Induced by Sleep Deprivation. *Neural Plast* 2019; **2019**: 7030286 [PMID: 31915432 DOI: 10.1155/2019/7030286]

32 **Nechifor RE**, Ciobanu D, Vonica CL, Popita C, Roman G, Bala C, Mocan A, Inceu G, Craciun A, Rusu A. Social jetlag and sleep deprivation are associated with altered activity in the reward-related brain areas: an exploratory resting-state fMRI study. *Sleep Med* 2020; **72**: 12-19 [PMID: 32540632 DOI: 10.1016/j.sleep.2020.03.018]

33 **Qiu GB**, Liao WX, Liu YH, Chen JC. Study on resting brain function in chronic partial sleep deprivation Imaging. *Yanjiu Yu Yixueyingyong* 2021; **5**: 61-62

34 **Xu YQ**, Wang XR, Hu WZ, Yin H, Zhu YQ. The cognitive neural mechanism of short-term sleep deprivation affecting sustained attention: based on resting state functional MRI low-frequency amplitude fraction analysis. *Fangshexue Shijian* 2021; **36**: 158-163 [DOI: 10.13609/j.cnki.1000-0313.2021.02.003]

35 **Zeng B**, Zhou J, Li Z, Zhang H, Yu P. Altered Percent Amplitude of Fluctuation in Healthy Subjects After 36 h Sleep Deprivation. *Front Neurol* 2020; **11**: 565025 [PMID: 33519662 DOI: 10.3389/fneur.2020.565025]

36 **Cai Y**, Mai Z, Li M, Zhou X, Ma N. Altered frontal connectivity after sleep deprivation predicts sustained attentional impairment: A resting-state functional magnetic resonance imaging study. *J Sleep Res* 2021; **30**: e13329 [PMID: 33686744 DOI: 10.1111/jsr.13329]

37 **Nechifor RE**, Popita C, Bala C, Vonica C, Ciobanu D, Roman G, Mocan A, Sima D, Inceu G, Craciun A, Pop RM, Craciun C, Rusu A. Regional homogeneity and degree of centrality in social jetlag and sleep deprivation and their correlations with appetite: a resting-state fMRI study. *Bio Rhythm Res* 2022; **53**: 966-986 [DOI: 10.1080/09291016.2020.1854991]

38 **Xin KK**, Wang L, Sun ZH, Kang F, Quan ZY, Zhu YQ, Mu Y, Wang J. The percentage change of low-frequency oscillation amplitude in the resting state frontoparietal network after sleep deprivation. *Shenjing Jiepouxue Zazhi* 2022; **38**: 549-554 [DOI: 10.16557/j.cnki.1000-7547.2022.05.010]

39 **Yan FX**, Lin JL, Lin JH, Chen HJ, Lin YJ. Altered dynamic brain activity and its association with memory decline after night shift-related sleep deprivation in nurses. *J Clin Nurs* 2023; **32**: 3852-3862 [PMID: 36081313 DOI: 10.1111/jocn.16515]

40 **Chen J**, Gong X, Wang L, Xu M, Zhong X, Peng Z, Song T, Xu L, Lian J, Shao Y, Weng X. Altered Postcentral Connectivity after Sleep Deprivation Correlates to Impaired Risk Perception: A Resting-State Functional Magnetic Resonance Imaging Study. *Brain Sci* 2023; **13** [PMID: 36979324 DOI: 10.3390/brainsci13030514]

41 **Cirelli C**, Tononi G. The why and how of sleep-dependent synaptic down-selection. *Semin Cell Dev Biol* 2022; **125**: 91-100 [PMID: 33712366 DOI: 10.1016/j.semcdb.2021.02.007]

42 **Nissen C**, Piosczyk H, Holz J, Maier JG, Frase L, Sterr A, Riemann D, Feige B. Sleep is more than rest for plasticity in the human cortex. *Sleep* 2021; **44** [PMID: 33401305 DOI: 10.1093/sleep/zsaa216]

43 **Santisteban JA**, Brown TG, Ouimet MC, Gruber R. Cumulative mild partial sleep deprivation negatively impacts working memory capacity but not sustained attention, response inhibition, or decision making: a randomized controlled trial. *Sleep Health* 2019; **5**: 101-108 [PMID: 30670158 DOI: 10.1016/j.sleh.2018.09.007]

