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Promoting recovery from severe mental illness: Implications from research on metacognition and metacognitive reflection and insight therapy

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Abstract

Research indicates that individuals with schizophrenia recover. Recovery, however means different things to different individuals and regardless of what kind of experiences define recovery, the individual diagnosed with the serious mental illness must feel ownership of their recovery. This raises the issue of how mental health services should systematically promote recovery. This paper explores the practical implications for research on metacognition in schizophrenia for this issue. First, we present the integrated model of metacognition, which defines metacognition as the spectrum of activities which allow individual to have available to themselves an integrated sense of self and others as they appraise and respond to the unique challenges they face. Second, we present research suggesting that many with schizophrenia experience deficits in metacognition and that those deficits

compromise individuals' abilities to manage their lives and mental health challenges. Third, we discuss a form of psychotherapy inspired by this research, Metacognitive Reflection and Insight Therapy which assists individuals to recapture the ability to form integrated ideas about themselves and others and so direct their own recovery. The need for recovery oriented interventions to focus on process and on patient's purposes, assess metacognition and consider the intersubjective contexts in which this occurs is discussed.

Key words: Schizophrenia; Rehabilitation; Self; Psychosis; Metacognition; Recovery; Psychotherapy; Social cognition

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Core tip: Impairments in metacognitive processes challenge the abilities of individuals with schizophrenia to form and sustain an integrated sense of self and others. These deficits in metacognition compromise individuals' abilities to manage their lives and mental health challenges. Treatments which help individuals with schizophrenia recapture metacognitive abilities can assist those individuals to regain access to the kinds of integrated ideas about themselves and others which assists them to meaningfully direct their own recovery. Metacognitive Reflection and Insight Therapy is an example of this kind of treatment.

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INTRODUCTION

Serious mental illness, whether referring to schizophrenia spectrum disorders or psychosis more broadly, is by definition tied to a multitude of psychological and social challenges. Regardless of whether we are considering matters at the cellular level, larger brain structures, phenomenology, or complex social and environmental structures, individuals diagnosed with these conditions experience disruptions, which culminate in the interruption not only of their lives but also of the lives of their families, partners, friends, and others living in their communities.

For decades, these conditions were assumed to involve progressive decline and dysfunction. Individuals held out little hope for wellness and it was assumed that individuals diagnosed with these conditions could at best hope for stability. If operationalized, this seemed to consist only of freedom from acute distress

and institutionalization^[1]. Multiple levels of evidence, including careful long-term follow-up, qualitative and quantitative clinical research, and a multitude of first person accounts, however, have offered a very different picture. Taking an optimistic turn, this work has suggested that no matter how ill a person can be at a particular moment, individuals with serious mental illness can recover in a personally meaningful manner regardless of the limitations imposed upon an individual's life by the disorder^[2].

These studies of outcome and recovery have also highlighted the complexity of the concept of recovery itself^[3,4]. Among other things, it is clear that recovery can and does mean different things to different people^[5]. Recovery, for some people, is mostly a matter of changes in objective phenomena. For example, to recover could mean that symptoms remit or that individuals attain certain psychosocial milestones, such as returning to work or school. Recovery can also involve a host of subjective experiences including attaining a self-appraised acceptable quality of life or reasonable sense of social rank. Recovery could mean no longer feeling tainted or different from others, or at a more subjective level, it could involve recapturing a cohesive sense of oneself as a valuable person in the world^[6,7]. For many, these subjective and objective aspects of recovery are complementary and interact with each other^[1,8]. Despite the complexity and individual variation of the concept of recovery, there do appear to be three things that are inevitably true about recovery: (1) It happens; (2) its meaning is contextualized; and (3) regardless of what kind of experiences define recovery, the person diagnosed with the serious mental illness must feel a sense of ownership of their recovery^[2]. This is to say that the person diagnosed with mental illness must direct their own recovery. In this sense, recovery is a matter undertaken by an agent in the world^[9]. Recovery consequently is not just "fixing" something or finding solutions for any number of dilemmas. Recovery requires individuals to make sense, in the moment and over time, of the experiences that surround mental illness. Sense and meaning has to be made of psychiatric and social challenges, changes in the person's own mind and body, the minds of others and about what is happening in the larger world. Meaning-making is necessary, both implicitly and explicitly, for decisions to be made about how to respond to challenges^[2,10]. To sum up: Recovery from serious mental illness requires that the person diagnosed with the condition be an active agent in that process.

This knowledge is freeing but also adds extra responsibility for clinical care^[11]. If recovery is possible, naturally it should be the goal of treatment. But given the different meanings recovery has and its requirement that the individual in treatment be in charge in some meaningful way, what is the clinician to do beyond offering general support and attending

to the other common factors of treatment? How can clinical care systematically promote something that differs from person to person and which has to be ultimately directed by the person with serious mental illness?

This paper explores how research on the integrative model of metacognition and related developments in individual psychotherapy may offer a partial answer to this question by offering a larger framework for thinking about how individuals form a sense of what recovery means to them and then how they should pursue it. The integrative model of metacognition frames metacognitive processes as a spectrum of activities that enable a sense of self and others to be available to individuals in the moment that can be used to understand and respond to life's challenges. Metacognition in the integrative model is, therefore, foundational for meaning making within a given moment, for a sense of agency and ultimately the ability to decide about the meaning of psychosocial challenges and the most effective response^[7].

To explore how research on this model might help inform recovery oriented care, we will first offer a more nuanced definition of the integrative model of metacognition. We will then discuss a decade of quantitative research on the prevalence and psychosocial consequences of reductions in metacognitive capacity for adults with serious mental illness and detail the development of a specific integrative form of recovery-oriented individual psychotherapy inspired by this research. We will then suggest that this work suggests five general principles that could inform change in traditional practice in order to genuinely support recovery. Finally, we will discuss how these principles and implications of this research converge and diverge with other emerging approaches.

As an initial caveat, we think it is important to clarify two points regarding terminology. This paper will use the term schizophrenia. Many suggest the word schizophrenia is stigmatizing and questions whether there is a scientific basis for suggesting it is a medical entity. Recognizing this controversy, we will employ the word schizophrenia given that, in part, one of its later ancient Greek roots suggests the splitting or shattering of the mind, which seems a valid attempt to characterize fragmentation which those diagnosed with these conditions confront^[12]. Second, when describing people engaged in treatment we use the word "patient." This also is a controversial term as many have found mental health care to be both stigmatizing and marginalizing. This has led to other terms being commonly used including consumers, experts by experience, service users, clients, and psychiatric survivors. We chose to use the word "patient" given its roots in Latin and Greek meaning "to suffer," believing again that this characterizes the often profound suffering individuals diagnosed with these

conditions experience. We do reject any suggestion that wellness in the face of mental illness comes from being a passive recipient of care.

Metacognition

Original term: Metacognition was first used to describe the experience of having a cognition or thoughts about other cognitions. In education research it was used to examine how people are aware of their own learning and how that awareness is utilized^[13]. The term was subsequently applied to other phenomena including self-regulation^[14], the ability to monitor and correct reasoning and behavior^[15], and to reflect upon memory^[16] as well as to describe attentional biases or general interpersonal stances sometimes referred to as metacognitive beliefs^[17].

Integrated model of metacognition: As metacognition has continued to be studied across a variety of disciplines including educational, developmental, neurocognitive, and abnormal psychology the term metacognition has emerged to take on many meanings^[18]. In an effort to form an integrated model of metacognition we have proposed that metacognition is a spectrum of activities^[19]. One end of that spectrum involves awareness of discrete mental experiences that can be distinguished from one another, such as a specific thought, certain feeling or a particular desire. At the other end of that spectrum is the integration of those discrete experiences into a larger complex sense of oneself and others^[20]. These different ends of the spectrum continuously influence one another, as for any larger sense individuals have of themselves must account for discrete experience, while the meaning of a discrete experience is always influenced by a larger understanding of the individual having that experience.

In this model, metacognitive processes are what allows an integrated and cohesive sense of self and others to be available to an individual in a given moment^[7]. When metacognitive processes are fully functional they allow individuals to engage effectively in a number of mental operations simultaneously and automatically. These include the ability to recognize and distinguish specific mental experiences, to perceive how those mental experiences are changing or not changing, to contrast those mental states with the demands of reality, to see how all of that is happening in a larger context, and to see how those concrete situations fit into a larger narrative of our lives and the lives of others. Metacognition thus allows individuals access to a sense of themselves (and of others) which is multifaceted and multidimensional, while also allowing for that sense of self and others to change responsively and adaptively as contexts change. Metacognition in the integrated model is not a form of disembodied cognition or set of calculations that exist in isolation. They are vital activities that enable individuals to respond to psychological and

social challenges and ultimately function as members of the human community^[19].

For the purposes of thinking about recovery from serious mental illness, the integrative model suggests metacognitive processes have at least three distinguishing characteristics. First, metacognitive acts occur and evolve intersubjectively. The ideas individuals have of themselves or others, whether elemental and complex, are formed with others in mind, others who may be either present or implicitly imagined, such that those ideas can be shared with and acknowledged by other people^[21-23].

Second, metacognitive processes can be differentiated from one another according to their focus. As Semerari *et al.*^[24] have described, there are four discernable objects or domains of metacognition which can be distinguished from one another. These include groups of metacognitive acts, which are focused on the self, others, one's larger community and the use of knowledge about self and others to respond to life's problems, or mastery.

Third, synthetic metacognitive processes are holistic in nature and involve a series of hierarchical steps. These steps are conceptualized, per domain, as a series of levels with each level incorporating something larger into what was incorporated into the step before it. For example, the fourth step of the metacognitive processes which are focused on the self adds and incorporates something new to what was incorporated in the third step allowing for a more complex sense of self to be available in the moment. A key implication of this is that for a given step to be operating successfully the step below it also has to be operating successfully. Consequently, once a step is not operating successfully then no higher step can operate in a fully successful manner given that those higher steps would necessarily be missing the information that was supposed to be provided by the more basic or lower step. This conceptual framework allows for individual differences in metacognitive capacity to be quantified and characterized as more or less functional on the basis of an identified level of metacognition which is not fully operational. Importantly, this is not to say that individuals with lesser metacognitive capacity have less experience of the self or others, but instead that their experience of self and others is less integrated or more fragmented. It is also not to imply a purely developmental model of metacognition, as individuals with lesser metacognitive abilities may have previously held these abilities but lost them for any number of different social, biological or psychological reasons^[7].

Measuring metacognition: The Metacognition Assessment Scale (MAS^[24]) was one of the first scales that incorporated metacognition as a core construct to characterize how individuals form an evolving and multidimensional sense of self and others. The MAS offered multiple advances. First, it was explicitly

interested in the psychological processes that go beyond momentary self-awareness and facilitate the emergence of a broader sense of self and others. It also operationally differentiated metacognitive acts based on their focus and allowed for the measurement of changes in how often particular metacognitive acts were being performed. This scale was adapted by Lysaker and colleagues^[25], who transformed the original MAS into an ordinal scale referred to as Metacognition Assessment Scale Abbreviated (MAS-A). The MAS-A retained the original distinctions offered by Semerari *et al.*^[24] and so contained four scales: Self-reflectivity (S), Understanding other's minds (O), Decentration (D), and Mastery (M).

While the MAS was originally designed to detect the presence or proportion of times a metacognitive act could have been used vs was used within a psychotherapy session, the MAS-A is used to rate metacognitive capacity as it is manifest within an interview (e.g., Indiana Psychiatric Illness Interview; IPII^[25]) which provides opportunities for participants to reflect about their life and psychological challenges. Training for rating using the MAS-A consists of the completion of an established set of transcripts followed by supervision and the establishment of inter-rater reliability.

Concerning the content of the scale, the MAS-A, in contrast to the MAS, follows the integrated model of metacognition, and considers each item of each scale to reflect a more complex metacognitive act than the one before it. Each item describes a metacognitive act that requires the integration of a new kind of information that was not included in the previous item. Concretely then, a rater scores each item in the MAS-A as adequately functioning or attained ("1") if they judge the participant to be capable of performing that act or as not attained ("0") if they judge the participant to not be capable of performing that act and once a score of "0" is given for an item no further levels can be scored as attained. Thus, the scores from the MAS-A indicate participants' maximal level of metacognitive function, or the last level before their metacognitive processes were judged to fail to fully operate and so the scores on each MAS-A subscale allows for the degree of fragmentation (or lack of integration in a given metacognitive domain to be measured dimensionally.

Research on metacognition in schizophrenia:

Research has found the MAS-A has fully acceptable psychometric properties^[20] and assesses phenomenon which are distinct from the social cognition^[26,27] as well as content specific metacognitive beliefs^[28]. To date, research using this scale has addressed two broad research questions: (1) Are individuals with schizophrenia spectrum disorders more likely to experience disruptions in earlier or more basic aspects of metacognitive capacity; and (2) when disruptions occur at more basic levels of metacognitive function

are individuals more likely to experience greater levels of impairment in current and future function.

In response to the first question, research has revealed that individuals experiencing both first episode psychosis and prolonged schizophrenia experience significantly greater metacognitive deficits relative to others. Specifically, individuals with first episode psychosis and prolonged schizophrenia tend to experience disruptions in more basic levels of metacognitive capacity more often than individuals without any significant mental health concerns^[26,28], minor anxiety and affective disorders^[29] or with serious and prolonged non-psychiatric medical conditions^[30]. Other mental health conditions have been found to involve metacognitive deficits including depression^[31] substance use, borderline personality disorder^[32,33], posttraumatic stress disorder^[34], and bipolar disorder^[28], though these deficits occur in less basic elemental levels than what is seen in schizophrenia spectrum disorders.

Concerning the relationship with function, disruptions observed in basic or more elemental levels of metacognition (referred to as more severe metacognitive deficits) have been found to predict generally poorer function^[35]. This includes greater reductions in functional competence^[36], reports of poorer subjective sense of recovery^[37], a weaker therapeutic alliance in cognitive-behavior therapy^[38], less reported ability to reject stigma^[39], anhedonia in the absence of depression^[40], a more sedentary life style^[41], reduced awareness of negative changes in psychological and social function states^[42] and lesser levels of behavior that is driven by internal rewards^[43], all regardless of concurrent symptom severity. Individuals with schizophrenia spectrum disorders who experience disruptions in basic metacognitive function have also been found to be more likely to have future problems with vocational function^[44], more likely to develop negative symptoms^[45-47], and to experience reduced intrinsic motivation^[48], regardless of baseline assessments of these phenomena.

Metacognitive reflection and insight therapy: An illustration of an emerging recovery-oriented treatment that targets metacognition in psychosis.

Application of metacognitive research to treatment: Inspired by both research on metacognition and emerging models of recovery, efforts commenced to develop a form of integrative psychotherapy that could promote recovery through stimulating metacognition. The core assumption was individuals with a more fragmented sense of self and others would struggle to make sense of psychiatric and social challenges and thus struggle to move toward recovery. Put another way, a treatment enabling the processes which allow individuals to form a more integrated sense of self and others (*i.e.* metacognition) would promote recovery. What was proposed then was a process oriented

therapy referred to as Metacognitive Reflection and Insight Therapy (MERIT)^[7], a therapy focused on enabling the metacognitive processes which would allow individuals diagnosed with schizophrenia spectrum disorders to determine what recovery meant to them, what steps they needed to take and to take charge of their own recovery.

As described elsewhere^[7] this therapy was developed through a series of international conversations among clinicians with extensive experience providing long-term psychotherapy to individuals with serious mental illness. It was conceptualized as integrative in that it would describe principles that could be adapted by therapists from other perspectives in order to promote metacognition. These principles were explicitly described as core activities that offered patients maximal opportunity for the development of metacognition which should be present in any given psychotherapy session rather than a rigid set of activities to be carried out in a certain order. In this sense treatment does not approach metacognition as something someone has or does not have. Instead, MERIT approaches metacognition as something a person possesses to a varying degree and something they can further cultivate with time and practice.

Structure and principles of MERIT: The central assumption of MERIT is that patients can gain metacognitive capacity by practicing metacognitive acts within the flow of a psychotherapy session^[7]. Following the integrative model of metacognition, it is assumed that as patients become able to perform a level of metacognitive acts, they will begin to be able to perform more complex metacognitive acts and consequently have a richer sense of self and others available to them as they seek to recover. Analogous to processes in physical therapy, patients could be expected over time to become able to perform more complex metacognitive acts, as physical therapy builds upon existing ability and stretches to the next level of function^[49].

MERIT is grounded in several general principles including foremost that recovery from serious mental illness is expected, regardless of the severity of the mental health condition^[7]. Consistent with the material presented above, MERIT also assumes patients must be active agents who direct their own recovery during all phases of illness and that this requires the rejection of stigma, as well as a non-hierarchical therapist-patient relationship in which the therapist's role is best understood as one of a co-participant or consultant. It is thus a therapy for any patient who consents and there are no particular preconditions before therapy can begin^[7]. Importantly, MERIT is not intended as a replacement for other treatments but can be offered both on its own or in combination with other rehabilitative practices depending on unique patient needs and clinic resources.

In MERIT, eight elements should be present in any given session, each of which is assumed to uniquely assist adults with psychosis to recapture damaged, atrophied, or undeveloped metacognitive abilities. Each element describes a measurable activity that can occur regardless of the unique problem or dilemma a patient is experiencing or wanting to discuss in psychotherapy. The elements are conceptually and synergistically inter-related, but each can be considered and assessed independently^[7].

The eight elements are divided into three classes. The first class includes what are referred to as content elements. These include four specific elements that call for the session to focus upon and discuss (E1) the patient's agenda, or wishes and needs in the moment, (E2) the patient's experience of the therapist's thoughts and feelings about the patient and his or her agenda, (E3) the patient's experience of life as revealed within specific and minimally abstract personal narrative episodes and (E4) the psychological challenges which emerge from the first three content elements. The second set of elements includes what are referred to as the process elements. The process elements include a discussion (E5) of the therapeutic relationship in which the patient is thinking about their sense of themselves and others and (E6) discussion of progress, including resultant changes in their minds and bodies. The final two elements are considered superordinate elements and call for reflections about (E7) self and others and (E8) mastery to be stimulated at a level consonant with the patient's metacognitive ability as assessed in the moment. In other words, efforts to meaningfully engage patients in conversations about their sense of themselves and others need to match the patient's metacognitive capacity.

Regarding treatment mechanisms, it is assumed that these elements will have the ability to enhance metacognitive capacity that will result in a more integrated sense of self and others becoming available to patients in the moment. This integrated and flexible understanding of self and others will then enhance the opportunities for more effective self-management culminating in recovery. An adherence scale has been developed which allows for assessment of whether a given session sufficiently conforms to the session guidelines and is available in the MERIT guidebook^[7]. This adherence scale can be self-rated by therapists or by others in order to allow for fidelity to the MERIT procedures to be formally assessed between therapists.

Research evidence: Though still emerging as a treatment, research has indicated that MERIT can be delivered under routine conditions in natural clinical settings and that patients with severe mental illness will accept this treatment and demonstrate improvements in metacognition^[50-53]. Exploring the first-person experience of MERIT, a qualitative study has examined the self-reported experience of patients who received at least one year of either

MERIT or supportive psychotherapy^[54]. This study found that MERIT, in contrast to supportive therapy, leads to improvements in sense of agency and the ability to tolerate and manage previously disabling levels of emotional distress. Studied at the level of individuals and their own unique needs, detailed case reports have indicated that participation in MERIT is associated with improvements in the unique goals patients set for themselves in both early and later phases of serious mental illness^[10,55-61]. Concerning patients who deny they have a mental illness, Vohs and colleagues^[53] randomly assigned adults with first episode psychosis with poor clinical insight to receive a 6-mo trial of MERIT vs treatment as usual. They found that the treatment completion rate for MERIT was 80% with statistically significant improvements in objective measures of awareness of illness without any concurrent increases in hopelessness or emotional distress.

Implications for developing and implementing recovery-oriented care in serious mental illness

At the outset of this paper we suggested that conventional treatment models for serious mental illness are challenged to account for three aspects of recovery: (1) Recovery is to be expected; (2) recovery means different things to different people; and (3) recovery must be self-directed to be meaningful. We then summarized research suggesting metacognitive deficits may hinder a person's abilities to form the kinds of complex ideas about self and others needed to direct one's own recovery effectively. We then offered an illustration of a form of integrative therapy, MERIT designed to target metacognition and promote a kind of recovery that is personally meaningful and self-directed. Consistent with the need for integrative approaches in the treatment of serious mental illness^[62], MERIT offers principles which can be incorporated into different approaches in psychotherapy and hence does not require yet another new treatment approach unrelated to others^[22,63].

Returning to the issue of how treatment can promote unique, individualized, and self-directed recovery, we would suggest this body of research on metacognition suggests at least five general principles that conventional treatments could potentially embrace.

Treatment must be process oriented: First, if treatment is to be concerned with how people understand their psychiatric and social challenges it has to begin with curiosity and inquiry about what patients think about those challenges. How does the patient experience challenges? How do they think about challenges now and how have they thought about challenges in the past? Thus, what therapy is trying to provoke or support is a process and not specific content such as accepting a fact. It is as much about how people think as what they think. Moreover,

that process is about making meaning of often complex and painful material.

This is not to say that content is irrelevant. Certain content may prove helpful for supporting the process of meaning making but those contents are likely different from patient to patient. Whereas one patient may find psychoeducation and support helpful, another may find it destructive and marginalizing. Some may find a particular skill based approach helpful, but others may experience that as useless or harmful. Content in fact should differ from person to person depending upon any number of individual differences in ages, gender, education, cultural background, trauma history, socio-economic status, talents, family history *etc.* Nevertheless, because understanding challenges involves making meaning and not the grasping of facts, treatment cannot be conceptualized as primarily following a curriculum seeking to “teach” patients to perform certain acts or “getting them” to think certain things. This requires the clinicians to “give up” the knowing attitude^[63] and let themselves be taken by surprise^[64].

Treatment must be concerned with purposes beyond problems: Given that it is the meaning of challenges and the best response to them is at stake, a recovery-oriented approach also needs to be at least as focused on patients’ purposes as it is on problems. In other words, it is vital for therapy to address not just what has gone wrong discretely, but what the patient is seeking, both in the moment and in recovery more broadly. Here the conventional assumption that the patient-clinician dyad should identify the problem and then the solution can be seen to risk undermining recovery and meaning making. For example, two patients could agree that they have the same problem, such as being anxious or hearing voices. Yet each may come to treatment and approach life with very different purposes. One patient may primarily want to avoid any future humiliation by keeping within the safety of the patient role and the other be primarily concerned only with finding a romantic partner. Clinician blindness to patient’s purposes could then obviously derail the chances for joint meaning making.

Accordingly, an explicit requirement of recovery-oriented therapy seems likely to be that it involves direct and continuous discussions of patient’s purposes and wishes, assuming that those wishes and purposes are likely to be complex. It is more likely than not that patients will have multiple purposes which may be contradictory, complementary or unrelated^[65]. These purposes may be more or less in awareness and may change over time. In parallel, the purposes patients have for their therapists are also likely to be fluid and changing. Accordingly, an intervention which promoted the process of meaning making at one point might not at a later point and vice versa.

This is not to say that clinicians should unconditionally support any patient agenda. For example,

patients may want to remain in the sick role, for the therapist to provide endless support, or to avoid guilt for neglecting real life responsibilities such as child support. What is essential is that what the patient is seeking is directly discussed and those discussions are employed in the service of understanding what the patient is facing and what he or she wants to do about that.

Process of recovery-oriented treatment is fundamentally intersubjective: The process of making meaning of challenges and purposes should be further understood as one that occurs between people. As noted above, individuals do not make meaning of themselves and their lives in isolation. Thus, the clinician has a clear role beyond blanket support or reassurance. In fact, supporting everything anyone thinks is never likely to be a successful strategy for promoting reflection.

What is necessary instead is an open and genuine dialogue which allows for disagreement but in which the clinician does not derail conversation by virtue of their power in the relationship. In this relationship, disagreement should not be confused as an expression of disrespect. Indeed, challenging individuals to think more deeply about their lives may be among the most respectful things human beings can offer one another.

The process promoted by recovery-oriented treatments should be conceptualized as taking place within the therapeutic intersubjective space, between the clinician and patient^[63,66]. A deepening sense of self and others does not first occur in the mind of the therapist to then be shared with the patient. It is understanding that emerges from and within the encounter of unique persons. This allows for the therapeutic relationship to be a vehicle for a reflective dialogue.

Goals and outcomes will appear and change fluidly over time: Given that recovery-oriented treatment is concerned with meaning and purpose as well as the relationship within which it is taking shape, patients’ goals within and outside of therapy are likely to evolve in ways that cannot be anticipated. It is likely that with more integrated ways of understanding oneself and others, or in the face of unexpected emotional pain, patients will find themselves with a different set of purposes and potentially very different goals. For example, a patient might originally seek to improve a relationship with an adult child but then suddenly on her own realize she needs to drive. This new goal may then shift the focus as he or she considers buying a car and learning to drive, despite that never having been a goal at any earlier part of treatment. Another patient may, with more awareness, suddenly take a more active role in thinking about medication he or she needs while another may decide it is time to try to manage his or her life without medication.

Interventions should match a patient’s meta-cognitive capacity: Finally, if metacognitive

processes are what allow individuals to have an integrated sense of self and others, then interventions which seek to facilitate metacognitive capacity, need to continuously assess patients' level of metacognitive capacity and offer interventions that match that level of metacognitive capacity. Practically, asking a patient to question their own thoughts and perceptions is likely to only lead to frustration and misunderstanding rather than reflection if that patient is unable to see that their emotions and affects change over time and that their mental states are accordingly subjective and transitory.

This would require the assessment of metacognition and its responsiveness to changes within and between sessions. Certainly, the MAS-A is not the only means for assessing changes in metacognition but it does exist as a method of identifying points where metacognition fails to fully function and therefore the MAS-A can be used as a guide for intervention. The MAS-A further distinguishes metacognitive acts pertaining to the self, others, the community, and the use of that knowledge. This instrument has the benefit of responding to awareness of self and others as something more nuanced than a vague monolithic phenomenon. It allows clinicians to respond differently to patients based on clearly delineated levels of metacognitive capacity.

In this way recovery interventions may come to take on an usual character. Whereas most interventions tend to be considered in terms of high structure vs. low structure, the need to appraise metacognition and respond differently to individuals given their capacities in the moment give the clinician a highly structured task while the patient's task of making sense of what they face and need to do about it is clearly a highly unstructured task.

In summary, research suggests that many with schizophrenia experience deficits in metacognition, and that while these deficits are tied to poorer outcomes they may be the target of treatment leading to self-directed and personally meaningful recovery. In this paper we have suggested that this research offers some important directions for clinical interventions which could support recovery in serious mental illnesses such as schizophrenia. We have proposed this research suggest that these interventions need to be focused on process and on patient's purposes as well as the intersubjective context in which this is occurring. Further, these interventions need to allow for the fluid formation and evolution of goals while imposing on clinicians the highly structured task of assessing metacognitive capacity and responding accordingly to patients as they seek to make sense of what recovery means to them and how they should pursue it.

While these ideas may appear radical in some ways, it is worth noting that the metacognitive model of schizophrenia does not differ terribly from key features of Bleuler's^[67] original model of schizophrenia which attributed the interruption of the lives in schizophrenia

to disturbances in associative process or the ability to link ideas together *via* associative threads. The model of therapy inspired by this work, MERIT, shares this understanding with the practices of other contemporary approaches. For example, like Cognitive Behavior Therapy for Psychosis (CBT-P)^[68], MERIT focuses on normalizing distressing experiences^[69]. It also shares with mindfulness^[70] and Acceptance Commitment Therapy^[71,72] a focus on patients' relationship to their experience. MERIT and these therapies, sometimes called third wave Cognitive Behavior Therapy^[73], seek to address matters that go beyond individual cognition and require curiosity about mental experience with the expectation that patients will have unique responses to psychological and social challenges^[69]. MERIT, also like psychodynamic mentalization-based approaches, is interested in the ideas people form about one another in an explicitly intersubjective context. Like traditional humanistic practices^[74,75] MERIT is concerned with self-actualization, agency, and understanding experience in the context of the human condition. Similar to skills based approaches to rehabilitation, MERIT is focused on real world outcomes, the rejection of stigma and the patient's movement beyond the sick role.

However, MERIT and treatments driven by its supporting research do diverge from these views. Unlike CBT-P, MERIT is expressly interested in understanding how individuals synthesize or integrate information, above and beyond particular beliefs considered in isolation. In contrast to the third wave of CBT, MERIT is explicitly concerned with joint reflection about self-experience in the moment, as it occurs in the relationship with the therapist and across patients' personal narratives^[69]. Unlike ACT, MERIT is not concerned with abstractions about values but instead explores the larger complex web of meanings that span the course of an individual life. In contrast to mindfulness, MERIT is interested in patients' experiences as they occur in the mind in the moment, in response to the therapist's mind, and further asks about the meaning of those mental experiences in relation to one another, again in the context of a unique narratized life. MERIT also thinks about self-knowledge differently than other cognitive therapies. The self-knowledge that emerges from MERIT is not a knowledge of a true self or a matter of a more transparent perception of a self but instead the availability of a diverse self, which is able to respond to what is emerging at any point in a unique life^[69]. In contrast to psychodynamic and mentalization based treatment^[76], MERIT's use of the MAS-A to operationalize metacognition differentiates thoughts about the self, others, the community, and ability to use this knowledge to respond to life's challenges. Further differentiating MERIT from mentalization approaches is the assumption that difficulties in reflectivity can occur outside of the context of disturbed attachment and emotion dysregulation and have a bidirectional relationship with both constructs^[77].

Concerning self-actualization and the development of agency, MERIT also moves beyond some of the classic humanistic approaches to psychotherapy^[74,75], in that it proposes a method for scaffolding a complex and nuanced sense of self that could be actualized. Finally, the suggestions offered here are potentially at odds with rehabilitative skills based approaches which directly seek to “get” people to “do” particular things or to exercise certain skills that a clinician thinks are needed. Indeed, the work detailed above suggests that when those approaches take on the responsibility for deciding what patients need to think or do, that those approaches, regardless of how benevolent the clinician's intentions are, may do a significant disservice by reinforcing the patient's lack of agency and positioning them as stigmatized and not fully competent adults.

While considering the strengths and evidences of metacognitive approaches to recovery focused treatment such as the MERIT, limitations should be mentioned. Randomized controlled trials of MERIT are needed in a broad range of settings. Despite being an integrative psychotherapy, it is unclear how easily clinicians from different disciplines and with different backgrounds can make the adaptations we suggest. Methods for assessing treatment adherence exist but it remains to be determined how these affect therapists from different perspectives. It is also unclear how to make these adaptations in settings that do not allow extended contact with patients but instead offer only brief and intermittent contact, such as inpatient units. There is further need for replication and further study of both the methods for assessing metacognition and for delivering metacognitive therapies.

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Complex posttraumatic stress disorder: The need to consolidate a distinct clinical syndrome or to reevaluate features of psychiatric disorders following interpersonal trauma?

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Abstract

Complex posttraumatic stress disorder (Complex PTSD) has been recently proposed as a distinct clinical entity in the WHO International Classification of Diseases, 11th version, due to be published, two decades after its first initiation. It is described as an enhanced version of the current definition of PTSD, with clinical features of PTSD plus three additional clusters of symptoms namely emotional dysregulation, negative self-cognitions and interpersonal hardship, thus resembling the clinical features commonly encountered

in borderline personality disorder (BPD). Complex PTSD is related to complex trauma which is defined by its threatening and entrapping context, generally interpersonal in nature. In this manuscript, we review the current findings related to traumatic events predisposing the above-mentioned disorders as well as the biological correlates surrounding them, along with their clinical features. Furthermore, we suggest that besides the present distinct clinical diagnoses (PTSD; Complex PTSD; BPD), there is a cluster of these comorbid disorders, that follow a continuum of trauma and biological severity on a spectrum of common or similar clinical features and should be treated as such. More studies are needed to confirm or reject this hypothesis, particularly in clinical terms and how they correlate to clinical entities' biological background, endorsing a shift from the phenomenologically only classification of psychiatric disorders towards a more biologically validated classification.

Key words: Complex posttraumatic stress disorder; Posttraumatic stress disorder; Borderline personality disorder; Trauma; Complex trauma

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Core tip: A cluster of complex posttraumatic stress disorder (PTSD), PTSD and borderline personality disorder that have in common a history of trauma, is proposed, as a clinical and biological continuum of symptom severity, to be classified together under trauma-related disorders instead of just distinct clinical diagnoses. Trauma depending on biological vulnerability and other precipitating risk factors is suggested that it can lead to either what we commonly diagnose as PTSD or to profound and permanent personality changes, with complex PTSD being an intermediate in terms of its clinical presentation and biological findings so far.

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INTRODUCTION

Complex posttraumatic stress disorder (Complex PTSD), has been originally proposed by Herman^[1], as a clinical syndrome following precipitating traumatic events that are usually prolonged in duration and mainly of early life onset, especially of an interpersonal nature and more specifically consisting of traumatic

events taking place during early life stages (*i.e.*, child abuse and neglect)^[1].

In order to develop a new psychiatric diagnosis, it requires carrying a certain extent of validity as a distinct entity with a clinical utility^[2], providing essential additions to already established diagnoses especially regarding biological aetiology, course and treatment options.

Several psychiatric disorders overlap in terms of symptomatology and there is a high comorbidity present to most, if not all, especially when precipitating factors are common or similar. Furthermore, until now, psychiatric diagnoses have been traditionally described as theoretical constructs, mostly to facilitate communication of professionals working in the field, with the exact psychopathological processes and biological background research only currently blooming. This also carries the question whether already established psychiatric diagnoses need to be re-evaluated and re-grouped following newly suggested research findings, aiming to offer more efficient treatment plans to patients in question.

It has been questioned^[2,3] whether complex PTSD can form a distinct diagnosis, since its symptomatology often overlaps with several mental disorders following trauma, mainly with PTSD which is usually correlated to single event trauma as well as Axis II disorders, mainly borderline personality disorder (BPD). The latter besides the high comorbidity with complex PTSD^[4], also shares some of the core symptoms described in complex PTSD especially related to impaired relationships with others, dissociative symptoms, impulsive or reckless behaviours, irritability and self-destructive behaviours.

Complex PTSD is defined by symptom clusters mainly resembling an enhanced PTSD, with symptoms such as shame, feeling permanently damaged and ineffective, feelings of threat, social withdrawal, despair, hostility, somatisation and a diversity from the previous personality. It also regularly presents with serious disturbances in self-organisation in the form of affective dysregulation, consciousness, self-perception with a negative self-concept and perception of the penetrator(s), often causing dysfunctional relations with others leading to interpersonal problems^[1,5-7].

The aim of this paper is to review the until now research on complex PTSD and its correlation to other trauma-related mental disorders mainly PTSD and BPD, primarily regarding the diagnostic frame and biological correlates, in order to examine whether there is sufficient data to approve the need of establishing a distinct clinical mental syndrome or to address the need to reassess and expand the diagnostic criteria of trauma-related disorders to include clinical features of complex PTSD currently missing from the already confirmed clinical entities.

CLINICAL DESCRIPTIONS AND BIOLOGICAL CORRELATES OF COMPLEX PTSD, PRECIPITATING TRAUMATIC EVENTS AND CLINICAL DIVERGENCE FROM PTSD

Complex PTSD is already suggested as a distinct diagnostic entity, in the World Health Organization (WHO) International Classification of Diseases, 11th version, (ICD-11)^[5], which is due to be published in 2018 and currently under review, classified under disorders specifically associated with stress. It is grouped together along with PTSD, prolonged grief disorder, adjustment disorder, reactive attachment disorder, disinhibited social engagement disorder and others. The disorders mentioned above are all associated with stress and exposure to distressing traumatic events. The clinical features following the stressful experience result in serious functional impairment regardless whether the traumatic event precipitating the disorder, falls under the normal range of life experiences (such as grief) or encompasses events of a menacing nature (*i.e.*, torture or abuse).

According to ICD-11^[5], complex PTSD follows exposure to a traumatic event or a series of events of an extremely threatening nature most commonly prolonged, or repetitive and from which escape is usually impossible or strenuous^[6].

Two decades ago when it was first proposed, precipitating traumatic events were described strictly as being prolonged in time usually taking place during early developmental stages (*i.e.*, childhood)^[1]. The literature describing complex PTSD ever since, following its first initiation as a cluster of symptoms beyond classic PTSD, began to also include entrapping events taking place during adulthood^[8] and argued against their prolonged nature *per se*, referring to single event traumas as well as repeated series of single complex trauma that could be so severe and catastrophic in nature leading to profound personal effects, such as personality modification, even after the conclusion of major developmental stages^[9]. A recent study of Palic *et al.*^[10], argues of the complex PTSD association, not only with childhood trauma but with exposure to all forms of adulthood trauma, predominately having in common the interpersonal intensity of the stress induced and the severity of prolonged trauma exposure. Another study of van der Kolk *et al.*^[11], correlated the presence of complex trauma in adulthood to complex PTSD symptomatology, specifically dissociation, suggesting a potential link to the dissociative subtype of PTSD.

Complex trauma, which summates a total of precipitating traumatic events to complex PTSD, is currently being described as a horrific, threatening, entrapping, deleterious and generally interpersonal traumatic event, such as prolonged domestic violence,

childhood sexual or physical abuse, torture, genocide campaigns, slavery *etc.* along with the victim's inability to escape due to multiple constraints whether these are social, physical, psychological, environmental or other^[12,13].

Complex PTSD includes most of the core symptoms of PTSD, specifically flashbacks (*i.e.*, re-experiencing the traumatic event), numbness and blunt emotion, avoidance and detachment from people, events and environmental triggers of the predisposing trauma as well as autonomic hyperarousal. Furthermore, due to the nature of the complex trauma experienced, it also includes affective dysregulation, adversely disrupted belief systems about oneself as being diminished and worthless, severe hardship in forming and maintaining meaningful relationships along with deep-rooted feelings of shame and guilt or failure^[7]. Its distinct characteristics added upon PTSD symptomatology, often interfere to separate it from BPD (*i.e.*, affective dysregulation) and PTSD alone, which in cases with a chronic course will eventually transit to a lasting personality change^[14].

Therefore it is speculated that prolonged exposure to complex trauma and/or chronic PTSD, would, therefore, lead to personality alterations that are often also seen clinically in complex PTSD patients (such as feelings of being permanently damaged and alienation), even when the traumatic experiences are taking place during adulthood^[14]. It is speculated that complex trauma has to be present for a sufficient amount of time to cause a clinically evident diversion from the already established personality traits, towards traits that seem to either help the victim cope with trauma or as an expression of disintegration which might express as the dysregulation of emotion processing and self-organisation, two of the core symptoms added to the already established PTSD diagnostic criteria^[10,15]. Complex trauma, especially childhood cumulative trauma and exposure to multiple or repeated forms of maltreatment, has been shown to affect multiple affective and interpersonal domains^[12]. Also, chronic trauma is more strongly predictive of complex PTSD than PTSD alone, while complex PTSD is associated with a greater impairment in functioning^[16].