44 **Hennecke E**, Lange D, Steenbergen F, Fronczek-Poncelet J, Elmenhorst D, Bauer A, Aeschbach D, Elmenhorst EM. Adverse interaction effects of chronic and acute sleep deficits on spatial working memory but not on verbal working memory or declarative memory. *J Sleep Res* 2021; **30**: e13225 [PMID: 33169493 DOI: 10.1111/jsr.13225]

45 **Scullin MK**, Gao C. Dynamic Contributions of Slow Wave Sleep and REM Sleep to Cognitive Longevity. *Curr Sleep Med Rep* 2018; **4**: 284-293 [PMID: 31737466 DOI: 10.1007/s40675-018-0131-6]

46 **Pizzagalli DA**, Roberts AC. Prefrontal cortex and depression. *Neuropsychopharmacology* 2022; **47**: 225-246 [PMID: 34341498 DOI: 10.1038/s41386-021-01101-7]

47 **Lee MH**, Lee KH, Oh SM, Seo MC, Lee H, Jeon JE, Lee YJ. The moderating effect of prefrontal response to sleep-related stimuli on the association between depression and sleep disturbance in insomnia disorder. *Sci Rep* 2022; **12**: 17739 [PMID: 36272992 DOI: 10.1038/s41598-022-22652-9]

48 **Yeung MK**, Lee TL, Cheung WK, Chan AS. Frontal Underactivation During Working Memory Processing in Adults With Acute Partial Sleep Deprivation: A Near-Infrared Spectroscopy Study. *Front Psychol* 2018; **9**: 742 [DOI: 10.3389/fpsyg.2018.00742]

49 **Roussy M**, Corrigan B, Luna R, Gulli RA, Sachs AJ, Palaniyappan L, Martinez-Trujillo JC. Stable Working Memory and Perceptual Representations in Macaque Lateral Prefrontal Cortex during Naturalistic Vision. *J Neurosci* 2022; **42**: 8328-8342 [PMID: 36195438 DOI: 10.1523/JNEUROSCI.0597-22.2022]

50 **Friedman NP**, Robbins TW. The role of prefrontal cortex in cognitive control and executive function. *Neuropsychopharmacology* 2022; **47**: 72-89 [PMID: 34408280 DOI: 10.1038/s41386-021-01132-0]

51 **Sander TH**, Zhou B. Linking neuroimaging signals to behavioral responses in single cases: Challenges and opportunities. *Psych J* 2016; **5**: 161-169 [PMID: 27678481 DOI: 10.1002/pchj.143]

52 **Li B**, Zhang L, Zhang Y, Chen Y, Peng J, Shao Y, Zhang X. Decreased Functional Connectivity Between the Right Precuneus and Middle Frontal Gyrus Is Related to Attentional Decline Following Acute Sleep Deprivation. *Front Neurosci* 2020; **14**: 530257 [PMID: 33408600 DOI: 10.3389/fnins.2020.530257]

53 **Wang L**, Wu H, Dai C, Peng Z, Song T, Xu L, Xu M, Shao Y, Li S, Fu W. Dynamic hippocampal functional connectivity responses to varying working memory loads following total sleep deprivation. *J Sleep Res* 2023; **32**: e13797 [PMID: 36528854 DOI: 10.1111/jsr.13797]

54 **Li Y**, Ma M, Shao Y, Wang W. Enhanced effective connectivity from the middle frontal gyrus to the parietal lobe is associated with impaired mental rotation after total sleep deprivation: An electroencephalogram study. *Front Neurosci* 2022; **16**: 910618 [PMID: 36248651 DOI: 10.3389/fnins.2022.910618]

55 **Sun J**, Zhao R, Yang X, Deng H, Zhu Y, Chen Y, Yuan K, Xi Y, Yin H, Qin W. Alteration of Brain Gray Matter Density After 24 h of Sleep Deprivation in Healthy Adults. *Front Neurosci* 2020; **14**: 754 [PMID: 32903801 DOI: 10.3389/fnins.2020.00754]

56 **Chen WH**, Chen J, Lin X, Li P, Shi L, Liu JJ, Sun HQ, Lu L, Shi J. Dissociable effects of sleep deprivation on functional connectivity in the dorsal and ventral default mode networks. *Sleep Med* 2018; **50**: 137-144 [PMID: 30055480 DOI: 10.1016/j.sleep.2018.05.040]

57 **Szczupak D**, Iack PM, Rayêe D, Liu C, Lent R, Tovar-Moll F, Silva AC. The relevance of heterotopic callosal fibers to interhemispheric connectivity of the mammalian brain. *Cereb Cortex* 2023; **33**: 4752-4760 [PMID: 36178137 DOI: 10.1093/cercor/bhac377]

58 **Bruce HA**, Kochunov P, Kvarta MD, Goldwaser EL, Chiappelli J, Schwartz A, Lightner S, Endres J, Yuen A, Ma Y, Van der Vaart A, Hatch KS, Gao S, Ye Z, Wu Q, Chen S, Mitchell BD, Hong LE. Frontal white matter association with sleep quality and the role of stress. *J Sleep Res* 2023; **32**: e13669 [PMID: 35698853 DOI: 10.1111/jsr.13669]

59 **Zhu Y**, Ren F, Zhu Y, Zhang X, Liu W, Tang X, Qiao Y, Cai Y, Zheng M. Gradually Increased Interhemispheric Functional Connectivity During One Night of Sleep Deprivation. *Nat Sci Sleep* 2020; **12**: 1067-1074 [PMID: 33262670 DOI: 10.2147/NSS.S270009]

60 **Vargas I**, Drake CL, Lopez-Duran NL. Insomnia Symptom Severity Modulates The Impact of Sleep Deprivation on Attentional Biases to Emotional Information. *Cogn Ther Res* 2017; **41**: 842-852 [DOI: 10.1007/s10608-017-9859-4]

61 **Taraku B**, Zavaliangos-Petropulu A, Loureiro JR, Al-Sharif NB, Kubicki A, Joshi SH, Woods RP, Espinoza R, Narr KL, Sahib AK. White matter microstructural perturbations after total sleep deprivation in depression. *Front Psychiatry* 2023; **14**: 1195763 [PMID: 37457774 DOI: 10.3389/fpsyt.2023.1195763]

62 **Li G**, Zhang X, Zhang J, Wang E, Zhang H, Li Y. Magnetic resonance study on the brain structure and resting-state brain functional connectivity in primary insomnia patients. *Medicine (Baltimore)* 2018; **97**: e11944 [PMID: 30142814 DOI: 10.1097/MD.0000000000011944]

63 **Bellesi M**, Haswell JD, de Vivo L, Marshall W, Roseboom PH, Tononi G, Cirelli C. Myelin modifications after chronic sleep loss in adolescent mice. *Sleep* 2018; **41** [PMID: 29741724 DOI: 10.1093/sleep/zsy034]

64 **Biswal B**, Yetkin FZ, Haughton VM, Hyde JS. Functional connectivity in the motor cortex of resting human brain using echo-planar MRI. *Magn Reson Med* 1995; **34**: 537-541 [PMID: 8524021 DOI: 10.1002/mrm.1910340409]

65 **Zang Y**, Jiang T, Lu Y, He Y, Tian L. Regional homogeneity approach to fMRI data analysis. *Neuroimage* 2004; **22**: 394-400 [PMID: 15110032 DOI: 10.1016/j.neuroimage.2003.12.030]

World Journal of Psychiatry

Submit a Manuscript: https://www.f6publishing.com

World J Psychiatry 2024 February 19; 14(2): 330-333

DOI: 10.5498/wjp.v14.i2.330

ISSN 2220-3206 (online)

LETTER TO THE EDITOR

Using ChatGPT to promote college students' participation in physical activities and its effect on mental health

Yi-Fan Zhang, Xin-Qiao Liu

Specialty type: Psychiatry

Provenance and peer review: Invited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

Grade A (Excellent): A
Grade B (Very good): 0
Grade C (Good): 0
Grade D (Fair): 0
Grade E (Poor): 0

P-Reviewer: Tasijawa FA, Indonesia

Received: September 12, 2023
Peer-review started: September 12, 2023
First decision: December 12, 2023
Revised: December 19, 2023
Accepted: January 23, 2024
Article in press: January 23, 2024
Published online: February 19, 2024

Yi-Fan Zhang, Xin-Qiao Liu, School of Education, Tianjin University, Tianjin 300350, China