Up to now, there is a lack of investigation of biological correlates to complex PTSD, referring to neuroimaging studies, autonomic and neurochemical measures and genetic predisposition^[17]. The only data so far, consist of neuroimaging studies mainly in groups of child abuse-related subjects that mostly argue for the hippocampal dysfunction and decreased gray matter density observed, activation disturbances in the prefrontal cortex^[18-20], as well as findings suggesting of more a severe neural imaging correlate in complex PTSD than those observed in PTSD patient studies, primarily involving brain areas related to emotional regulation and cognitive defects, symptoms that have been additionally added in

complex PTSD symptomatology vs PTSD^[17]. Structural brain abnormalities in complex PTSD seem to be more extensive with brain activity after complex trauma being distinctive than the one seen in PTSD patients who had experienced only single trauma^[21] with higher functional clinical impairment in complex PTSD independently described but confirming the biological results mentioned above^[22,23].

The three additional clusters of symptoms beyond core PTSD symptoms refer to emotional regulation, negative self-concept and interpersonal relational dysfunction^[24].

PTSD has been re-evaluated in DSM-5^[15], adding a cluster D of PTSD symptoms including altering in mood and cognition following the traumatic experience, as well as the dissociative PTSD subtype (*i.e.*, depersonalisation and/or derealisation), a subtype that clinically resembles the cluster of symptoms that are commonly encountered in the complex PTSD^[25]. A recent study of Powers *et al.*^[26] though, concluded that the ICD-11 Complex PTSD diagnosis is different than the DSM-5 PTSD diagnosis, in all clinical domains, showing more severe emotion regulation and dissociation, and more severe impairment in relational attachment, suggesting that they present two distinct constructs. More studies are needed to investigate the biological basis of complex PTSD as a clinical entity and its differences from trauma-induced disorders such as PTSD.

RE-CONCEPTUALISING BPD AS A COMPLEX TRAUMA SPECTRUM DISORDER

BPD is characterized by emotional dysregulation, oscillating between emotional inhibition and extreme emotional lability which has been often associated with prolonged childhood trauma^[27], such as child abuse and neglect as well as adverse childhood experiences, present in a range within 30 to 90% of BPD patients^[28-30]. Emotional dysregulation, an unstable sense of identity, difficulties in interpersonal relationships as core features of BPD^[15] and precipitating complex interpersonal traumatic victimisation, a cluster of symptoms that overlaps with symptomatology described in complex PTSD, has led into a series of arguments whether BPD represents a comorbidity of trauma-related disorders or it actually duplicates complex PTSD, a clinical entity already introduced as a separate trauma-related diagnosis in ICD-11^[31].

The WHO International Classification of Diseases, 11th version, (ICD-11), includes a slightly different spectrum of personality disorders classification, including BPD into a wider spectrum of the Emotionally Unstable Personality Disorder, carrying all of the characteristics that BPD has been known by, so far, but distinguishing two types; the impulsive type, defined

by emotional instability and impulsiveness and the borderline type with an unstable sense of self and the environment, self-destructive tendencies and intense and unstable relations. Still again, while traumatic stress exposure is fundamental in Complex PTSD and has been added to its diagnostic criteria, it is not included in the definition of BPD, albeit the multiple references that trauma, especially during early life stages, plays a crucial role in the development of the borderline personality even if epigenetically added upon a temperamental vulnerability^[32]. Especially childhood trauma such as, sexual and physical abuse, maladaptive parenting, neglect, and parental conflict has been correlated to BPD multiple times in literature as risk if not etiological factors^[33].

The long-term stress response mechanism activation, mediated by the hypothalamic-pituitary-adrenal (HPA) axis, due to chronic stress exposure, can predispose to multiple stress-related psychiatric entities, including PTSD^[34]. Stress early in life due to childhood trauma has been reported to result in an adjustment dysfunction of the HPA axis responsiveness upon stress states encountered, with patients with BPD. There seems to be an increased activation of the HPA axis^[35,36], suggesting the association of the main stress regulating mechanism to childhood trauma and a biological correlation to the development of the borderline personality. Furthermore, several interacting neurotransmitter systems are shown to be affected in BPD^[37,38], resulting to a disruption of emotional regulation and social interaction as well as cognitive impairments evident mainly in spatial memory, modulation of vigilance and negative emotional states mediated through the hippocampus and amygdala^[39], symptomatology that is present in complex PTSD even in the lack of similar biological studies to support this, at least in terms of neuromodulation alterations in complex PTSD.

Additionally, neuroimaging studies on BPD, confirm the reduction in hippocampus and amygdala volumes as well as in the temporal lobes^[39-42], while a recent study of Kreiser *et al.*^[43], found that BPD patients with a comorbid lifetime history of PTSD had smaller hippocampal volumes compared to the ones that didn't. Additionally, a study of Kuhlmann *et al.*^[44], correlated the history of trauma to BPD, showing a modification of grey matter at stress regulating centers, including the hippocampus, the amygdala, the anterior cingulate cortex and the hypothalamus.

Likewise, studies indicate that epigenetic changes upon the brain derived neurotrophic factor^[45], which is a key mediator in brain plasticity, are associated to prolonged early stage trauma, contributing to the cognitive dysfunction which is often described in BPD patients^[46,47].

Altogether, the similarities between studies concerning BPD and complex PTSD^[17-20], in terms of the common underlying systems affected along with the clinical analogy in both disorders, both associated

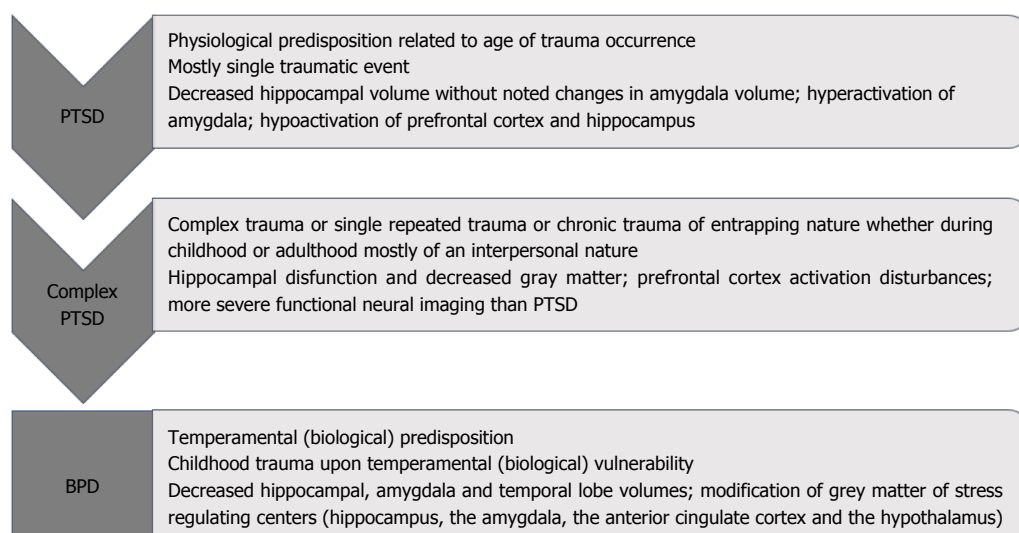


Figure 1 Proposed development of the clinical phenomenology based on trauma history and biological correlates. PTSD: Posttraumatic stress disorder; BPD: Borderline personality disorder.

to prolonged stress and trauma exposure, suggest the need to re-classify subgroups of patients with BPD, especially the ones that show comorbidity with PTSD, as possible cases of complex PTSD or, as it will be discussed below, added on a spectrum of trauma-related clinical entities carrying a similar biological background with complementary clinical expression.

CONCLUSION

The new proposed diagnosis of complex PTSD in ICD-11, re-conceptualises a previous ICD-10 diagnosis namely “enduring personality change after catastrophic experience”, which carries characteristic clinical features of self-organisation dysfunction and exposure to multiple and chronic or repeated and entrapping, for the individual, traumatic events (*e.g.*, child abuse, domestic violence, imprisonment, torture). The ICD-11 complex PTSD shares three core symptom clusters of PTSD (re-experiencing, avoidance and sense of threat), adding three additional clusters of symptoms, specifically emotional dysregulation, negative self-concept and relational disturbances. Even if a clear personality change is not required for the diagnosis of complex PTSD, the sustainable and pervasive alteration in self-organisation, especially within the group of patients who have experienced long-lasting early life complex trauma, according to the authors, suggesting that a personality change is unavoidable, essentially while even chronic PTSD alone can lead to the change of personality eventually as it has been noted in the literature^[14]. Therefore, complex PTSD, often clinically resembles a subtype of BPD.

There lies the question whether complex PTSD is a clearly defined distinct entity or a PTSD comorbid with BPD. The debate focuses mainly on the fact that even if both conditions share core symptoms, such as affect dysregulation and self-organization disturbances, BPD

has been traditionally described by an unstable sense of self oscillating between highly positive and highly negative self-evaluation and a relational attachment style vacillating between idealizing and denigrating perceptions of others when complex PTSD on the other hand, is defined by a deeply negative sense of self and an avoidant attachment style that are stable in nature and follow complex trauma, something that is not described in the diagnostic criteria of BPD.

However, BPD seems to be a heterogeneous diagnostic category, which can include many subtypes of patients, such as patients with bipolar disorder, depression or other personality disorders such as narcissistic personality disorder, with an accurate clinical diagnosis being difficult under practical pressures posed upon physicians and the comorbidity present among the above mentioned disorders^[48]. BPD clinical features do not seem to be stable over time, and this is suggested to be influenced by the underlying biological temperament^[49,50], while the comorbidity with PTSD is common but not present in all of the BPD cases^[51], therefore arguing for conceptualizing some of the BPD cases belonging to a trauma spectrum disorder instead^[52].

Since the etiological background for most if not all psychiatric disorders, is not linear but instead it consists of many biological, psychological and social factors, interacting between each other and continuously adjusting, shifting and varying among individuals on top of brain plasticity and ever-changing circumstances, the authors suggest that the biological correlates of disorders appearing with similar phenomenology should be better investigated.

The different clinical profiles described in the most recent classification systems (Table 1) even if sharing many common clinical features, that surround PTSD, complex PTSD and BPD, are all associated with different levels of impairment and different risk

Table 1 Phenomenology of posttraumatic stress disorder, complex posttraumatic stress disorder and borderline personality disorder; DSM-5 clinical features and proposed criteria of ICD-11

	DSM - 5	ICD - 11
PTSD	Exposure to traumatic events; Intrusion symptoms; Persistent avoidance of stimuli; Negative alterations in cognitions and mood (dissociation, persistent negative beliefs of oneself, others or the world, distorted cognitions about the traumatic event, persistent negative emotional state, detachment from others, diminished interest or participation in previously enjoyed activities <i>etc.</i>); Alterations in arousal and reactivity; aggressive verbal and/or physical behaviour, reckless or self-destructive behaviour; depersonalisation or derealisation; Significant impairment in all areas of functioning	Exposure to an extremely threatening or horrific event or series of events; vivid intrusive memories, flashbacks, or nightmares, which are typically accompanied by strong and overwhelming emotions; avoidance of thoughts and memories, events, people, activities, situations reminiscent of the event(s); persistent perceptions of heightened current threat, hypervigilance or an enhanced startle reaction. Significant impairment in personal, family, social, educational, occupational or other important areas of functioning
Complex PTSD	Not included as a diagnostic entity	Exposure to an event(s) of an extremely threatening or horrific nature, most commonly prolonged or repetitive, from which escape is difficult or impossible; All diagnostic requirements for PTSD are and additionally: severe and pervasive affect dysregulation; persistent negative beliefs about oneself; deep-rooted feelings of shame, guilt or failure; persistent difficulties in sustaining relationships and in feeling close to others. Significant impairment in all areas of functioning
BPD	Pervasive pattern of instability of interpersonal relationships, self-image and affects and impulsivity; frantic efforts to avoid abandonment, unstable and intense interpersonal relations oscillating between idealisation and devaluation, unstable self-image or sense of self, self-harming behaviour, affective instability and marked reactivity of mood, chronic feelings of emptiness, poor anger management, transient paranoid ideation or severe dissociation	Emotionally unstable personality disorder, Borderline type: Maladaptive self and interpersonal functioning, affective instability, and maladaptive regulation strategies: Frantic efforts to avoid abandonment; unstable interpersonal relations (idealisation/devaluation); unstable self-image; impulsivity; self-damaging behaviours; marked reactivity of mood; chronic feelings of emptiness; anger management issues; dissociative symptoms

PTSD: Posttraumatic stress disorder; BPD: Borderline personality disorder.

factors mainly in the trauma history precipitating the phenomenology that finally occurs, which is evident in the neuroimaging findings of each disorder (Figure 1).

Since even chronic PTSD will eventually lead to personality modification, it is suggested that complex trauma exposure, even during adulthood, is a predisposing factor for complex PTSD occurring, which will, eventually, if relatively prolonged in time, lead to more severe personality changes often clinically similar to BPD. We suggest that the time of the traumatic events occurrence (*i.e.*, early developmental stages vs adulthood), their severity and context, their duration in time and whether they are of an entrapping and interpersonal nature, posed upon a genetically predisposed background will eventually progress into enduring or permanent personality modifications. Therefore, we suggest that within the heterogeneous group of cases classified as BPD, there is a subgroup that could be possibly classified under trauma-related disorders and be therapeutically treated as such.

Concluding, the authors suggest a continuum of clinical severity and symptoms' development in trauma-related disorders, within a spectrum of clinical features, biological background and precipitating trauma, from classic PTSD towards a subtype of BPD; especially concerning cases supposing a comorbidity with PTSD. We also suggest of complex PTSD being an "intermediate" in its phenomenological manifestation, with biological analogies seemingly supporting these hypotheses.

More studies are needed focusing on the biological background of complex PTSD and how this relates to its newly proposed clinical entity and how it correlates to the extended findings in the literature around the biology of PTSD and BPD. This is essential for examining the validity of it as a distinct and separated entity altogether or to confirm the hypothesis of a spectrum surrounding the disorders discussed above, at least within the range of cases having a history of trauma present.

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Clinical Practice Study

Repeatability of two-dimensional chemical shift imaging multivoxel proton magnetic resonance spectroscopy for measuring human cerebral choline-containing compounds

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Abstract

AIM

To investigate the repeatability of proton magnetic resonance spectroscopy in the *in vivo* measurement of human cerebral levels of choline-containing compounds (Cho).

METHODS

Two consecutive scans were carried out in six healthy resting subjects at a magnetic field strength of 1.5 T. On each occasion, neurospectroscopy data were collected from 64 voxels using the same 2D chemical shift imaging (CSI) sequence. The data were analyzed in the same way, using the same software, to obtain the values for each voxel of the ratio of Cho to creatine. The Wilcoxon related-samples signed-rank test, coefficient of variation (CV), repeatability coefficient (RC), and intraclass correlation coefficient (ICC) were used to assess the repeatability.

RESULTS

The CV ranged from 2.75% to 33.99%, while the

minimum RC was 5.68%. There was excellent reproducibility, as judged by significant ICC values, in 26 voxels. Just three voxels showed significant differences according to the Wilcoxon related-samples signed-rank test.

CONCLUSION

It is therefore concluded that when CSI multivoxel proton neurospectroscopy is used to measure cerebral choline-containing compounds at 1.5 T, the reproducibility is highly acceptable.

Key words: Cerebral metabolites; Chemical shift imaging; Choline; Neurospectroscopy; Neuropsychiatric disorders

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Core tip: Proton neurospectroscopy is a powerful tool allowing the assessment of cerebral metabolites. As such, it is increasingly being introduced into the practice of psychiatry for the investigation of cerebral choline-containing compounds in patients, as well as being used as a research tool. However, it is important to establish the reproducibility of this sensitive technique. In the present study, we show that this technique (using 2D chemical shift imaging) gives a level of reproducibility that is highly acceptable. These results should further encourage the use of this technique, which, in principle, is available on all standard MRI scanners, in psychiatric practice.

Puri BK, Egan M, Wallis F, Jakeman P. Repeatability of two-dimensional chemical shift imaging multivoxel proton magnetic resonance spectroscopy for measuring human cerebral choline-containing compounds. *World J Psychiatr* 2018; 8(1): 20-26 Available from: URL: <http://www.wjgnet.com/2220-3206/full/v8/i1/20.htm> DOI: <http://dx.doi.org/10.5498/wjp.v8.i1.20>

INTRODUCTION

In vivo magnetic resonance proton spectroscopy studies of the human brain pose a technical challenge given that the water signal is four orders of magnitude greater than signals from metabolites of interest, and also because of the narrow range of the chemical shift, spin-spin coupling complicating the spectral pattern, and the higher scalp lipid signal compared with cerebral metabolite signals; nevertheless, choline-containing compounds (Cho) such as phosphoryl- and glycerophosphoryl-choline can be measured using this technique^[1].

In contrast to the commonly used method of single-voxel spectroscopy (SVS), chemical shift imaging (CSI) is a multi-voxel technique. Thus, in neuroimaging, 2D-CSI has the distinct advantage over

SVS of allowing larger areas of the brain to be studied during scanning, so that areas showing abnormal signals and also those appearing normal in structural magnetic resonance images can be included^[2]. CSI can also be carried out in three dimensions, which should improve spatial resolution and the signal-to-noise ratio; however, 2D-CSI is more resistant to motion artefact, which can be a problem when scanning the brain, than 3D-CSI^[3]. Furthermore, image quality is better with 2D-CSI compared with 3D-CSI at a usual magnetic field strength of 1.5 T or 3 T^[4-6].

Choline is an alcohol which, in the human brain, is particularly abundant in phosphatidylcholine (in which it is attached, as a polar head group, *via* a phosphate group, to the Sn3 position of the glycerol backbone) membrane phospholipid molecules; Cho take part in membrane biosynthesis and breakdown^[1]. Thus, measurement of Cho has clinical and research value. One example is in relation to chronic fatigue syndrome (also known as myalgic encephalomyelitis or systemic exertion intolerance disease), which is currently of unknown etiology. The first systematic proton neurospectroscopy study of this condition showed a significantly higher level of Cho in the occipital cortex in patients compared with matched healthy controls, and also loss of the spatial variation of Cho that is normally expected^[7]. Given that such increased levels are associated with abnormal membrane phospholipid metabolism^[8], this finding, which was essentially confirmed later by another group in respect of the basal ganglia^[9], suggests that chronic fatigue syndrome/myalgic encephalomyelitis is associated with abnormal phospholipid metabolism in neuroglial membranes^[1,7]. It has been suggested that this, in turn, might result from chronic viral infection^[10]. Based on this Cho finding, a potential therapeutic approach to this difficult-to-treat disorder, involving long-chain polyunsaturated fatty acids, has been suggested^[11,12]. A second example relates to dyslexia, which is another important neuropsychiatric disorder of unknown etiology, in which the first systematic proton neurospectroscopy study revealed decreased Cho in the left temporo-parietal lobe^[13]. This finding could have resulted from reduced left temporo-parietal phospholipid metabolism^[14], which would be consistent with the findings from the first systematic 31-phosphorus neurospectroscopy study of this disorder^[15]. In turn, this has led to suggestions of potential therapeutic interventions^[16].

2D-CSI may also be useful clinically in evaluating patients with acute onset of neuropsychiatric systemic lupus erythematosus^[2]. Another important clinical use of 2D-CSI is in relation to grading gliomas when used in combination with diffusion kurtosis imaging and dynamic susceptibility-weighted contrast-enhanced MRI^[17]. Indeed, in a brain histopathological study, it has been shown that 2D-CSI combined with perfusion MRI are associated with high sensibility and high specificity

in differentiating between glioblastoma multiforme and cerebral metastases and also in distinguishing between grade III and grade IV gliomas^[18]. It is therefore important to ascertain the reproducibility of 2D-CSI.