Corresponding author: Xin-Qiao Liu, PhD, Associate Professor, School of Education, Tianjin University, No. 135 Yaguan Road, Jinnan District, Tianjin 300350, China. xinqiaoliu@pku.edu.cn

Abstract

As one of the most famous large language models, ChatGPT has great potential for application in physical education. It can provide personalized exercise plans, a variety of exercise options, and interactive support. The integration of ChatGPT into the teaching process can promote college students' participation in physical activities and improve their mental health while expanding the traditional teaching environment and promoting the reform of traditional teaching methods. However, the application of ChatGPT faces challenges and obstacles in physical education. To make full use of ChatGPT in physical education, it can be combined with wearable devices and sports equipment to enhance the efficiency of interactions with users. Relevant policies are urgently needed to avoid the improper use of users' data.

Key Words: ChatGPT; College students; Physical education; Mental health

Core Tip: ChatGPT has great potential for application in physical education. This article argues that the integration of ChatGPT into college physical education has great benefits for both students and teachers. To make full use of ChatGPT in the future, interactions with users should be further enhanced, and relevant policies should be released to prompt the proper use of ChatGPT.

Citation: Zhang YF, Liu XQ. Using ChatGPT to promote college students' participation in physical activities and its effect on mental health. *World J Psychiatry* 2024; 14(2): 330-333
URL: https://www.wjgnet.com/2220-3206/full/v14/i2/330.htm
DOI: https://dx.doi.org/10.5498/wjp.v14.i2.330

TO THE EDITOR

We reviewed the article titled "Effect of exercise prescription teaching on exercise quality and mental health status of college students", published in Volume 13, Issue 5 of the *World Journal of Psychiatry*[1]. By randomly assigning students to an experimental group of exercise prescription teaching and a control group of routine teaching, this study examined the effects of exercise prescription teaching on students' exercise quality, cardiopulmonary function, and psychological status. The authors observed that exercise prescription teaching can formulate teaching content for students and effectively improve their physical quality. Interestingly, personalized exercise teaching for students can also benefit their mental health[1]. With the deep integration of artificial intelligence (AI) and education, we believe that ChatGPT has great potential for application in physical education.

We strongly agree with the conclusion of this study that college students' poor physical fitness, poor living habits, and mental health problems urgently require attention[2,3]. Traditional physical education mainly focuses on competitive sports and tends to ignore college students' subjectivity[4]. In contrast, exercise prescription teaching involves teaching content based on college students' physical qualities and health status[1,5]. First, the intensity of physical exercise is designed based on college students' physical qualities; that is, targeted teaching content can effectively improve college students' enthusiasm for participating in physical activities, decrease the probability of injury due to excessive intensity of exercise, and play a role in preventing chronic diseases[6,7]. Second, exercise prescriptions have been widely used to treat mental diseases[8-10], and the effect of exercise prescription teaching on students' mental health has attracted attention. Some studies note that participating in physical exercise has a significant positive impact on relieving depression and anxiety[11,12]. Furthermore, different physical activities have an impact on different aspects of physical and mental health[13,14].

In exercise prescription teaching, since students' feedback on their physical state and the effects of exercise are not always timely, teachers' adjustments of exercise plans may lag behind students' feedback. With the integration of artificial intelligence and education, AI-facilitated physical education has become a widely discussed topic in research and has brought new opportunities for physical teaching reform[15-17]. ChatGPT is currently one of the most popular large language models. It is worth further exploring the application prospects of ChatGPT or generative AI (represented in this paper by ChatGPT) in teaching[18]. First, ChatGPT can produce personalized plans based on college students' basic information[19]. By dialoging with students, ChatGPT collects specific information about them, including their physical fitness, health status, daily exercise, and exercise goals, and develops personalized exercise plans. In addition, as Khan *et al*[20] noted, when students' physical fitness and health status change, ChatGPT can receive timely feedback from students and modify their exercise plans. Second, as a conversational artificial intelligence model, ChatGPT can provide timely and interactive support[21]. Zheng *et al*[22] suggested that continuous support from ChatGPT could help users stay motivated and self-manage, and some empirical studies have reported that chatbot-assisted interventions can increase college students' interest in participating in physical activities and improve their health[18,23,24]. ChatGPT can also use dialog to encourage college students to participate in physical activities and increase their enthusiasm. Moreover, since ChatGPT is not limited by time or space, college students can have conversations with ChatGPT on their mobile phones at any time, and ChatGPT can track students' exercise after PE class and adjust their exercise plans according to students' feedback. Third, ChatGPT can provide a variety of exercise options that benefit college students' mental health. Proper physical exercise is a critical way to alleviate psychological problems[25]. ChatGPT can suggest different physical activities according to different psychological problems. Fourth, the integration of ChatGPT into the teaching process has many benefits for teachers as well because it not only expands the traditional teaching environment but also promotes the reform of traditional teaching methods[26,27].