We present the results of the first study to investigate the repeatability of proton magnetic resonance spectroscopy 2D-CSI in the *in vivo* measurement of human cerebral levels of Cho at a magnetic field strength of 1.5 T.

MATERIALS AND METHODS

Study design

This study was a repeated-measures pilot study in six individuals. The study was approved by the Research Ethics Committee. All participants gave written informed consent. Immediately after undergoing MRI scanning (including 2D-CSI), each participant remained lying in the scanner and the scanning protocol, including the 2D-CSI, was repeated.

Volunteers

The cohort consisted of six healthy volunteers, three males and three females. Their mean age was 44.1 years (range 26 to 58 years).

MR spectroscopy

All measurements were carried out using a 1.5-T Siemens Symphony TIM (Total Imaging Matrix) scanner (Siemens Medical Systems, Erlangen, Germany) using a standard head matrix coil. Proton spectra were acquired using a 64-voxel 2D-CSI spin-echo spectroscopy sequence with TE = 30 ms, TR = 1500 ms, number of averages = 4, field of view = 160 mm × 160 mm, and thickness = 15 mm. Figure 1 shows the location of the voxels. Spectral analysis was carried out using the Siemens spectroscopy task card (Siemens Medical Systems, Erlangen, Germany). This automated software analysis was objective and clearly obviated the need for inter-observer analysis.

Statistical analysis

The main endpoint of this study was the ratio of Cho to creatine (Cr) for each voxel. The coefficient of variation (CV), repeatability coefficient (RC), and intraclass correlation coefficient (ICC) were used to assess the repeatability. The repeatability coefficient was calculated as $1.96 \times$ (standard deviation of the mean difference between two measurements), after the method proposed by Bland and Altman as being more appropriate than the correlation coefficient when assessing the level of agreement between two methods of clinical measurement^[19]. The CV was calculated as (the standard deviation of the mean difference between two measurements)/(the mean of all measurements) and was assessed in order to allow comparison of the results of the present study with those of previous studies of the reproducibility

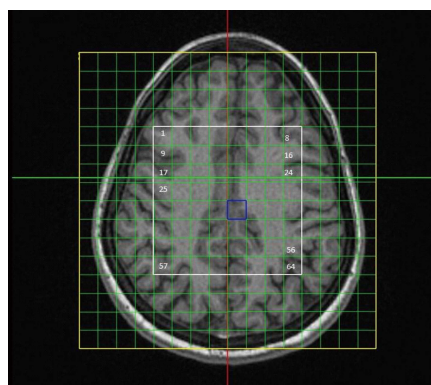


Figure 1 Location and numbering of voxels.

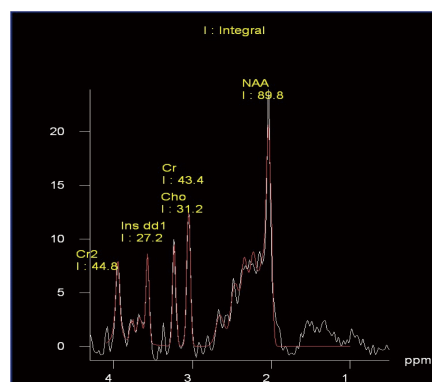


Figure 2 A fitted ¹H-MR spectrum.

of proton magnetic resonance (albeit without CSI). Differences between the results of the two scans were analyzed using the Wilcoxon related-samples signed-rank test (a repeated-measures nonparametric test). A *P*-value of less than 0.05 was taken to be statistically significant. Statistical tests were carried out using the software package IBM SPSS Statistics for Windows, version 21 (IBM Corp., Armonk, NY, United States).

RESULTS

There were no technical difficulties in carrying out this study and all 2D-CSI proton neurospectroscopy data were included in the analyses. Figure 2 illustrates an example of a fitted spectrum from this study using the Siemens software.

The Wilcoxon related-samples signed-rank test results for all 64 voxels are shown in Table 1, using the voxel nomenclature given in Figure 1. Three voxels showed a significant difference between successive scans, namely voxels 3, 10 and 21.

The values of the mean CV, RC and ICC (together with corresponding *P* values) are given in Table 2. The CV ranged from 2.75% (voxel 3) to 33.99% (voxel 58). The minimum RC was 5.68% (voxel 3). Many of the ICC values were statistically significant, particularly for central and more caudal voxels, but also for some rostral voxels.

Table 1 Wilcoxon related-samples signed-rank test results

Voxel	Median Cho/Cr at first scan	Median Cho/Cr at second scan	Wilcoxon related-samples signed-rank test (<i>P</i> value)
1	0.681	0.624	0.345
2	0.825	0.836	0.917
3	0.897	0.924	0.046
4	0.819	0.785	0.917
5	0.822	0.812	0.753
6	0.998	1.060	0.917
7	0.868	0.902	0.600
8	0.661	0.708	0.463
9	0.751	0.579	0.075
10	0.878	0.799	0.028
11	0.970	1.043	0.173
12	0.793	0.860	0.173
13	0.822	0.765	0.600
14	0.993	0.989	0.753
15	0.923	0.894	0.600
16	0.714	0.682	0.463
17	0.760	0.644	0.249
18	0.947	0.855	0.116
19	1.027	1.045	0.345
20	0.751	0.828	0.173
21	0.898	0.816	0.046
22	1.063	1.056	0.173
23	0.942	1.022	0.917
24	0.728	0.747	0.116
25	0.713	0.705	0.249
26	0.941	0.984	0.917
27	0.940	0.961	0.345
28	0.808	0.831	0.753
29	0.853	0.851	0.600
30	1.030	1.083	0.600
31	0.991	0.929	0.249
32	0.709	0.696	0.173
33	0.660	0.660	0.600
34	0.892	0.922	0.345
35	0.948	0.905	0.917
36	0.732	0.718	0.600
37	0.750	0.724	0.345
38	1.032	0.904	0.173
39	0.982	0.946	0.345
40	0.700	0.744	0.116
41	0.627	0.597	0.917
42	0.866	0.854	0.249
43	0.871	0.793	0.600
44	0.591	0.595	0.600
45	0.573	0.584	0.753
46	0.793	0.875	0.600
47	0.903	0.940	0.249
48	0.563	0.686	0.075
49	0.571	0.575	0.463
50	0.779	0.817	0.345
51	0.740	0.777	0.116
52	0.539	0.533	0.463
53	0.546	0.500	0.463
54	0.767	0.752	0.463
55	0.812	0.838	0.046
56	0.530	0.583	0.345
57	0.498	0.507	0.917
58	0.692	0.715	0.463
59	0.607	0.683	0.463
60	0.466	0.472	0.173
61	0.569	0.451	0.173
62	0.825	0.677	0.753
63	0.638	0.639	0.753
64	0.530	0.625	0.600

Table 2 Mean coefficient of variation, repeatability coefficient, and intraclass correlation coefficient for all voxels

Voxel	Mean coefficient of variation	Repeatability coefficient	Intraclass correlation coefficient (<i>P</i> value)
1	0.080	0.159	0.492 (0.236)
2	0.057	0.194	0.866 (0.032)
3	0.028	0.057	0.982 (< 0.0001)
4	0.115	0.386	-1.877 (0.822)
5	0.101	0.260	-0.066 (0.523)
6	0.117	0.446	0.372 (0.335)
7	0.053	0.171	0.829 (0.046)
8	0.076	0.206	0.158 (0.429)
9	0.191	0.607	-0.233 (0.612)
10	0.049	0.113	0.901 (0.003)
11	0.071	0.191	0.702 (0.081)
12	0.091	0.225	0.509 (0.197)
13	0.076	0.213	0.724 (0.100)
14	0.078	0.233	0.696 (0.124)
15	0.089	0.277	0.735 (0.105)
16	0.091	0.236	-0.024 (0.509)
17	0.290	1.287	-3.314 (0.949)
18	0.095	0.226	0.811 (0.029)
19	0.058	0.226	0.816 (0.052)
20	0.058	0.137	0.370 (0.273)
21	0.058	0.106	0.569 (0.071)
22	0.064	0.214	0.780 (0.048)
23	0.055	0.238	0.941 (0.005)
24	0.258	6.467	0.152 (0.43)
25	0.192	0.305	0.866 (0.028)
26	0.044	0.129	0.974 (0.001)
27	0.062	0.205	0.833 (0.033)
28	0.087	0.242	0.652 (0.159)
29	0.059	0.170	0.749 (0.088)
30	0.061	0.205	0.851 (0.034)
31	0.046	0.114	0.983 (< 0.001)
32	0.093	0.174	0.907 (0.007)
33	0.126	0.244	0.872 (0.024)
34	0.057	0.146	0.829 (0.033)
35	0.066	0.230	0.793 (0.071)
36	0.063	0.151	0.883 (0.024)
37	0.036	0.079	0.960 (0.002)
38	0.096	0.314	0.397 (0.284)
39	0.087	0.269	-0.162 (0.584)
40	0.122	0.222	0.643 (0.116)
41	0.185	0.225	0.917 (0.011)
42	0.055	0.138	0.950 (0.002)
43	0.083	0.235	0.691 (0.132)
44	0.106	0.217	0.553 (0.216)
45	0.106	0.369	0.229 (0.397)
46	0.182	0.547	-0.256 (0.588)
47	0.054	0.136	0.942 (0.003)
48	0.175	0.274	-0.074 (0.555)
49	0.102	0.134	0.961 (0.002)
50	0.053	0.121	0.970 (0.001)
51	0.039	0.081	0.946 (0.001)
52	0.056	0.116	0.870 (0.03)
53	0.068	0.134	0.795 (0.064)
54	0.071	0.171	0.928 (0.007)
55	0.083	0.117	0.945 (0.001)
56	0.148	0.277	0.108 (0.448)
57	0.195	0.296	0.887 (0.022)
58	0.340	0.547	0.582 (0.188)
59	0.177	0.384	0.143 (0.43)
60	0.135	0.177	0.883 (0.011)
61	0.143	0.230	0.620 (0.135)
62	0.200	0.691	0.512 (0.253)
63	0.180	0.432	0.833 (0.046)
64	0.273	0.714	-0.957 (0.73)

DISCUSSION

There have been no previous studies of the repeatability of proton neurospectroscopy 2D-CSI in the *in vivo* measurement of human cerebral levels of Cho at a magnetic field strength of 1.5 T. Previous *in vivo* studies of the reproducibility of proton magnetic resonance spectroscopy measurements have used single voxel techniques and have reported “within day” CV values for human hepatic fat of between 0.3% and 8.5%^[20-25]. Thus the results of the present study compare favorably with these reports, which is all the more impressive given that cerebral tissue is more heterogeneous than hepatic tissue. There have been few cerebral single-voxel proton reproducibility studies. Schirmer and Auer reported CVs for absolute human brain concentrations of the main metabolites Cho, Cr and N-acetylaspartate, ranging from 3.8% to 6.4%^[26]; the present results compare very well with these.

Van Werven and colleagues reported a “within day” RC value for hepatic fat (using a single voxel technique at 3 T) of 0.4%. Again, the present result of a minimum voxel RC of over 5% compares very well this result. Twenty-six of the voxels in the present study had an ICC which was statistically significant, indicating a high level of agreement for these voxels.

Just three voxels had median Cho to Cr ratios which were different between scans. From Figure 1 it can be seen that these voxels (numbers 3, 10 and 21) have locations in sulcal regions of the brain. It is therefore possible that the poor reproducibility in these three voxels might be a function of “bleeding” in the neurospectroscopy data acquisition. Voxel “bleeding” refers to contamination with signals derived from any of the six adjacent voxels, and is an analogue of artifactual Gibbs ringing in structural MRI^[27]. In the present case, the contaminating signals could have arisen from the low-signal sulcal spaces.

In conclusion, in this first study of its type, the reproducibility of proton magnetic resonance spectroscopy in the *in vivo* measurement of human cerebral levels of Cho at a field strength of 1.5 T using 2D-CSI has been found to be very acceptable. These findings should further encourage the use of this technique in psychiatric clinical practice as well as in research studies of neuropsychiatric disorders. Already, neurospectroscopy is proving helpful in studies of schizophrenia, major depressive disorder, forensic psychiatry (*e.g.*, posttraumatic stress disorder), chronic fatigue syndrome (myalgic encephalomyelitis or systemic exertion intolerance disease), and neuropsychiatric presentations in organic disorders, in which it has an important role to play in aiding diagnosis^[16,28,29]. Given the present finding of a highly acceptable level of reproducibility of 2D-CSI, it would be appropriate in future to apply this technique to the follow-up of such patients, including monitoring their response to treatment.

ARTICLE HIGHLIGHTS

Research background

In vivo magnetic resonance proton spectroscopy studies of the brain can be used to measure Cho. In contrast to the commonly used method of SVS, CSI is a multi-voxel technique. Thus, compared with SVS, 2D-CSI allows larger areas of the brain to be studied, so that areas showing abnormal signals and also those appearing normal in structural MRI can be included. Compared with 3D-CSI, 2D-CSI is more resistant to motion artefact, which can be a problem when scanning the brain, and image quality is better at a usual clinical magnetic field strength of 1.5 T or 3 T.

Research motivation

Brain choline is particularly abundant in phosphatidylcholine membrane phospholipid molecules; Cho take part in membrane biosynthesis and breakdown. Thus, measurement of Cho has clinical and research value. For example, in chronic fatigue syndrome (also known as myalgic encephalomyelitis or systemic exertion intolerance disease), which is of unknown etiology, the first systematic proton neurospectroscopy study showed a significantly higher level of Cho in the occipital cortex in patients compared with matched healthy controls, and also loss of the spatial variation of Cho that is normally expected. This finding, which was essentially confirmed later by another group in respect of the basal ganglia, suggests that this disorder is associated with abnormal phospholipid metabolism in neuroglial membranes and has led to the suggestion of a potential therapeutic approach. A second example is dyslexia, also of unknown etiology, in which the first systematic proton neurospectroscopy study revealed decreased Cho in the left temporo-parietal lobe. This finding could have resulted from reduced left temporo-parietal phospholipid metabolism, which would be consistent with the findings from the first systematic 31-phosphorus neurospectroscopy study of dyslexia. In turn, this has led to suggestions of potential therapeutic interventions. 2D-CSI may also be useful clinically in evaluating patients with acute onset of neuropsychiatric symptoms. Another important clinical use of 2D-CSI is in relation to grading gliomas. It is therefore important to ascertain the reproducibility of 2D-CSI.

Research objective

The aim of this study was to investigate the repeatability of proton magnetic resonance spectroscopy 2D-CSI in the *in vivo* measurement of human cerebral levels of Cho.

Research methods

A repeated-measures study in six individuals was carried out using a 1.5-T Siemens Symphony TIM scanner and a standard head matrix coil. Proton spectra were acquired using a 64-voxel 2D-CSI spin-echo spectroscopy sequence. Spectral analysis was carried out using the Siemens spectroscopy task card. The main endpoint was the ratio of Cho to Cr for each voxel. The CV, RC, and ICC were used to assess the repeatability. There have been no previous studies of the repeatability of proton neurospectroscopy 2D-CSI in the *in vivo* measurement of human cerebral levels of Cho at a magnetic field strength of 1.5 T.

Research results

There was a minimum voxel RC of over 5%, which compared favorably with previous studies of the liver; the present results were all the more impressive given the much more heterogeneous nature of the brain compared with hepatic tissue. Twenty-six voxels had an ICC which was statistically significant, indicating a high level of agreement for these voxels. Just three voxels had median Cho to Cr ratios which were significantly different between scans. These three voxels were located in sulcal brain regions. Thus the poor reproducibility in these three voxels might be a function of “bleeding” in the neurospectroscopy data acquisition.

Research conclusions

In this first study of its type, the reproducibility of proton magnetic resonance spectroscopy in the *in vivo* measurement of human cerebral levels of Cho at a field strength of 1.5 T using 2D-CSI has been found to be very acceptable. Overall, the present findings should further encourage the use of this technique

in psychiatric clinical practice as well as in research studies of neuropsychiatric disorders.

Research perspectives

Overall, the results of this study are highly encouraging for the use of this technique in neuropsychiatric research and clinical practice. Further studies should be carried out to determine whether sulcal voxels should routinely be omitted from longitudinal comparison studies.

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Clinical Practice Study

Audit of physical health monitoring in children and adolescents receiving antipsychotics in neurodevelopmental clinics in Northumberland

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Abstract

AIM

To ascertain performance against the standards set by National Institute for Clinical Excellence (NICE) guidelines on physical health monitoring of thirty children and adolescents prescribed antipsychotics in neurodevelopmental clinics in Northumberland and identifying areas for improvement in practice.

METHODS

The audit involved a review of recorded documentation pertaining to physical health monitoring in patient electronic records pertaining to children and adolescents attending neurodevelopmental clinics in Northumberland prescribed antipsychotics. Clients were also contacted by telephone if relevant documentation could not be identified or retrieved to confirm the details. 32 case notes were perused of which 2 were excluded as they had refused to have venepuncture which was documented in the electronic records.

RESULTS

The overall audit results demonstrated partial compliance with NICE guidelines on physical health monitoring in children and adolescents prescribed antipsychotics. Bi-annual recording of height, weight, blood pressure, pulse rate and review of side effects

was completed in 100% of subjects. However, annual monitoring for blood tests including liver function, renal function full blood count as well as biannual monitoring of serum prolactin, serum lipid profile was completed only in 56% of subjects. Comparative baseline characteristics between the two groups (compliant and non-compliant with guidelines) found no differences based on any socio-demographic or clinical variables. However, the proportion of patients in the group compliant to guidelines was higher in the age group of 12-17 years as compared to < 12 years (70.58% *vs* 38.46%), though not statistically significant ($\chi^2 = 1.236$; $P = 0.24$).

CONCLUSION

Development of tailored and specific guidelines for physical health monitoring in children and adolescents prescribed antipsychotics taking into consideration clinical effectiveness and safety profile is likely to improve adherence rates.

Key words: Antipsychotic; Children; Physical health; Guidelines

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Core tip: A number of clinical guidelines have been developed for physical health monitoring in children and adolescents on antipsychotics. However, none of them capture the intricacies and complexities involved in prescribing antipsychotics to children and adolescents, which is distinct from adults. The typically shorter duration of prescribing, lower doses used and lack of data on long term adverse effects with antipsychotics in this population have not been taken into account. This audit aimed to ascertain if physical health of children and adolescents attending neurodevelopmental clinics in Northumberland and prescribed antipsychotics followed National Institute for Clinical Excellence guidelines. The overall audit findings were partially compliant with the guidelines. Logistic and ethical challenges as well as lack of awareness about the guidelines could underpin these findings.

Gnanavel S, Hussain S. Audit of physical health monitoring in children and adolescents receiving antipsychotics in neurodevelopmental clinics in Northumberland. *World J Psychiatr* 2018; 8(1): 27-32 Available from: URL: <http://www.wjgnet.com/2220-3206/full/v8/i1/27.htm> DOI: <http://dx.doi.org/10.5498/wjp.v8.i1.27>

INTRODUCTION

Despite limited literature on long term effectiveness and side effects of antipsychotics in children and adolescents, antipsychotics are frequently used in this population in Europe and North America. In fact,

recent trends of increased antipsychotic prescribing for this population has been well-documented. In a recent German nation-wide prescribing audit by health care insurers it was demonstrated that the rise in antipsychotic prescriptions was particularly marked among 10- to 14-year-olds (from 0.24% to 0.43%) and among 15- to 19-year-olds (from 0.34% to 0.54%)^[1]. Psychosis, challenging behaviour in autism spectrum disorder (ASD) and Tourette's syndrome are the most common reasons for child and adolescent psychiatrists to prescribe antipsychotics. In addition, use of antipsychotics in other neurodevelopmental disorders like attention deficit hyperactivity disorder (ADHD) is not uncommon though "off-label" for this purpose^[2]. In terms of symptom profiles targeted by antipsychotic use in this population, the most common indications were chronic behavioural disturbance with persistent aggression (34%), followed by agitation/anxiety (31%) and psychotic symptoms (31%) in a recent nation-wide audit of antipsychotic prescribing in children and adolescents in United Kingdom^[3].