Although ChatGPT has excellent application prospects in physical education, it faces some challenges and obstacles in the teaching process. First, the reliability of the exercise plans developed by ChatGPT should be verified. The official website of OpenAI emphasizes that ChatGPT may yield incorrect or meaningless answers due to the limitations of machine training and other reasons, which may mislead students. If ChatGPT's recommendations are harmful to students' health, it is unclear who is responsible for the consequences[28]. Second, ChatGPT may lead to adverse effects on students' development. Overreliance on ChatGPT hinders the development of students' critical thinking and creativity [29]. In addition, the use of ChatGPT in education presents higher requirements for students' self-control, and it remains unclear whether ChatGPT will exacerbate educational inequity. Third, students' excessive reliance on ChatGPT will pose a challenge to traditional teaching and teacher-student relationships[30].

ChatGPT has been iterated to GPT-4. Some studies have applied it in clinical practice[31,32], and its impact on the field of education has attracted increasing attention[20,21,33]. To promote the application of ChatGPT in educational practice, we present the following suggestions for its future development. First, to better integrate ChatGPT into reality, it can be combined with wearable devices and sports equipment to monitor students' physical status in real time and improve interaction efficiency. Second, the ethical and data protection issues that may be caused by ChatGPT have been widely discussed[34,35]. Therefore, it is urgent to develop relevant policies to restrict ChatGPT. Affiliated companies should pay attention to users' privacy issues to avoid the improper use of users' data.

As the latest product of the era of artificial intelligence, ChatGPT has great potential for application in college physical education. However, despite its ability to revolutionize education, ChatGPT also poses great challenges for schools, the government, and society. In the future, educators should further explore how ChatGPT can be integrated into education while promoting student development.

FOOTNOTES

Author contributions: Liu XQ designed the study; Zhang YF and Liu XQ wrote the manuscript; both authors contributed equally to this work and approved the final manuscript.

Conflict-of-interest statement: The authors declare no conflict of interests.

Country/Territory of origin: China

ORCID number: Yi-Fan Zhang 0000-0002-8870-9983; Xin-Qiao Liu 0000-0001-6620-4119.

S-Editor: Lin C
L-Editor: A
P-Editor: Chen YX

REFERENCES

1 **Zhong XL**, Sheng DL, Cheng TZ, Zhang ZW. Effect of exercise prescription teaching on exercise quality and mental health status of college students. *World J Psychiatry* 2023; **13**: 191-202 [PMID: 37303933 DOI: 10.5498/wjp.v13.i5.191]
2 **Liu XQ**, Guo YX, Wang X. Delivering substance use prevention interventions for adolescents in educational settings: A scoping review. *World J Psychiatry* 2023; **13**: 409-422 [PMID: 37547731 DOI: 10.5498/wjp.v13.i7.409]
3 **Cao X**, Liu X. Time Use and Cognitive Achievement among Adolescents in China: Depression Symptoms as Mediators. *J Intell* 2023; **11** [PMID: 37233337 DOI: 10.3390/jintelligence11050088]
4 **Wu Y**, Zhang F. Research on the Influence of Sports and Nutrition Matching on Improving Students' Physique Based on Intelligent Sensor. *Comput Intell Neurosci* 2021; **2021**: 3556131 [PMID: 35003241 DOI: 10.1155/2021/3556131]
5 **Schneider M**, Schmalbach P, Godkin S. Impact of a personalized versus moderate-intensity exercise prescription: a randomized controlled trial. *J Behav Med* 2017; **40**: 239-248 [PMID: 27481104 DOI: 10.1007/s10865-016-9776-0]
6 **Abonie US**, Edwards AM, Hettinga FJ. Optimising activity pacing to promote a physically active lifestyle in medical settings: A narrative review informed by clinical and sports pacing research. *J Sports Sci* 2020; **38**: 590-596 [PMID: 31997716 DOI: 10.1080/02640414.2020.1721254]
7 **Phillips EM**, Kennedy MA. The exercise prescription: a tool to improve physical activity. *PM R* 2012; **4**: 818-825 [PMID: 23174544 DOI: 10.1016/j.pmrj.2012.09.582]
8 **Radovic S**, Melvin GA, Gordon MS. Clinician perspectives and practices regarding the use of exercise in the treatment of adolescent depression. *J Sports Sci* 2018; **36**: 1371-1377 [PMID: 28945524 DOI: 10.1080/02640414.2017.1383622]
9 **Garvey L**, Benson AC, Benger D, Short T, Banyard H, Edward KL. The perceptions of mental health clinicians integrating exercise as an adjunct to routine treatment of depression and anxiety. *Int J Ment Health Nurs* 2023; **32**: 502-512 [PMID: 36369663 DOI: 10.1111/inm.13089]
10 **Stanton R**, Happell B, Reaburn P. Investigating the exercise-prescription practices of nurses working in inpatient mental health settings. *Int J Ment Health Nurs* 2015; **24**: 112-120 [PMID: 25639383 DOI: 10.1111/inm.12125]
11 **Cao X**, Zhang Q, Liu Q. Cross-lagged relationship between physical activity time, openness and depression symptoms among adolescents: Evidence from China. *Int J Ment Health Promot* 2023; **25**: 1009-1018 [DOI: 10.32604/ijmhp.2023.029365]
12 **Herring MP**, Gordon BR, McDowell CP, Quinn LM, Lyons M. Physical activity and analogue anxiety disorder symptoms and status: Mediating influence of social physique anxiety. *J Affect Disord* 2021; **282**: 511-516 [PMID: 33433380 DOI: 10.1016/j.jad.2020.12.163]
13 **Zhang Z**, Min HJ. Effects of Different Physical Exercises on Physical and Mental Health of Female College Students. *J Healthc Eng* 2022; **2022**: 7812005 [PMID: 35273785 DOI: 10.1155/2022/7812005]
14 **Couto N**, Monteiro D, Cid L, Bento T. Effect of different types of exercise in adult subjects with fibromyalgia: a systematic review and meta-analysis of randomised clinical trials. *Sci Rep* 2022; **12**: 10391 [PMID: 35725780 DOI: 10.1038/s41598-022-14213-x]
15 **Yu S**. Application of artificial intelligence in physical education. *Int J Electr Eng Educ* 2021; **60**: 1-10 [DOI: 10.1177/0020720921996604]
16 **Deng C**, Yu Q, Luo G, Zhao Z, Li Y. Big data-driven intelligent governance of college students' physical health: System and strategy. *Front Public Health* 2022; **10**: 924025 [PMID: 36033780 DOI: 10.3389/fpubh.2022.924025]
17 **Hsia LH**, Hwang GJ, Hwang JP. AI-facilitated reflective practice in physical education: An auto-assessment and feedback approach. *Interact Learn Envir* 2023 [DOI: 10.1080/10494820.2023.2212712]
18 **Vandelanotte C**, Trost S, Hodgetts D, Imam T, Rashid M, To QG, Maher C. Increasing physical activity using an just-in-time adaptive digital assistant supported by machine learning: A novel approach for hyper-personalised mHealth interventions. *J Biomed Inform* 2023; **144**: 104435 [PMID: 37394024 DOI: 10.1016/j.jbi.2023.104435]
19 **Cascella M**, Montomoli J, Bellini V, Bignami E. Evaluating the Feasibility of ChatGPT in Healthcare: An Analysis of Multiple Clinical and Research Scenarios. *J Med Syst* 2023; **47**: 33 [PMID: 36869927 DOI: 10.1007/s10916-023-01925-4]
20 **Khan RA**, Jawaid M, Khan AR, Sajjad M. ChatGPT - Reshaping medical education and clinical management. *Pak J Med Sci* 2023; **39**: 605-607 [PMID: 36950398 DOI: 10.12669/pjms.39.2.7653]
21 **Lee H**. The rise of ChatGPT: Exploring its potential in medical education. *Anat Sci Educ* 2023 [PMID: 36916887 DOI: 10.1002/ase.2270]
22 **Zheng Y**, Wu Y, Feng B, Wang L, Kang K, Zhao A. Enhancing Diabetes Self-management and Education: A Critical Analysis of ChatGPT's Role. *Ann Biomed Eng* 2023 [PMID: 37553556 DOI: 10.1007/s10439-023-03317-8]