A survey of antipsychotic prescribing among child and adolescent psychiatrists in the United Kingdom found that over 95% had prescribed antipsychotics over a 12 mo period with the majority (almost 90%) choosing one of the second generation antipsychotics (SGAs)^[4]. Risperidone followed by aripiprazole and olanzapine are the favoured antipsychotics in this population^[4]. There is a relatively limited but gradually expanding evidence-base of randomised clinical trials to support antipsychotic prescribing in children and adolescents with non-psychotic illnesses. This includes management of challenging behaviour in ASD with risperidone; aripiprazole and risperidone for management of aggression with conduct disorder and learning disability^[5-8].

It is to be noted that, children and adolescents are more sensitive to antipsychotic-related adverse effects than adults. This includes extrapyramidal side effects (EPS) with first generation antipsychotics (FGAs) and metabolic side effects with SGA^[9,10]. However, it is also worth noting that most literature relating to tolerability of antipsychotics in children and adolescents are based on the treatment of severe mental illnesses like psychotic disorders in typically short-term clinical trials lasting 6 to 12 wk. There is scant literature on the adverse effects associated with longer term prescribing of antipsychotics (the distal health outcomes as opposed to more proximal health outcomes) and more particularly, involving lower doses that are typically used in non-psychotic developmental disorders in children and adolescents. Possibly, as an extension to this, we do not know if these physical side effects are reversible, partially or completely with discontinuation of antipsychotics or are these irreversible side effects.

Individual antipsychotics (even within the same class) differ in terms of side effect profiles when prescribed to children and adolescents. For example, in this population, EPS are more common with haloperidol and high-

dose risperidone than with olanzapine. Weight gain is more common in olanzapine than with risperidone^[10,11]. There is also some evidence for differential response to same medication based on age groups. For example, children and adolescents experience more weight gain on second generation antipsychotics than do adults^[10]. However, most of the guidelines do not differentiate their physical health monitoring requirements, particularly in the maintenance phase between those on different antipsychotics or between different age groups. Also, first and second generation antipsychotics are different chemically and heterogeneous with respect to safety profile. Hence, having common monitoring requirement seems flawed, in practical terms.

The commonly followed guidelines for physical health monitoring in children and adolescents receiving antipsychotics include NICE (National institute for clinical excellence guidelines) (CG155); AACAP (American academy of child and adolescent psychiatry) - practice parameter for the use of atypical antipsychotic medications in children and adolescents; CAMESA - Canadian Alliance for Monitoring Effectiveness and Safety of Antipsychotics in Children and TRAAY (Treatment recommendations for the use of antipsychotics for aggressive youth) centre for the Advancement of Children's Mental Health^[12-14]. The specificity of recommendations for ongoing monitoring for metabolic parameters varies, with some guidelines recommending "appropriate" monitoring while others identifying specific tests and pre-determined follow-up intervals.

The parameters specified in these guidelines include physical measurements like height, weight, blood pressure and pulse rate as well as those measured in laboratory with a blood sample like liver function test, renal function tests and blood glucose. Usually, there are specifications for monitoring parameters at baseline as well as during the maintenance phase in the guidelines mentioned above.

This audit was identified with a view to ascertaining performance against the standards set by National Institute for Clinical Excellence (NICE) guidelines on physical health monitoring of thirty children and adolescents prescribed antipsychotics in neurodevelopmental clinics in Northumberland and identifying areas for improvement in practice^[15]. The audit focused only on those clients who had already been initiated and stabilised on a dose of antipsychotic medication for at least a period of one year prior to the time frame chosen for audit. The time frame covered was from 1st November 2015 to 30th October 2016.

MATERIALS AND METHODS

The audit involved a review of recorded documentation pertaining to physical health monitoring in patient electronic records pertaining to those children and adolescents attending neurodevelopmental clinics in Northumberland prescribed antipsychotics. Clients were

also contacted by telephone if relevant documentation could not be identified or retrieved to confirm the details. Thirty-two case notes were perused of which 2 were excluded as they had refused to have venepuncture which was documented in the electronic records. Hence, the total number of clients included in the audit was 30. The sample was collated by means of consecutive sampling of convenience. Data collection took place from 1 November 2016 to 30 March 2017 and data analysis was completed in 30 April 2017. A quality review of the results of this audit was undertaken by the second author during July 20, 2017 to August 03, 2017 to provide assurance on the accuracy of the findings in this report. The audit was registered with the audit department of Northumberland, Tyne and Wear NHS foundation trust.

The NICE guidelines recommend annual physical health monitoring of following parameters for patients already stabilised on antipsychotic medications: Biannual monitoring for weight, height, pulse, blood pressure, fasting blood glucose, HbA1c and blood lipid levels, review of side effects and annual monitoring for liver function tests, renal function tests and serum electrolytes as well as full blood count. The expected compliance rate was 100% (gold standard) with respect to all the above parameters.

Statistical analysis

The data was analysed using SPSS 15.0 (Statistical package for social science). The data was analysed using appropriate parametric and non-parametric tests based on the distribution of data including χ^2 test for categorical variables and *t*-test for continuous variables. *P* < 0.05 was considered significant.

RESULTS

The study sample included 28 males and 2 female clients (male: female ratio of 14:1). The two antipsychotics prescribed were risperidone (77%) (*n* = 23) and aripiprazole (23%, *n* = 7). The daily dose range for risperidone was 0.25-2 mg and for aripiprazole was 0.5-4 mg. The mean dose of risperidone used was 0.88 mg (SD: 0.11) and mean dose of aripiprazole used was 1.87 mg (SD: 0.23). The mean age of initiation of antipsychotic in this sample was 13.45 years (SD: 1.23). The average duration of antipsychotic use in months was 15.67 mo (SD: 1.98) (Table 1).

Bi-annual recording of height, weight, blood pressure, pulse rate and review of side effects was completed in 100% of subjects. However, annual monitoring for blood tests including liver function, renal function full blood count as well as biannual monitoring of serum prolactin, serum lipid profile was completed only in 56% of subjects. It was also noted that in five of the subjects in whom the physical health monitoring was carried out according to guidelines, the initial lab result summary did not contain serum prolactin which

Table 1 Baseline characteristics of the audit sample (*n* = 30)

Variable	Mean	SD
Age (yr)	13.45	1.23
Duration of antipsychotic use (mo)	15.67	1.98
Average number of clinical reviews	3.43	0.46
Variable	<i>n</i>	%
Age groups (yr)		
12-17	17	56.67
< 12	13	43.33
Gender		
Male	28	93.33
Female	2	6.67
Antipsychotic		
Risperidone	23	76.67
Aripiprazole	7	23.33
Psychiatric diagnosis		
ADHD	12	40.00
ASD	4	13.33
ADHD + ASD	6	20.00
ADHD + other diagnosis	6	20.00
ASD + other diagnosis	2	6.67

ADHD: Attention deficit hyperactivity disorder; ASD: Autism spectrum disorder.

was subsequently carried out after a second request (possibly missed out initially due to oversight).

Comparing the baseline characteristics between the groups for whom antipsychotic physical monitoring guidelines were followed and not followed, there were no differences based on antipsychotic prescribed, duration of antipsychotic use or number of reviews carried out in the neurodevelopmental clinics. However, the proportion of patients who were monitored for physical health according to guidelines was higher in the age group of 12-17 years as compared to < 12 years, though not statistically significant ($\chi^2 = 1.236$; $P = 0.24$). There were also no significant differences in the proportion monitored for physical health based on the diagnosis (ADHD; ASD; ADHD+ASD; ADHD + other mental health disorders; ASD + other mental health disorders) ($\chi^2 = 1.345$; $P = 0.27$). The "other" diagnoses included oppositional defiant disorder ($n = 3$), tic disorder ($n = 3$) and conduct disorder ($n = 2$). We did not carry out a gender-wise comparison, since there were only two female clients in the audit sample (Table 2).

The overall audit results demonstrated partial compliance with NICE guidelines on physical health monitoring in children and adolescents prescribed antipsychotics. However, it was interesting to note that, the monitoring guidelines were followed in a larger proportion of patients in 12-17 year age range as compared to < 12 years (though not statistically significant). To summarise, there was no statistical difference between the groups that completed and did not complete physical health monitoring according to NICE guidelines based on any baseline socio-demographic or clinical variables.

Table 2 Factors associated with likelihood of testing

Age groups (yr)	Total number	Number monitored
12-17	17	12
< 12	13	5
Antipsychotic		
Risperidone	23	13
Aripiprazole	7	4
Psychiatric diagnosis		
ADHD	12	7
ASD	4	2
ADHD + ASD	6	3
ADHD + other diagnosis	6	4
ASD + other diagnosis	2	1
Average duration of antipsychotic use	Mean	SD
Group A ¹	15.98	1.21
Group B ²	15.42	1.32
Average number of clinical reviews	Mean	SD
Group A ¹	3.52	0.32
Group B ²	3.31	0.36

¹Group A: Group that completed physical health monitoring requirements according to National Institute for Clinical Excellence (NICE) guidelines;

²Group B: Group that did not complete physical health monitoring requirements according to NICE guidelines. ADHD: Attention deficit hyperactivity disorder; ASD: Autism spectrum disorder.

DISCUSSION

The findings from our audit are broadly similar to previous published literature. A similar audit carried out recently in an inpatient setting in United Kingdom on children and adolescents prescribed antipsychotics demonstrated adherence rates of 20%-60% on different parameters^[16]. In comparison, an audit of similar parameters in a community based setting focusing on adult patient's demonstrated partial adherence to guidelines in around half the patients^[17]. Both the above audits were carried out with standards set by NICE as the reference.

Outside the United Kingdom, there are studies or audits published from North America and Europe on the same theme. A large scale longitudinal retrospective cohort study using data from 2000-2006 from the PharMetrics data base (an insurance claims database) in United States demonstrated 12 wk lipid and blood sugar monitoring rates of 6.8% and 9% respectively in patients under 65 years (which also includes children and adolescents) receiving second generation antipsychotics^[18]. It also interestingly demonstrated rise in these rates to 14.1% and 17.9% post introduction of ADA (American diabetic association) guidelines in 2004. Of even more importance, is the fact that 0-11 years and 11-17 years fared the worst when different age groups were compared for 12 wk monitoring of blood glucose and blood lipids^[18].

The limitations of our audit include a small sample size and lack of representation from female patients with neurodevelopmental disorders, receiving an

antipsychotic. Also, the results are specific for our service and cannot be generalised to other parts of the country considering the heterogeneity in the way neurodevelopmental services as well as physical health services are organised in different parts of the country.

Several guidelines based on available evidence base have been developed (mentioned earlier) for both baseline and ongoing monitoring of physical health parameters for children and adolescents prescribed antipsychotics. However, most of these guidelines are extrapolated at least in part from the equivalent guidelines for adults. They fail to capture the complexities and intricacies of antipsychotic prescribing, particularly in younger children, especially the usually short term symptomatic use.

The common barriers cited for non-adherence to guidelines on physical health monitoring in children and adolescents prescribed antipsychotics include ethical and practical difficulties in taking blood from children (*e.g.*, In children with autism and challenging or oppositional behaviours)^[3]. This could also be the possible basis for the audit finding that a higher proportion of adolescents on antipsychotics were monitored for physical health parameters than younger children on antipsychotics (though not statistically significant). This could also possibly reflect the tendency of mental health professionals to treat adolescents more like young adults while in case of children, the attitude of clinicians is generally quite different. There is also uncertainty regarding the impact of abnormal results on clinical management (*e.g.*, asymptomatic hyperprolactinaemia)^[3]. Sometimes, logistic challenges including inadequate number of skilled phlebotomists and lack of a reliable pathway for carrying out these investigations and retrieving the results could be a barrier to following these guidelines (for example, in many cases psychiatrists depend on general practitioners or hospitals for organising blood tests while in some services in house phlebotomy and lab services are offered). However, most clinicians do support the development of physical health monitoring guidelines for antipsychotic use in children and adolescents, albeit advocating guidelines more appropriately constructed for this target population and taking into account the complexities involved.

Some published literature on quality improvement projects in this regard demonstrated simple methods like a visual prompt questionnaire tool along with review paperwork, new formatting of clinical letters to general practitioners, psychoeducation of both clinical practitioners and patients, easy read leaflets and posters which did produce a significant improvement in adherence to clinical guidelines^[16,17]. On a larger scale, in Europe, the Therapeutic Drug Monitoring (TDM) run by the German-Austrian Swiss "Competence Network on TDM in Child and Adolescent Psychiatry" and the Paediatric Atypical Antipsychotic Monitoring Safety Study (PAMS) in the United Kingdom have been developed as pharmacovigilance projects^[19,20].

Development of tailored and specific guidelines for physical health monitoring in children and adolescents prescribed antipsychotics based on age of initiation, dose and type of antipsychotic is likely to improve adherence rates. Some room for flexibility, taking into consideration appropriate clinical judgement on a case by case basis may also be beneficial in this regard. Similarly, understanding attitudes and psychological barriers in both patients and clinicians to regular monitoring, particularly blood parameters can provide useful insight in addressing the generally low compliance rates to these guidelines worldwide. We also need further studies to identify those children and adolescents with a possibly higher risk of side effects (*e.g.*, a positive family history of physical morbidity) to allow us to tailor a more intensive monitoring regimen for this subset of population receiving antipsychotics. Tailored guidelines for children and adolescents and a customised approach is needed to match clinical effectiveness and safety profile.

ARTICLE HIGHLIGHTS

Research background

Despite limited literature on long term effectiveness and side effects of antipsychotics in children and adolescents, antipsychotics are frequently used in this population in Europe and North America. In fact, recent trends of increased antipsychotic prescribing for this population has been well-documented. These medications are associated with physical health side effects though the extent of these side effects when used in lower doses or prolonged duration in children and adolescents have not been adequately studied. However, a number of popular guidelines exist pertaining to physical health monitoring in children and adolescents on antipsychotics.

Research motivation

The current study is an audit of physical health monitoring in children and adolescents prescribed antipsychotics in neurodevelopmental clinics in Northumberland. A comparative review of similar audits carried out from different regions can address pertinent issues like association between standards set by different guidelines and the concordance rates with the same.

Research objectives

To ascertain performance against the standards set by National Institute for Clinical Excellence (NICE) guidelines on physical health monitoring of thirty children and adolescents prescribed antipsychotics in neurodevelopmental clinics in Northumberland and identifying areas for improvement in practice.

Research methods

The audit involved a review of recorded documentation pertaining to physical health monitoring in patient electronic records pertaining to those children and adolescents attending neurodevelopmental clinics in Northumberland prescribed antipsychotics. Clients were also contacted by telephone if relevant documentation could not be identified or retrieved to confirm the details. 32 case notes were perused of which 2 were excluded as they had refused to have venepuncture which was documented in the electronic records.

Research results

The overall audit results demonstrated partial compliance with NICE guidelines on physical health monitoring in children and adolescents prescribed antipsychotics. Bi-annual recording of height, weight, blood pressure, pulse rate and review of side effects was completed in 100% of subjects. However, annual monitoring for blood tests including liver function, renal function full blood count as well as biannual monitoring of serum prolactin, serum lipid profile was completed only in 56% of subjects. Comparative baseline characteristics

between the two groups (compliant and non-compliant with guidelines) found no differences based on any socio-demographic or clinical variables. However, the proportion of patients in the compliant group was higher in the age group of 12-17 years as compared to < 12 years (70.58% vs 38.46%), though not statistically significant ($\chi^2 = 1.236$; $P = 0.24$).

Research conclusions

Development of tailored and specific guidelines for physical health monitoring in children and adolescents prescribed antipsychotics taking into consideration clinical effectiveness and safety profile is likely to improve adherence rates.

Research perspectives

The methodology into development of tailored guidelines for antipsychotic monitoring in children and adolescents need to be adequately focused upon. A comparative review of the audits on antipsychotic physical health monitoring guidelines carried out till date in different regions of the world based on different guidelines might shed some light on this important topic.

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Clinical Practice Study

Factors associated with tobacco, alcohol, and other drug use among youth living in West Central Mexico

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Abstract

AIM

To determine the prevalence of drug and substance abuse among high school students in Jalisco and its association with the severity of health, behavior and psychosocial problems in order to provide evidence for possible prevention and treatment needs.

METHODS

A multi-stage random sample of Jalisco high school students was given a paper-and-pencil survey based upon an adapted version of the drug use screening inventory (DUSI) ($n = 24699$; $n = 2832$). The DUSI showed adequate psychometric characteristics in this population. The statistical analyses accommodated the complex survey design with attention to unequal probability of selection and clustering of participants within schools and regions.

RESULTS

An estimated 44% of the students had smoked tobacco, one in five students was a current smoker, and one in four students used to smoke but had not smoked for one year or more. By contrast, 6.8% of the students reported having used marijuana, cocaine, or both. Behavioral problems, deviant peer affiliation, and troubled families were independently associated with drug use. One in two students who used tobacco or alcohol had used these drugs in the past year (46% and 54%, respectively), and one in four students who used marijuana or cocaine in their lifetime had used those drugs in the past year (28% in both cases).

CONCLUSION

The rates of cocaine use as well as the proportion of current users were higher than expected among high school students and indicate changing patterns of drug use in Mexico. These results corroborate that the general trend of drug use by youth in Mexico is increasing. Results from this study help us better understand the needs of at-risk youth and the need for new treatment and prevention strategies.

Key words: Tobacco; Alcohol; Marijuana; Illegal drugs; Mexico; Students; Epidemiology

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Core tip: Drug and substance use is a public health problem around the world. Prevention efforts are carried out with varying results. One of the main targets in prevention is the risk factors associated with drug use. There are several instruments to study the risk factors which provide critical information to establish guidelines to control and prevent drug use. We used a well known validated and accepted instrument (drug use screening inventory) to investigate the prevalence and psychosocial factors associated with tobacco, alcohol and drug use in high school students in Mexico. We found higher prevalence of substance use than expected: 44% of the students had smoked tobacco and one in five students was a current smoker while over 40% had history of binge drinking. On the other hand, 6.8% of the students reported having used marijuana, cocaine, or both. Behavioral problems, deviant peer affiliation, and troubled families were independently associated with drug use. These results will help in the application of control and prevention

programs among high school students. This is the first survey representative of a West Central state in Mexico: Jalisco which is an important Mexican state because it has a significant drug production and trafficking problem, and on the other hand, it provides a great number of migrants to the United States creating social, cultural and health problems associated with risk behaviors.

Campollo O, Sheikhattari P, Alvarez C, Toro-Guerrero J, Sanchez Avila H, Wagner FA. Factors associated with tobacco, alcohol, and other drug use among youth living in West Central Mexico. *World J Psychiatr* 2018; 8(1): 33-42 Available from: URL: <http://www.wjgnet.com/2220-3206/full/v8/i1/33.htm> DOI: <http://dx.doi.org/10.5498/wjp.v8.i1.33>

INTRODUCTION

Drug use is a public health problem with increasing trends in Mexico^[1-3] where only tobacco and alcohol products are legally available while other drugs such as marijuana (except the recently legalized medical marijuana)^[4], cocaine, heroin, methamphetamines, and synthetic drugs of abuse are not. In fact, although the 2016-2017 National Drug, Alcohol and Tobacco Consumption Survey may not provide an accurate comparison with previous surveys on account of the modified methodology^[3], according to the National Addiction Surveys (Encuesta Nacional de Adicciones, ENA)^[1,2], the prevalence of cocaine and marijuana use almost doubled in the past decade. More specifically, in 2012, 43% of the individuals between the ages of 12-25 reported being exposed to drug use, among them half experimented with drugs, and 13% used drugs frequently^[1,2]. In spite of recent efforts to provide up-to-date epidemiologic information, since 1991 there has not been a published regional or state drug abuse survey performed in Jalisco, a state in the West Central Region of Mexico with a population of over 8 million. The most recent available information from the Mexican National Survey from 2016 estimated that 15.3% of the 12- to 65-year-old population in Jalisco had never used drugs^[3]. Among youths of high school age, the ENA estimated that 2.7% of males and 1.1 % of females have used illegal drugs^[2]. However, these figures may not apply directly to Jalisco given the significant heterogeneity within this particular region. To the extent that drug use differs across rural/urban areas in Mexico^[5-7], pooled drug use estimates for the region may mask important within-region differences.

Interest in drug use trends in the State of Jalisco is warranted in light of its large population and a very strategic geo-politic location as a narcotic production enclave and a route for drug trafficking directed to the United States^[8]. Jalisco is also a large contributor of documented and undocumented workers to the United States, many of which make frequent

roundtrips^[9]. In addition, drug use may correlate with other risk behaviors that increase the risk of HIV/AIDS, viral hepatitis, and other sexually transmitted infections^[10,11]. Therefore, it is important to recognize that health profiles and risk behaviors in one region, and even a sub-region, may have consequences in many other regions in spite of geographic, language, cultural, and legal barriers.

Surveys are one of the main sources of information to understand the nature and extent of drug abuse in different populations, and they support evidence-informed development of policies and practice guidelines^[12]. Thus, in this study, we sought to improve on the few existing studies about treatment needs for drug abuse among youths in Mexico. Hence, the aim of this study was to investigate the prevalence of substance use and associated factors amongst high school students from the Mexican West-Central State of Jalisco, to identify treatment and prevention needs, and to explore the association between drug involvement and selected psychosocial covariates. We conducted the first survey representative of Jalisco's sub-regions performed in the 21st century.

MATERIALS AND METHODS

Data were collected through a cross-sectional survey using a multi-stage, random sample of high school students, from 10 geo-political sub-regions in the State of Jalisco, Mexico. A total of 25 public high schools participated in the survey. The mean number of students per school was 524 with a maximum of 2242 and a minimum of 132 (the sample included regional high schools and smaller high school "modules"). The universe included 24699 students and a final sample of 2832 students participated. The project was approved by the University of Guadalajara's Research Committee of the Health Sciences Center. We obtained authorization from the principal of each participating high school, and no school refused to participate in the study. The inclusion criteria were regular attendance in the participating school and consenting to participate in the study. Irregular students and students who did not complete the survey were excluded. At the time of the survey, students were informed that their participation was voluntary and they could choose not to participate in the survey without any penalties. Almost all of the students consented to participate in the study (only 4 refused). Data confidentiality and anonymity were explained twice; once in their classroom at the time of randomization, and once in the auditorium where all participants were gathered.

Procedures

We used a self-administered, school-based paper-and-pencil anonymous questionnaire. In each school, the survey was conducted in one day, and it was administered by the principal investigator and

members of the research team. The survey was administered at the school's auditoriums. To assure and preserve confidentiality, no teachers or school staff members were allowed to be present in the auditorium at the time of the application, nor were they allowed to see the completed questionnaires. The questionnaires were scanned with an optical reader which recorded filled or blank dots.

Measures used

Students completed the abbreviated Spanish version of the drug use screening inventory (DUSI) for youth developed by Tarter^[13] and further adapted for the Mexican population by Diaz *et al.*^[14]. The abbreviated DUSI-RM includes 95 yes/no questions assessing the 10 domains of drug and alcohol use, psychiatric disorders, health status, behavior patterns, school performance, family system, peer relationships, social competence, work adjustment, and leisure/recreation. Of particular interest for the present analyses is the substance abuse domain which assesses the type and substance use on the day of the survey, as well as the past week, month, year, and before then. In addition, the survey questionnaire includes questions on demographics such as age, gender, high school grade, occupation, family income, school shift, and school location (urban vs rural).

As with the original DUSI and other adaptations for Latin American countries^[15], the DUSI-RM in this sample had good to excellent reliability, with a 0.79 Chronbach's alpha coefficient for the overall instrument and domain-specific scores^[16] ranging from 0.57 to 0.80. Due to non-normality of the data, each participant's domain-specific scores were recoded into three levels to contrast the bottom two deciles (No Problem) from the six subsequent deciles (Low Problem), and the highest two deciles (High Problem).

Statistical analysis

After exploratory data analyses to check for variable distribution and data preparation for multivariate analyses, logistic regression models were used to estimate the association of each DUSI-RM domain with tobacco use, alcohol use, as well as marijuana and cocaine use, while controlling for age, sex, and socio-economic status (SES). The analyses were done with STATA version 10.0 (STATA Corp, College Station, TX, United States), and they accommodated the complex survey design with attention to unequal selection probabilities and clustering of participants within schools^[17].

RESULTS

Table 1 summarizes results regarding drug involvement in the surveyed sample. More than half of the students (55.8%) had never used tobacco, one in five (20.2%) had smoked it in the past year, and about

Table 1 Drug and substance use by high school students in Jalisco, Mexico (*n* = 2816)

Prevalence	Tobacco use		Binge drinking		Marijuana		Cocaine		Any illegal	
	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	No.	%	<i>n</i>	%
Never	1564	55.77	1590	57.03	2596	92.48	2611	92.50	2517	89.47
Past year	556	20.21	984	35.01	129	4.41	127	4.84	191	6.83
Former	696	24.02	242	7.96	91	3.11	78	2.66	108	3.70

Table 2 Cross-tabulation of past-year tobacco, alcohol, and illicit drug use by socio-demographic characteristics and drug use screening inventory problem areas (*n* = 2816)

Variables	Total (<i>n</i> %)	Past year smoking (<i>n</i> %)			Past year alcohol use (<i>n</i> %)			Past year illicit drug use (<i>n</i> %)		
		No	Yes	<i>P</i> value	No	Yes	<i>P</i> value	No	Yes	<i>P</i> value
Total	2816 (100)	2260 (79.8)	556 (20.2)	n/a	1832 (65.0)	984 (35.0)	n/a	2721 (96.6)	191 (6.8)	n/a
Age (yr)										
>16	2358 (83.7)	1875 (79.2)	483 (20.8)	0.112	1482 (62.8)	876 (37.2)	< 0.001	2183 (92.5)	175 (7.5)	0.005
≤ 16	458 (16.3)	385 (82.8)	73 (17.2)		350 (76.1)	108 (23.9)		442 (96.3)	16 (3.7)	
Gender										
Female	1460 (52.0)	1223 (83.7)	237 (16.3)	< 0.001	1050 (71.8)	410 (28.2)	< 0.001	1413 (96.8)	47 (3.2)	< 0.001
Male	1356 (48.0)	1037 (75.5)	319 (24.5)		782 (57.6)	574 (42.4)		1212 (89.3)	144 (10.7)	
Employment										
Not working	1937 (69.5)	1590 (81.5)	347 (18.5)	0.013	1279 (65.9)	658 (34.1)	0.097	1828 (94.2)	109 (5.8)	0.01
Employed	879 (30.5)	670 (75.9)	209 (24.1)		553 (62.9)	326 (37.1)		797 (90.7)	86 (9.3)	
Behavioral pattern										
No problem	622 (22.5)	558 (89.6)	64 (10.4)	< 0.001	497 (79.5)	125 (19.5)	< 0.001	607 (98.0)	15 (2.0)	< 0.001
Low	1651 (58.2)	1341 (81.0)	310 (19.0)		1094 (66.3)	557 (33.7)		1556 (94.1)	95 (5.9)	
High	543 (19.3)	361 (64.7)	182 (35.3)		241 (44.2)	302 (55.8)		462 (84.8)	81 (15.2)	
Psychiatric disorder										
No problem	564 (19.9)	471 (83.4)	93 (16.6)	0.002	403 (71.6)	161 (28.4)	< 0.001	534 (94.7)	30 (5.3)	0.104
Low	1692 (60.1)	1377 (80.9)	315 (19.1)		1122 (65.9)	570 (34.1)		1585 (93.6)	107 (6.4)	
High	560 (20.0)	412 (72.9)	148 (27.1)		307 (55.8)	253 (44.2)		506 (90.4)	54 (9.6)	
Social competence										
No problem	565 (19.8)	463 (81.2)	102 (18.8)	0.44	364 (65.1)	201 (35.0)	0.016	525 (92.9)	40 (7.1)	0.741
Low	1683 (60.2)	1339 (79.2)	344 (20.8)		1074 (63.5)	609 (36.5)		1567 (93.1)	116 (6.9)	
High	568 (20.0)	458 (80.0)	110 (20.0)		394 (69.3)	174 (30.7)		533 (93.7)	35 (6.3)	
Family system										
No problem	574 (20.3)	510 (88.4)	64 (11.6)	< 0.001	474 (83.6)	100 (16.4)	< 0.001	560 (97.8)	14 (2.2)	< 0.001
Low	1676 (60.0)	1352 (80.2)	324 (19.8)		1083 (63.9)	593 (36.1)		1570 (93.6)	106 (6.5)	
High	566 (19.7)	398 (69.8)	168 (30.2)		275 (49.0)	291 (51.0)		495 (87.2)	71 (12.8)	
School adjustment										
No problem	824 (29.3)	747 (90.2)	77 (9.8)	0.001	659 (80.1)	165 (19.9)	< 0.001	805 (98.1)	19 (1.9)	< 0.001
Low	1425 (50.7)	1161 (81.1)	264 (18.9)		946 (66.2)	479 (33.8)		1364 (95.5)	61 (4.5)	
High	567 (20.0)	352 (61.2)	215 (38.8)		227 (39.7)	340 (60.3)		456 (80.1)	111 (19.9)	
Peer relationship										
No problem	596 (21.4)	543 (91.2)	53 (8.8)	< 0.001	481 (81.3)	115 (18.7)	< 0.001	592 (99.3)	4 (0.7)	< 0.001
Low	1656 (58.5)	1340 (80.3)	316 (19.7)		1089 (65.5)	567 (34.5)		1581 (95.5)	75 (4.5)	
High	564 (20.1)	377 (66.3)	187 (33.7)		262 (46.2)	302 (53.8)		452 (79.8)	112 (20.2)	
Leisure/recreation										
No problem	573 (19.9)	511 (88.6)	62 (11.4)	< 0.001	452 (80.3)	121 (19.7)	< 0.001	560 (98.3)	13 (1.7)	< 0.001
Low	1677 (60.2)	1362 (80.6)	315 (19.4)		1112 (65.8)	565 (34.2)		1571 (93.4)	106 (6.7)	
High	566 (19.9)	387 (68.4)	179 (31.6)		268 (47.2)	298 (52.8)		494 (87.5)	72 (12.5)	

one in four (24%) had used tobacco at some time more than a year before. Also, more than half (57.0%) stated they had never gotten drunk, one third (35.0%) had experienced it in the past year, and an additional 8% had gotten drunk at some time more than a year before. In total, 7.5% of the students reported to have used marijuana on at least one occasion, and 4.4% had used it in the past year. A similar proportion of students had a history of cocaine use, and 4.8% had used in the past year. Although there can be much overlapping between marijuana and cocaine use, it is important to note that close to one in 15 students

(6.8%) had ever used an illegal drug, the majority of them within the past year.

Table 2 provides data on sample characteristics and rates of past year use of tobacco, alcohol, and illicit drugs based on age, sex, working status, and DUSI domains. The age range of the participants was 14 to 22 years, and most (83.7%) were 16 years of age or older; 52% were female, and 48% were male. About a third of the students (30.5%) had a part-time or full-time job. The overall percentage distribution of students by DUSI-problem area score conformed to the expected 20% for the top scores (high problem),

Table 3 Association of past year tobacco, alcohol, illicit drug use and drug use screening inventory-RM domains among high school students in the State of Jalisco, Mexico (*n* = 2816)

Variables	Past year smoking				Past year alcohol use				Past year illicit drug use			
	aOR	95%CI		P value	aOR	95%CI		P value	aOR	95%CI		P value
Age (yr)												
>16	1.00				1.00				1.00			
≤ 16	0.94	0.70	1.24	0.628	0.56	0.46	0.69	< 0.001	0.56	0.34	0.90	0.020
Gender												
Female	1.00				1.00				1.00			
Male	1.26	0.93	1.72	0.127	1.61	1.36	1.91	< 0.001	2.28	1.44	3.61	0.001
Employment												
Not working	1.00				1.00				1.00			
Employed	1.14	0.83	1.56	0.412	0.81	0.66	1.01	0.058	1.03	0.73	1.46	0.870
Behavioral pattern												
No problem	1.00				1.00				1.00			
Low	1.63	1.21	2.19	0.002	1.43	1.09	1.88	0.012	2.04	1.03	4.02	0.040
High	2.62	1.91	3.59	< 0.001	2.34	1.72	3.18	< 0.001	3.11	1.51	6.40	0.004
Psychiatric disorder												
No problem	1.00				1.00				1.00			
Low	0.79	0.63	0.99	0.045	0.84	0.71	1.01	0.063	0.60	0.24	1.46	0.244
High	0.89	0.66	1.22	0.458	0.88	0.67	1.15	0.329	0.58	0.23	1.45	0.230
Social competence												
No problem	1.00				1.00				1.00			
Low	1.86	1.45	2.40	< 0.001	1.83	1.47	2.27	< 0.001	1.65	1.09	2.49	0.019
High	3.00	2.26	3.98	< 0.001	2.40	1.87	3.06	< 0.001	2.93	1.53	5.65	0.003
Family system												
No problem	1.00				1.00				1.00			
Low	1.23	0.91	1.65	0.168	2.01	1.60	2.53	< 0.001	1.70	0.91	3.16	0.092
High	1.53	1.04	2.24	0.031	2.75	2.16	3.50	< 0.001	2.29	1.29	4.06	0.007
School adjustment												
No problem	1.00				1.00				1.00			
Low	1.80	1.18	2.74	0.008	1.57	1.18	2.10	0.004	1.54	0.63	3.78	0.326
High	3.51	2.25	5.45	< 0.001	3.25	2.30	4.58	< 0.001	4.77	1.65	13.78	0.006
Peer relationship												
No problem	1.00				1.00				1.00			
Low	1.90	1.41	2.56	< 0.001	1.54	1.19	1.99	0.002	3.82	1.09	13.43	0.038
High	2.47	1.70	3.61	< 0.001	2.01	1.49	2.71	< 0.001	11.53	2.80	47.44	0.002
Leisure/recreation												
No problem	1.00				1.00				1.00			
Low	1.37	0.89	2.12	0.140	1.53	1.22	1.92	0.001	2.35	1.17	4.70	0.018
High	1.72	1.15	2.59	0.011	2.12	1.48	3.05	< 0.001	2.43	1.21	4.87	0.015

All estimates were obtained accommodating the complex sample design. aOR: Adjusted odds ratio.

50%-60% for those with intermediate scores (low problem) and 20% for those with the lowest scores (no problem level).

Results of the bivariate analyses for smoking tobacco in the past year are presented in columns 3 to 5 of Table 2. No statistically significant difference was observed based on age, but the rate was higher among males compared to females (24.5% vs 16.3% respectively; $P < 0.001$), and among youth who studied and worked, compared to those who did not (24.1% vs 18.5%, respectively; $P < 0.02$). The rate of smoking in the past year was also higher in the student population with the top 20% scores in DUSI problem areas compared to those with lower scores ($P < 0.001$).

As presented in columns 6 to 8 of Table 2, an estimated 35% of the students reported alcohol consumption within the past-year, and the rate was higher among older students (those 16 and older, 37.2%), males (42.4%), and those with higher DUSI

scores, except the "Social Competence" domain.

Results in terms of illegal drug use (mainly marijuana or cocaine) are summarized in the last three columns of Table 2. The overall prevalence of past-year illegal drug use (mainly marijuana or cocaine), was 6.8%. Similar to tobacco and alcohol use, the prevalence of illicit drug use was higher in older students compared to younger students (7.5% vs 3.7%, respectively, $P = 0.005$). The rates were also higher among males compared to their female counterparts (10.7% vs 3.2%, respectively, $P < 0.001$), those who worked and studied compared to those who did not (9.3% vs 5.8 %, respectively, $P < 0.001$), and those with higher DUSI scores ($P < 0.001$) in most problem areas.

Multivariate analyses were conducted to examine the association between different DUSI domains with past year tobacco, alcohol, and drug use while controlling for participants' socio-demographic characteristics. Table 3 summarizes the results,

including adjusted odds ratios (aOR) and 95%CI.

Past year tobacco use showed no statistically significant association with age, gender, or employment status. However, the odds were higher among students who had the top 20% scores in the DUSI problem areas, specifically on “*Behavioral Pattern*” (aOR = 2.62); “*Social Competence*” (aOR = 3.00); “*Family System*” (aOR = 1.53); “*School Adjustment*” (aOR = 3.51); “*Peer Relationships*” (aOR = 2.47) and “*Leisure/Recreation*” (aOR = 1.72) (Table 3). An association with tobacco smoking in the past year was also observed for the group with intermediate scores (*i.e.*, the 20-80 percentiles grouped together) in certain DUSI problem areas, such as “*Behavioral Patterns*” (aOR = 1.63); “*Social Competence*” (aOR = 1.86); “*School Adjustment*” (aOR = 1.80); and “*Peer Relationships*” (aOR = 1.90). On the other hand, an inverse association was observed between smoking in the past year and the students with top 20% scores on the “*Psychiatric Disorder*” domain (aOR = 0.89).

In terms of binge drinking in the past year, students who were 16 years and younger had about half the odds compared to older students (aOR = 0.56; 95%CI: 0.46-0.69; $P < 0.001$), and odds were higher in males than females (aOR = 1.61; 95%CI: 1.36-1.91; $P < 0.001$) (Table 3). Those employed had lower odds of alcohol consumption during the past year, albeit with borderline statistical significance (aOR = 0.81; 95%CI: 0.66-1.01; $P = 0.058$). The odds were also higher for students with the highest scores in the DUSI problem areas. Students who had the top 20% of scores on most DUSI domains had consistently higher odds of alcohol consumption in the past year compared to those in the lowest 20%; the domains included “*Behavioral Pattern*” (aOR = 2.34); “*Social Competence*” (aOR = 2.40); “*Family System*” (aOR = 2.75), “*School Adjustment*” (aOR = 3.25), “*Peer Relationships*” (aOR = 2.01), and “*Leisure/Recreation*” (aOR = 2.12). With somewhat attenuated associations, participants who scored within higher than 20% and lower than 80% in most domains, had higher odds of past year’s alcohol use compared to those who scored within the bottom 20%. For example, for students with intermediate scores in “*Behavioral Pattern*”, the odds of past year drinking were about 1.5 times higher (aOR = 1.43; 95%CI: 1.09-1.88; $P = 0.012$), and so forth.