23 **Krishnakumar A**, Verma R, Chawla R, Sosale A, Saboo B, Joshi S, Shaikh M, Shah A, Kolwankar S, Mattoo V. Evaluating Glycemic Control in Patients of South Asian Origin With Type 2 Diabetes Using a Digital Therapeutic Platform: Analysis of Real-World Data. *J Med Internet Res* 2021; **23**: e17908 [PMID: 33764306 DOI: 10.2196/17908]

24 **Kramer JN**, Künzler F, Mishra V, Smith SN, Kotz D, Scholz U, Fleisch E, Kowatsch T. Which Components of a Smartphone Walking App Help Users to Reach Personalized Step Goals? Results From an Optimization Trial. *Ann Behav Med* 2020; **54**: 518-528 [PMID: 32182353 DOI: 10.1093/abm/kaaa002]

25 **Liu XQ**, Guo YX, Zhang WJ, Gao WJ. Influencing factors, prediction and prevention of depression in college students: A literature review. *World J Psychiatry* 2022; **12**: 860-873 [PMID: 36051603 DOI: 10.5498/wjp.v12.i7.860]

26 **Celik I**. Towards Intelligent-TPACK: An empirical study on teachers' professional knowledge to ethically integrate artificial intelligence (AI)-based tools into education. *Comput Human Behav* 2023; **138**: 107468 [DOI: 10.1016/j.chb.2022.107468]

27 **Crompton H**, Burke D. Artificial intelligence in higher education: the state of the field. *J Educ Technol High Educ* 2023; **20**: 22 [DOI: 10.1186/s41239-023-00392-8]

28 **Arslan S**. Exploring the Potential of Chat GPT in Personalized Obesity Treatment. *Ann Biomed Eng* 2023; **51**: 1887-1888 [PMID: 37145177 DOI: 10.1007/s10439-023-03227-9]

29 **Cotton DRE**, Cotton PA, Shipway JR. Chatting and cheating: Ensuring academic integrity in the era of ChatGPT. *Innov Educ Teah Int* 2023 [DOI: 10.1080/14703297.2023.2190148]

30 **Chan CKY**, Hu W. Students' voices on generative AI: Perceptions, benefits, and challenges in higher education. *Int J Educ Technol High Educ* 2023; **20**: 43 [DOI: 10.1186/s41239-023-00411-8]

31 **Zhang L**, Tashiro S, Mukaino M, Yamada S. Use of artificial intelligence large language models as a clinical tool in rehabilitation medicine: a comparative test case. *J Rehabil Med* 2023; **55**: jrm13373 [PMID: 37691497 DOI: 10.2340/jrm.v55.13373]

32 **Ong H**, Ong J, Cheng R, Wang C, Lin M, Ong D. GPT Technology to Help Address Longstanding Barriers to Care in Free Medical Clinics. *Ann Biomed Eng* 2023; **51**: 1906-1909 [PMID: 37355478 DOI: 10.1007/s10439-023-03256-4]

33 **Sallam M**. ChatGPT Utility in Healthcare Education, Research, and Practice: Systematic Review on the Promising Perspectives and Valid Concerns. *Healthcare (Basel)* 2023; **11** [PMID: 36981544 DOI: 10.3390/healthcare11060887]

34 **Wang C**, Liu S, Yang H, Guo J, Wu Y, Liu J. Ethical Considerations of Using ChatGPT in Health Care. *J Med Internet Res* 2023; **25**: e48009 [PMID: 37566454 DOI: 10.2196/48009]

35 **Moldt JA**, Festl-Wietek T, Madany Mamlouk A, Nieselt K, Fuhl W, Herrmann-Werner A. Chatbots for future docs: exploring medical students' attitudes and knowledge towards artificial intelligence and medical chatbots. *Med Educ Online* 2023; **28**: 2182659 [PMID: 36855245 DOI: 10.1080/10872981.2023.2182659]

Published by **Baishideng Publishing Group Inc**
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-3991568
E-mail: office@baishideng.com
Help Desk: https://www.f6publishing.com/helpdesk
https://www.wjgnet.com