The last three columns of Table 3 convey the estimated association between past-year illegal drug use and DUSI psychosocial covariates, adjusted for all variables shown in the table. Younger students had lower odds of drug use than older students (aOR = 0.56; 95%CI: 0.34-0.90; $P = 0.02$). Males were estimated to have twice the odds of past-year drug use than females (aOR = 2.28; 95%CI: 1.44-3.61; $P = 0.001$). Most DUSI problem areas showed that students with higher scores had higher odds of illegal drug use than those with lower scores; these domains included “*Behavioral Patterns*” (aOR = 3.11; 95%CI: 1.51-6.40; $P = 0.004$); “*Social Competence*” (aOR =

2.93; 95%CI: 1.53-5.65; $P = 0.003$); “*Family System*” (aOR = 2.29; 95%CI: 1.29-4.06; $P = 0.007$); “*School Adjustment*” (aOR = 4.77; 95%CI: 1.65-13.78; $P = 0.006$); “*Peer Relationships*” (aOR = 11.53; 95%CI: 2.80-47.44; $P = 0.002$); and “*Leisure/Recreation*” (aOR = 2.43; 95%CI: 1.21-4.87; $P = 0.015$).

DISCUSSION

The DUSI has been used to measure the severity of problems in 10 different domains to allow identification of drug use problem areas and their relationship with psycho-social adjustment^[13,18]. The main findings of the present study demonstrate higher rates of tobacco (20.2%), alcohol (35%), and illegal drug use (6.8%) among high school adolescents in Jalisco, Mexico, compared to national rates reported by the ENA in 2002 (10.1%, 25.7%, and 4.6%, respectively), 2008 (alcohol 26.6%, illegal drugs 5.2%), and in 2012 (16%, 14.5%, and 1.6, respectively)^[1,2,19]. Compared to studies conducted in Mexico city with a similar research design to the present study, our findings are similar to those reported for tobacco (22.8%), alcohol (35.2%), and marijuana (3.95%) in high school students^[20]. The lifetime rate of cocaine use was higher than expected in this population (7.5%) and higher than the 1.6%-4.0% rates in comparable Mexico City surveys^[20,21]. This higher rate of cocaine use may indicate that the epidemiologic situation is changing and new patterns of drug use in Mexico are rising, which may be creating new treatment needs and complexities. The high combined rates of marijuana and cocaine use demonstrate a critical problem with illegal drug use in Jalisco’s high schools, which add to the already high rate of binge drinking in this population.

There has been an increasing trend in drug use in Mexico^[3,22]. Reasons for this increase may be multi-factorial including the transition from a mainly trafficking country to a user country^[21,23,24], as well as the increased use of addictive “legal” substances, such as alcohol and tobacco, by youth. Therefore, it is important to understand the psychological and socio-demographic profile of youth at risk of developing substance use disorder in order to propose and develop effective local treatment and prevention interventions.

In this study, older age was significantly associated with past year use of alcohol, which is consistent with other studies^[25-28]. This may mean that older students in Jalisco also face a higher risk of alcohol-related consequences (*e.g.*, aggression, unprotected sexual activities, *etc.*) compared to younger students^[21,28]. Smoking among young people in Mexico increased from 10.1% in 2002 to 14.9% in 2008, and to 16% in 2012^[1,2,19]. This evidence calls for targeted school-based preventive interventions, along with better enforcement of regulatory measures, which has been recognized as a weak point in public health

policy^[30]. The results showed no age differences in the past year use of tobacco. This is problematic because it may be due to one or a combination of the following possibilities: (1) Youths are experimenting tobacco at younger ages; (2) those who initiate may be transitioning faster to regular tobacco use; (3) starting younger students may be finding it harder to quit. Each of these possibilities would require further investigation. In addition, it is important to note that these students are still within the age range with highest risk for experimenting or becoming a regular tobacco user, which highlights the importance of prevention and cessation interventions^[31].

Gender was found to be an important factor associated with higher odds of alcohol and illegal drug use, but not the use of tobacco products (Table 3), which is not consistent with findings from other studies^[26,27,32,33]. Replication of these findings and future research is needed to understand if there have been changes in cultural norms that have protected women from being exposed to opportunities to use tobacco (and other drugs)^[34,35].

The psychosocial factors explored in this study were found to be associated with the outcome measures in most of the domains. The predictive values and validity of the DUSI have been well documented in prior reports^[13,18,36,37]. Consistent with other research, higher scores in the subscale measuring problems of *Behavior Pattern* (aggressiveness and impulsivity) were found to be associated with substance use and could serve as a tool for screening, early detection, and intervention design^[26,27,38-41]. Higher scores in the subscale of *Psychiatric Disorders* were also associated with drug involvement. The utility of the DUSI for implicating current psychiatric diagnosis in adolescents has been demonstrated^[42]. In prior research, individuals with behavior and affection problems were estimated to be at a greater risk of using illegal drugs^[32,38,39]. In the present study, the bivariate analyses showed an association between "*Psychiatric disorders*" and both past-year smoking and alcohol use, but even with this large sample size, the study lacked sufficient statistical power to detect associations with past-year substance abuse. We could not find a significant association between this domain and past year use of any substances in the multivariate analyses either, but this could be due to the strong correlation between psychiatric disorders and the other DUSI domains simultaneously controlled for in the analysis, in addition to the relatively low statistical power. Of note is that there may be a misclassification of problem substance use disorders for up to 28% of the cases, which may as well bias the estimates towards the null hypothesis^[13]. Another explanation could be related to neurobehavioral disinhibition as explained by indicators of executive cognitive functioning, emotion regulation, and behavior control^[43], which we did not explore in this study. It has also been reported that the correlates from the psychiatric domain have not been able to

differentiate between experimenters and users^[44], which could be another possibility in our study.

Nevertheless, the findings highlight the importance of detecting mental health problems earlier and referring cases for specialized care^[26]. In this study, consistent with previous research, problems with "*Family System*" were associated with higher odds of using tobacco, alcohol, and illegal drugs. Family factors have been demonstrated to influence drug and substance use particularly at younger ages^[27]. Family issues are major risk factors to the overall health among children and adolescents, and they include parental adjustment problems, inadequate parental communication and affection, negative family interaction patterns, and poor relationship or weak parent-child bonding^[26,38-41]. On the other hand, family factors such as family attention, parental monitoring, and living in a two-parent household can also act as resilient factors^[25,32,45]. The subscale on "*Social Competence*" measures problems in areas such as social skills, assertiveness, and social interaction. In this study, participants with the highest scores in "*Social competence*" problems had higher odds of substance use. However, the opposite has also been observed by other researchers: those with stronger social competence skills had lower risks of alcohol use^[40]. These factors are important internal resources and can inform preventive interventions that specifically support those students in greater need.

The relationship between the use of substances such as tobacco products, alcohol, and illegal drugs and health problems is well documented^[26,46]. Tobacco is the leading cause of death globally, killing almost 480000 individuals every year in the United States alone^[47]. There is evidence of higher likelihood of disease and more severe addiction among those with early initiation of substance use^[25,28,38]. Programs that include school-based interventions have been shown to reduce tobacco use amongst youths and subsequently decrease the burden of diseases^[48]. Using alcohol and illegal drugs have severe social implications as well, including violence, absenteeism, poor academic performance, crime, and family disruptions^[16,38,39,49]. The social consequences increase with the level of abuse and addiction^[50,51]. Therefore, early identification and treatment of students with substance abuse will have greater impact on the individual lives, families, schools, and society. Control and prevention of drug use could be achieved using standardized screening instruments to identify those students with treatment needs and those with higher risk of getting involved with substances, followed by school-based interventions^[52]. However, interventions should be coordinated among different providers such as the National Prevention Program based on Clinics for the Attention and Prevention of Addictions and other organizations like the education department with its *Safe School* program^[53], in close collaboration with families and the surrounding community. Finally,

environmental interventions have proven to be very effective in reducing the risk of substance use. Some examples include enforcing age restrictions for sale and consumption to limit the access to and reduce the use of alcohol and tobacco products among high school students and correcting the exaggerated perception of normative values for using substances by peers^[54] to mention a few. Intervening through social networks, especially in partnership with student leaders, may be a promising approach in promoting healthy behaviors by influencing the social norms and reducing peer pressure in high schools^[55].

Mexico is a large and populous country, and there are stark regional differences (*i.e.*, North, Central, and South). Those differences are particularly evident in terms of the epidemiology and prevalence of drug use. Jalisco is one of the largest and most resourceful states in Mexico, but generalizing the results from the present study to other States should be done with caution. Another limitation of this study is that we only included youths at school, and there is an important segment of the youth population with no school access or attendance. Also, we are aware of the limitations of a cross-sectional study in terms of looking at "risk factors" as opposed to a longitudinal study. Nevertheless, data for the present analyses come from the first survey on drug use in the State of Jalisco in the 21st century, which used a probability sampling and is representative of the high school population of the State of Jalisco. The data were collected using a standardized questionnaire that was adapted and tested for the Mexican population. One limitation of this questionnaire (DUSI-RM) is that it asks about the time of use, but it does not measure frequency or the amount of substance use, or in the case of tobacco, the number of cigarettes. It does, however explore the relation of psycho-social factors with drug or substance use.

This study confirms trends of increasing prevalence of alcohol, tobacco, and illegal drug use among Mexican youths, with new patterns of drug use in Jalisco that may be creating new treatment needs. Drug use problems in Jalisco may be becoming more complex, requiring a set of prevention alternatives and control programs (as opposed to a one-fits-all approach). Appropriate interventions for both legal and illegal substances should be planned and executed accordingly. New prevention efforts are urgently needed to target youth at the early stages of drug use to stop or delay their further involvement. This is a new need as the proportion of new users is increasing.

ARTICLE HIGHLIGHTS

Research background

We sought to improve on the few existing studies about drug and substance abuse among high school students in Jalisco, Mexico; particularly its association with health, behavior and psychosocial problems in order to provide evidence for possible prevention and treatment needs. Jalisco is an important

state in Mexico for its strategic geo-politic location as a narcotic production enclave and a route for drug trafficking directed to the United States, and also because it is a large contributor of documented and undocumented workers to that country. The socio-economic change from a from a production entity to a consumer one could be taking place.

Research motivation

There has not been a published regional or state drug abuse survey performed in Jalisco, a state in the West Central Region of Mexico, for more than a decade. The most recent available information comes from the Mexican National Survey. However, the figures may not apply directly to Jalisco given the significant heterogeneity within this particular region on the one hand and on the other, because of the limitations of the methodology utilized for the national surveys: household and, most frequently, indirect interviews.

Research objectives

The aim objectives were to investigate the prevalence of substance use and associated factors amongst high school students from the Mexican West-Central State of Jalisco, to explore the association between drug involvement and selected psychosocial factors, and to identify treatment and prevention needs.

Research methods

We designed a cross-sectional survey using a multi-stage, random sample of 2832 high school students, from 25 public high schools distributed in 10 geo-political sub-regions in the State of Jalisco, Mexico. The participants were given a paper-and-pencil survey based upon an adapted version of the drug use screening inventory (DUSI-RM). The DUSI showed adequate psychometric characteristics in this population. The statistical tests included multivariate analyses with logistic regression models to estimate the association of each DUSI-RM domain with the use of tobacco, alcohol, as well as marijuana and cocaine use, while controlling for age, sex, and socio-economic status. The analyses were done with STATA version 10.0 (STATA Corp, College Station, TX, United States).

Research results

An estimated 44% of the students had smoked tobacco and 35% of the students reported alcohol consumption within the past-year. The rate of alcohol use was higher among older students, males, and those with higher DUSI scores. By contrast, 6.8% of the students reported having used marijuana, cocaine, or both. Of all 10 DUSI domains behavioral problems, deviant peer affiliation, and troubled families were independently associated with drug use.

Research conclusions

The main findings of the present study demonstrate higher rates of tobacco, alcohol, and illegal drug use among high school students in Jalisco, Mexico, compared to national rates although similar to those reported for tobacco, alcohol, and marijuana in México city, the largest city in the country. Appropriate interventions for the use of both legal and illegal substances in young people should be planned and executed accordingly. New prevention efforts are urgently needed to target youth at the early stages of drug use to stop or delay their further involvement. These results suggest that there is an epidemiological transition in the prevalence and patterns of drug use in the state of Jalisco which could be influenced by geographical and economical factors like the local production of legal (alcohol) and illegal drugs (marijuana and methamphetamines). This is the first study representative of the West Central area in Mexico. These data corroborate national trends of increased prevalence of illegal drug use and, in some cases (cocaine), even higher rates. The results however, are similar to those from studies conducted in Mexico city, the largest city in the country. Some areas of the country, like Jalisco, may be changing from a predominantly productive area to a mixed productive-consumer area. We conducted a study in an area with a relatively high production of illegal drugs (marijuana and synthetic drugs) and obtained results of higher use rates than the national surveys and comparable to those obtained in the largest urban area of the country (Mexico city). Similar studies should be conducted in other high and low production areas to investigate the influence of production factors on drug use prevalence. With this study we could confirm the hypothesis that the prevalence of drug use in the State of Jalisco was higher than that reported

in national surveys. One of the reasons for those differences could be in the methods employed: confidential direct anonymous questionnaires in this case compared to home indirect interviews in the national surveys. The methodology used for designing and conducting drug and substance use national surveys should be improved.

Research perspectives

We suggest that epidemiological studies by independent researchers with up-to-date methodology, similar to the one presented herein should be conducted in other Mexican states independently from official national surveys.

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Observational Study

Bullying among people with visual impairment: Prevalence, associated factors and relationship to self-efficacy and life satisfaction

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Informed consent statement: All participants gave their informed consent to take part in the study.

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to the informed consent given by each respondent, the data is to be stored properly and in line with the Norwegian Law of Privacy Protection. However, anonymized data is available to researchers who provide a methodological sound proposal in accordance with the informed consent of the respondents. Interested researchers can contact project leader Trond Heir (trond.heir@medisin.uio.no) with request for our study data.

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Abstract

AIM

To examine associated factors of bullying and to determine associations between bullying and psychosocial outcomes among individuals with visual impairments (VI).

METHODS

We conducted an age-stratified cross-sectional survey of adults with VI who were recruited from the Norwegian Association of the Blind and Partially Sighted. Data were collected through structural telephone interviews in the period between February and May, 2017. Linear regression models were used to examine factors related to bullying and associations of bullying with self-efficacy and life satisfaction.

RESULTS

A total of 736 individuals were interviewed. The lifetime and 6-mo prevalence of bullying was 41.7% and 8.2%, respectively. The majority of bullied participants reported VI-specific bullying (65.1%). Victimization of bullying was associated with young age, early onset-age of VI, and having other impairments. Participants who reported bullying had lower levels of self-efficacy [Adjusted relative risk (ARR): 0.40, 95% confidence interval (CI): 0.19-0.85] and life satisfaction (ARR: 0.68, 95%CI: 0.51-0.91).

CONCLUSION

Bullying is highly prevalent among individuals with VI. Our findings suggest that interventions to reduce bullying may be beneficial for improving the well-being and life quality of people with VI.

Key words: Blindness; Bullying; Life satisfaction; Risk factors; Self-efficacy; Victim; Visual impairment

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Core tip: People with impairments are at risk of social exclusion. A high rate of bullying of people with visual impairment (VI) demonstrates how deviations from the social norm can lead to sanctions from the environment. The more different, the higher the risk of bullying, illustrated by the fact that people with functional impairments in addition to VI were even more prone to bullying. For those who are victimized, the consequences may be serious in terms of lower self-esteem and lower quality of life. A continuous focus on bullying is necessary to protect people with VI from bullying.

Brunes A, Nielsen MB, Heir T. Bullying among people with visual impairment: Prevalence, associated factors and relationship to self-efficacy and life satisfaction. *World J Psychiatr* 2018; 8(1): 43-50 Available from: URL: <http://www.wjgnet.com/2220-3206/full/v8/i1/43.htm> DOI: <http://dx.doi.org/10.5498/wjp.v8.i1.43>

INTRODUCTION

Bullying represents an extreme form of systematic and enduring social alienation which is assumed to exceed the boundaries of other forms of interpersonal

aggression such as incivility, social undermining, and verbal abuse^[1]. Formally, bullying is defined as a situation in which one or several individuals persistently and over a period of time, perceives to be on the receiving end of negative actions from another person and where the target of the bullying finds it difficult to defend him/herself against these actions^[2]. Although there is no definitive list of bullying behaviors, bullying may involve actions like harmful physical contact, verbal harassment, rumour spreading, and intentionally excluding a person from a group^[3]. In many cases, it is the accumulated exposure that constitutes the threat, not the specific behaviours.

Research on bullying has mainly been conducted in school and working life. Based on data from a large cross-national study, the percentage of 11 to 15 year old children who reported bullying at least once in the past 2 mo was 29%, ranging from 8% to 60% across the European countries^[4]. Research on bullying among adults has mainly been restricted to working life. A meta-analysis on the occurrence of workplace bullying showed that 11% to 18% of employees on a global basis perceived themselves as victims of bullying^[5]. Depending on measurement method, a 6-mo prevalence between 2% and 14% has been established among a representative sample of Norwegian employees^[6]. As most studies on prevalence have examined bullying within a six to 12 mo timeframe, there is a shortage of studies on lifetime prevalence of bullying.

Bullying may have considerable impact on the health and well-being for those being affected, including a higher risk of anxiety^[7-9], depression^[8,9], suicidal ideation^[9,10], headache^[9,11], and sleep problems^[9,12,13]. In a meta-analysis it was found that exposure to bullying predicted subsequent increase in mental health complaints (OR = 1.68; 95%CI: 1.35-2.09) and somatic complaints (OR = 1.77; 95%CI: 1.41-2.22) after adjusting for baseline health status^[14]. Insufficient evidence exists of bullying in its association with life satisfaction and psychosocial functions like self-esteem^[7,9,15].

Persons with impairments, such as visual impairment (VI), are more likely to be seen as different and of lower social rank by peers, and therefore become trapped into an ongoing victimization of bullying. In a meta-analysis of 7 studies involving people with VI, Pinquart^[16] showed that children with VI had an 80% greater risk of experiencing peer victimization compared with sighted children. However, VI is a heterogeneous condition in terms of cause, onset-age, and progression rate of the vision loss^[17], and is usually classified into moderate VI, severe VI, blindness, and unspecific VI^[18]. Since the previous studies have assessed only a few VI-related (e.g., wearing eye patches) and non-VI related factors^[19-21], more research is needed to determine whether some forms of VI are more strongly associated with bullying than others.

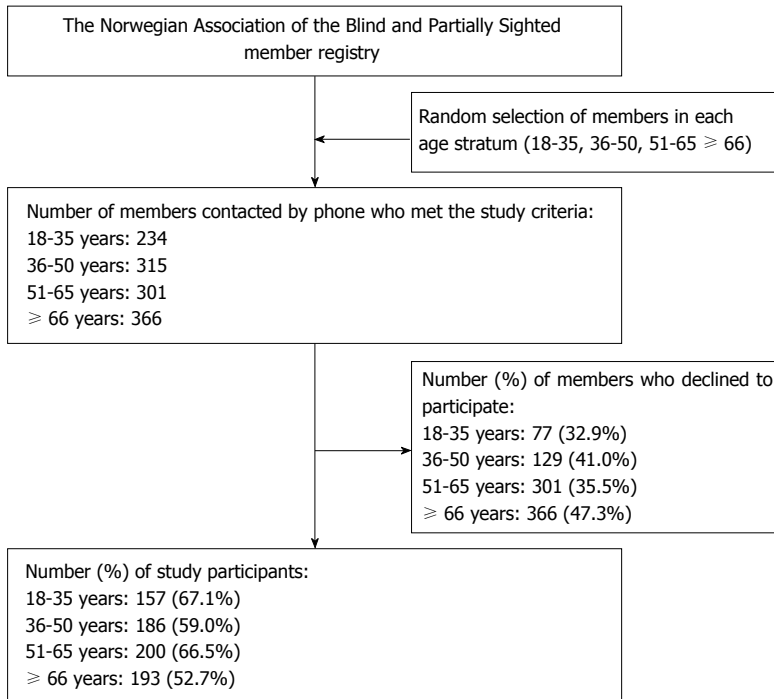


Figure 1 Selection of study participants.

To our knowledge, the possible consequences of bullying among people with VI have been assessed in two studies^[21,22], and both studies included convenience samples of children or adolescents. Consequently, the impact of bullying on the health and functioning in adult life remains to be studied. In order to add to the current knowledge, this cross-sectional study examined prevalence, associated factors, and psychosocial outcomes of bullying using a large age-stratified, probability sample of adults with VI. The study had the following three aims: (1) To study the prevalence of bullying; (2) to describe demographic and visual factors associated with lifetime bullying; and (3) to examine the association of lifetime bullying with self-efficacy and life satisfaction.

MATERIALS AND METHODS

Ethical considerations

The study was carried out anonymously and at request the Regional Committee for Medical and Health Research Ethics required no further formal ethical approval (Reference number: 2016/1615A). All participants gave their informed consent for taking part in the study. Study participation was voluntarily, and the participants were informed that they could withdraw from the study at any time.

Design and participants

This cross-sectional observational study included a sample of adults who were members of the Norwegian Association of the Blind and Partially Sighted. The organization has about 10000 members^[23], which

comprise 0.2% of the Norwegian population. Adults were eligible if they were aged ≥ 18 years and reporting a degree of VI. Data were collected *via* telephone interviews in the period between February and May, 2017. The interviews were carried out by experienced interviewers hired at a private survey company. The structured interview guide included questions about the participants' sociodemographic characteristics, type and nature of VI, bullying, and various aspects of quality of life. To ensure inclusion of participants at all age groups, a random sampling technique was performed within each of the following age strata: 18-35, 36-50, 51-65, and ≥ 66 . A total of 1216 adults with VI were contacted, and 736 (61%) participated by completing the interview. The response rate for each age group is displayed in Figure 1.

Assessment and evaluation

Bullying: Victimization from bullying was assessed by a single-item question retrieved from the General Nordic Questionnaire for Psychological and Social Factors at Work^[24]. This self-labelling approach has been considered a valid measurement of bullying^[25]. Before being presented to the question, the following definition of bullying were given to the participant: "To label something bullying or harassment, the offensive behaviour has to occur repeatedly over a period of time, and the person confronted has to experience difficulties defending himself/herself." Lifetime bullying was assessed through asking the participants whether they have been subjected to any bullying or harassment. The response alternatives were "yes" and "no". Those who responded "yes" to the question about

bullying were then asked to report whether they had been victims to bullying in the past 6 mo and whether the bullying was targeted towards their VI.

Self-efficacy: The participants' general perception of self-efficacy was measured by the General Self Efficacy Scale (GSE scale). The Norwegian version of the GSE scale has been shown to have a high test-retest reliability ($r = 0.82$) and acceptable correlations with life satisfaction ($r = 0.26$) and positive affect ($r = 0.40$)^[26]. The scale consists of 10 statements about the participant's belief in one's ability to adequately respond to novel or challenging situations and to cope with a variety of stressors, and is scored on a 4-point Likert scale from 1 (not at all true) to 4 (exactly true). A sum score was calculated based on all 10 items, with higher scores representing greater self-efficacy. The sum score was treated as an untransformed continuous variable in our main analyses. The GSE scale had a Chronbach's alpha of 0.89.

Life satisfaction: Cantril's Ladder of Life Satisfaction (CLLS) was used to measure current life satisfaction^[27]. The participants were asked to imagine themselves a ladder with 10 steps, of which the bottom of the ladder represented the worst possible life for them (a score of 0) and the top of the ladder represented the best possible life for them (a score of 10). Life satisfaction was treated as an untransformed continuous variable in the main analyses.

Covariates: The following covariates were identified as relevant in the current study: Gender, age (18-35, 36-50, 51-65, ≥ 66), current education level (< 10 years, 10-13 years, ≥ 14 years), marital status (single, married/partner, former married/partner), parental ethnicity (Norwegian, non-Norwegian), working or studying (no, yes, retired), urbanicity (< 50000 inhabitants, ≥ 50000 inhabitants), having other impairments (no, yes), severity of VI (moderate VI or other types of VI, severe VI, blindness), onset-age of VI (since birth, 1-24 years, ≥ 25 years), and VI stability (progressive, stable).

Statistical analysis

We tabulated lifetime and 6-mo prevalence of bullying with corresponding 95% binomial confidence intervals (CIs). Associated demographic and visual factors of past bullying experiences were assessed by using generalized linear models (GLMs) with a binomial distribution and log-link function. We selected a few important covariates prior to the analyses (age, gender, and severity of VI), as well as covariates having the best fit to the data in terms of Akaike's Information Criterion^[28].

GLMs with a Gaussian distribution and identity-link function were used to estimate mean scores of self-efficacy and life satisfaction among individuals who had experienced bullying compared with the

referent category of individuals not being bullied. The choice of distribution was determined by searching for the model that fitted the data best in terms of log-likelihood. The selection of possible confounding factors was based on previous publications and a priori reasoning^[12,16,19,21,29-31]. In order to produce better confidence limits^[28], we bootstrapped the CI estimates with 10000 replacements and a variance adjustment of 1.

A supplementary analysis was conducted of the association between bullying and self-efficacy and life satisfaction by using binomial GLM in order to check whether the choice of statistical model influenced our findings. In this analysis, all outcomes were dichotomized by its median value.

All regression analyses were either univariable or multivariable. The results were presented in terms of relative risks (RRs) and corresponding 95%CIs. The significance level was set at $P = 0.05$. The statistical analyses were carried out using Stata Version 14 (Stata Corp., Texas, United States).

RESULTS

Table 1 shows the characteristics of the study population. The lifetime prevalence of bullying was 41.7% (95%CI: 38.1-45.3) and the 6-mo prevalence of bullying was 8.2% (95%CI: 6.3-10.4). The majority of participants being bullied reported that the bullying experience was partly or completely related to their visual impairment (65.1%).

Associated factors of previous bullying experiences are presented in Table 2. In the univariable analyses, a significantly higher risk of bullying was found among participants with a lower age, having other impairments, having severe VI or blindness, and the onset of VI occurring early in life. All covariates, except for VI severity and residence, remained statistically significant in the multivariable models. The two strongest associated factors were lower age and early onset-age of VI. Bullying was not related to gender, parental ethnicity, or VI stability.

As shown in Table 3, compared with those not being bullied, individuals with past experiences of bullying had significantly lower scores on self-efficacy and life satisfaction. The strength of the associations remained fairly similar after adjusting for gender, age, current education level, working or studying, other impairments, marital status, severity of VI. The findings from the supplementary analysis showed that the association of bullying with self-esteem and life satisfaction became weaker, but remained statistically significant, in the binomial GLMs compared with the Gaussian GLMs (results not shown).

DISCUSSION

Key findings

Data from this cross-sectional study showed that four

Table 1 Study characteristics (n = 736)

Characteristics	n (%)
Age (yr)	
18-35	157 (21.3)
36-50	186 (25.3)
51-65	200 (27.2)
≥ 66	193 (26.2)
Gender	
Male	333 (45.2)
Female	403 (54.8)
Marital status	
Single	260 (35.3)
Married/partner	347 (47.2)
Former married/partner	129 (17.5)
Working or studying	
No	248 (33.7)
Yes	295 (40.1)
Retired	193 (26.2)
Urbanicity	
< 50000 inhabitants	400 (54.4)
≥ 50000 inhabitants	336 (45.7)
Parental ethnicity	
Norwegian	645 (87.6)
Non-Norwegian	91 (12.4)
Education	
< 10 yr	115 (15.6)
10-13 yr	286 (38.9)
≥ 14 yr	335 (45.5)
Age at VI onset	
Since birth	329 (44.7)
Childhood or youth (1-24 yr)	143 (19.4)
Adulthood (≥ 25 yr)	264 (35.9)
VI severity	
Moderate VI/other	186 (25.3)
Severe VI	296 (40.2)
Blindness	254 (34.5)
Stability of VI	
Progressive	231 (28.9)
Stable	523 (71.1)
Other impairments	
No	478 (65.0)
Yes	258 (35.0)

in ten Norwegian individuals with VI have experienced bullying, one in ten have experienced bullying during the past 6 mo, and more than sixty percent of those who have been bullied said that bullying was related to their VI. Bullying was associated with young age, early onset-age of VI, and having other impairments. Those who had experienced bullying had lower levels of self-efficacy and life satisfaction compared with those who had not experienced bullying.

Comparison with the literature

To our knowledge, this is the first study with a nationwide probability sampling addressing the prevalence and associated factors of bullying among individuals with VI, as well as the relation of bullying with well-being. Our findings demonstrate that bullying is frequent and potentially detrimental problem among people with VI, showing somewhat higher 6-mo prevalence rates than what have been found in comparable studies of general Scandinavian populations (2.8%-8.2%)^[6,32-34].

Thus, our results are in agreement with previous research suggesting that VI is a risk factor for bullying^[16].

The findings that early onset-age of VI, young age, and having additional impairments were associated with the risk of being bullied support the notion that childhood and young adulthood are vulnerable periods in life for persons with some sort of deviance from the social norm^[35,36] and that having additional impairments may reinforce those differences.

Some of the non-significant covariates need to be discussed. A noteworthy finding of this study was that the occurrence of bullying was similar for women and men with VI. This is in line with previous research^[19,20], and indicates that the risk of bullying following VI is not determined by gender.

The lack of association between severity of vision loss and the occurrence of bullying are not in line with the findings from previous research^[19,21]. For example, in an age-matched sample of 196 German students, Pinquart and Pfeiffer^[21] found that students with low vision reported on average more relational and overt bullying compared with students who were blind and students without vision loss. As we examined the lifetime prevalence of bullying, a possible explanation for our null findings may be that specific VI characteristics are important risk factors for bullying at different points in life.

Our findings of bullying being associated with poorer life satisfaction are in agreement with that of previous research including people with different impairments^[21,37]. Life satisfaction is a general evaluation of one's own life^[27] and bullying may have negative consequences on a wide-range of life domains^[9]. Furthermore, to our knowledge, this is the first study that have examined the relationship between bullying and general self-efficacy in populations with VI, showing lower levels of self-efficacy for those being bullied compared with those who have not been bullied.

Assuming bullying as a potential causal factor, as well as ignoring the possibilities for residual confounding and reversed effects, there may be several explanatory hypotheses for these relationships. First, models on stress and coping suggest that prolonged exposure to a given stressor, such as bullying, leads to a sustained cognitive activation^[38]. Problems handling this unbearable state of mind may reduce one's belief in coping with challenging situations, and the persistent activation could be subsequently manifested as reductions in well-being and unwanted behavioural reactions like social withdrawal^[7]. Second, the theory of learned helplessness may also explain the associations between bullying and the above indicators of well-being. Learned helplessness is a state of mind that may evolve when exposed to repeated and enduring painful or otherwise aversive stimuli which the targeted person is unable to escape or avoid^[39]. Consequently, a target of bullying who perceives him-/herself to be unable to defend him-/herself against the systematic

Table 2 Univariable and multivariable regression analyses of factors associated with lifetime bullying among individuals with VI (*n* = 736)

Covariates	% of bullying	Univariable RR (95%CI)	Multivariable RR (95%CI)
Age (yr)			
18-35	58.0	2.62 (1.95-3.51)	2.09 (1.53-2.85)
36-50	51.1	2.26 (1.68-3.05)	2.04 (1.51-2.77)
51-65	38.5	1.77 (1.30-2.41)	1.66 (1.12-2.26)
≥ 66	22.8	1.00	1.00
Gender			
Male	38.7	1.00	1.00
Female	44.2	1.14 (0.96-1.36)	1.15 (0.98-1.34)
Parental ethnicity			
Norwegian	41.2	1.00	1.00
Others	45.1	1.09 (0.86-1.40)	1.00 (0.81-1.25)
Urbanicity			
< 50000 inhabitants	46.3	1.00	1.00
≥ 50000 inhabitants	36.3	0.79 (0.66-0.94)	1.01 (0.84-1.21)
Other impairments			
No	38.1	1.00	1.00
Yes	48.5	1.27 (1.07-1.51)	1.35 (1.15-1.57)
Severity of VI			
Blind	41.9	1.19 (0.93-1.50)	1.05 (0.84-1.30)
Severe VI	47.0	1.33 (1.08-1.63)	1.18 (0.97-1.42)
Moderate VI/other	35.4	1.00	1.00
Age at VI onset			
Since birth	52.0	1.91 (1.53-2.38)	1.55 (1.22-1.96)
Childhood or youth (1-24 yr)	44.8	1.64 (1.26-2.15)	1.27 (0.98-1.68)
Adulthood (≥ 25 yr)	27.3	1.00	1.00
VI stability			
Stable	43.0	1.00	1.00
Non-stable	38.5	0.90 (0.74-1.19)	0.92 (0.76-1.11)

RR: Relative risk; VI: Visual impairment.

Table 3 Unadjusted and adjusted regression analyses addressing bullying exposure and its association with self-efficacy and life satisfaction among individuals with VI (*n* = 736)

Lifetime bullying	Mean (SD)	Unadjusted ¹ RR (95%CI)	Adjusted ^{1,2} RR (95%CI)
Self-efficacy			
No (<i>n</i> = 429)	32.0 (4.8)	Reference	Reference
Yes (<i>n</i> = 307)	30.8 (5.4)	0.28	0.41 (0.19-0.87)
Life satisfaction			
No (<i>n</i> = 429)	7.0 (1.9)	Reference	Reference
Yes (<i>n</i> = 307)	6.5 (2.2)	0.60	0.69 (0.52-0.91)

¹CI estimates were bootstrapped with 10000 replications and a variance multiplied by 1; ²Adjusted for gender, age (18-35, 36-50, 51-65, ≥ 66), current education level (< 10 years, 10-13 years, ≥ 14 years), working or studying (no, yes, retired), other impairments (no, yes), marital status (single, married/partner, former married/partner), and severity of VI (moderate VI/other, severe VI, blindness). RR: Risk ratio; SD: Standard deviation; VI: Visual impairment.

mistreatment should be more likely to resign and go into a state of helplessness. A third theory on the consequences of bullying is that of internalization, in which people accepts a belief or behavior and agrees with others both privately and publicly^[40]. For example, when perpetrators repeatedly tell the bully victim that

he/she is useless or unworthy, the victim may in turn accept and personally agree with the public opinion about his/her uselessness or unworthiness.

Strengths and limitations

The main strength of this study is the size and nature of the sample, which was selected through a probability mechanism and stratified on age. Furthermore, the use of validated assessment tools and the data collection procedure increase the credibility of our findings. While these characteristics may represent strengths of the study, it should be noted that studies using probabilistic sampling, including a definition of bullying, and recruiting participants from Scandinavian countries have established the lowest prevalence rates with regard to bullying^[5]. Hence, it is likely that our prevalence is relatively low compared to studies using other methods and samples.

Several limitations should be considered. In resemblance with all observational studies that analyses cross-sectional data, we had limited possibilities to address relationships of cause and effect, and, although we controlled for some potentially confounding factors, we cannot rule out the possibility of residual confounding. Second, the use of self-reports may have affected the accuracy of the estimates, and could lead to information biases like disclosure bias and recall bias. The possible impact of recall bias may have been greatest among the oldest participants, reflecting the low rates of bullying in this age group. Further, our data on bullying relied on a few validated questions about the overall exposure to bullying or harassment. We also lacked information about the perpetrator, as well as information related to how, when, where, and how often the participants had experienced bullying. With regard to the latter, including a behavioural experience checklist such as the Negative Acts Questionnaire^[41] would have provided specific information about the nature and content of the bullying. Third, we had limited information about the non-responders and do not know how non-responding might have influenced our results. Advance information contained general descriptions of topics such as coping with traumatic events, mental health and wellbeing, and did not specifically pinpoint bullying. Thus, we think it is less likely that prevalence estimates of bullying were biased by participations' motivation to share their history of being bullied. Also, we believe that bias in sample selection more likely may have affected the prevalence estimates of socioeconomic factors or VI characteristics and to lesser extent their associations to bullying^[42,43]. Fourth, the generalizability in studies of membership organizations may be questionable. We have no knowledge about how bullying and psychological consequences in people with VI who are not organized in the Norwegian Association of the Blind and Partially Sighted.

Implications

Bullying is a social problem with detrimental implications for the individual being affected. People with VI are at higher risk of bullying compared to the general population, and there should be increased awareness about this issue in school, social, and working life. There may be a need for interventions to prevent bullying, and for those who have been bullied, measures to increase self-efficacy.

In summary, our findings showed that bullying is highly prevalent among individuals with low vision and blindness, and especially among those with a young age, early onset-age of VI, and having other impairments. Furthermore, we found strong associations between lifetime bullying and lower levels of self-efficacy and life satisfaction. Increased awareness of bullying in school, social, and working life is recommended to protect people, and especially people from social minorities, from bullying. Future research should include longitudinal studies, focusing particularly on the risk and impact of bullying among those who have lost their vision at birth or during childhood.

ARTICLE HIGHLIGHTS

Research background

Persons with impairments, such as visual impairment (VI), may be more likely to be seen as different and of lower social rank by peers, and therefore become trapped into an ongoing victimization of bullying. To our knowledge, previous studies of risk of bullying in people with VI are restricted to include convenience samples of children and adolescents.

Research motivation

In order to add to the current knowledge, we conducted a cross-sectional study in the adult population of people with VI, having the following three main aims: (1) To study the lifetime prevalence of bullying, (2) to describe demographic and VI-related factors associated with lifetime bullying, and (3) to examine the association of lifetime bullying with self-efficacy and life satisfaction.

Research methods

The study was a cross-sectional interview-based survey conducted between February and May, 2017, including an age-stratified probability sample of adults with VI. All participants were recruited through the members list of the Norwegian Association of the Blind and Partially Sighted. A total of 736 (61%) adults with VI participated by completing the interview.

Research results

The lifetime and 6-mo prevalence of bullying was 41.7% and 8.2%, respectively. The rates are greater than what have been found in comparable studies of general Scandinavian populations. The majority of bullied participants (65.1%) reported that bullying was related to their vision loss. Victimization of bullying was associated with young age, early onset-age of VI, and having additional impairments. The findings illustrate that being different in terms of having visual impairment or other impairments in addition to the vision loss put individuals at increased risk of being victimized to bullying. Bullying was negatively associated with self-efficacy [adjusted relative risk (ARR): 0.40, 95% confidence interval (CI): 0.19-0.85] and life satisfaction (ARR: 0.68, 95%CI: 0.51-0.91). If bullying was the underlying causal factor, our results suggest that bullying may have profound adverse effects on personality and wellbeing in adult life.

Research conclusions

To our knowledge, this is the first research study demonstrating high rates

of bullying in people with VI, both in a lifetime perspective and in adult life. Individuals with young age, early onset age of VI, or other additional impairments were at greatest risk of bullying. Most of those who had been exposed perceived that bullying was related to their vision loss. Efforts should be made to increase awareness about this issue in school, social, and working life. Our findings that bullying was negatively related to outcomes of self-efficacy and life satisfaction emphasize the need of professional assistance of those who have been bullied. Universal design and access to professionals who are trained to the needs and challenges of people with VI are recommended.

Research perspectives

Our research findings should be supported by population-based cohort studies of individuals with and without VI. Moreover, future research should include longitudinal studies of the risk and impact of bullying in people with VI, especially among those who have lost their vision at birth or during childhood.

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