

Mental Pain as a Transdiagnostic Patient-Reported Outcome Measure

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Abstract

Patient-reported outcomes (PROs) refer to any report coming directly from patients about how they function or feel in relation to a health condition or its therapy. PROs have been applied in medicine for the assessment of the impact of clinical phenomena. Self-report scales and procedures for assessing physical pain in adults have been developed and used in clinical trials. However, insufficient attention has been dedicated to the assessment of mental pain. The aim of this paper is to outline the implications that assessment of mental pain may entail in psychiatry and medicine, with particular reference to a clinimetric index. A simple 10-item self-rating questionnaire, the Mental Pain Questionnaire (MPQ), encompasses the specific clinical features of mental pain and shows good clinimetric properties (i.e., sensitivity, discriminant and incremental validity). The preliminary data

suggest that the MPQ may qualify as a PRO measure to be included in clinical trials. Assessment of mental pain may have important clinical implications in intervention research, both in psychopharmacology and psychotherapy. The transdiagnostic features of mental pain are supported by its association with a number of psychiatric disorders, such as depression, anxiety, eating disorders, as well as borderline personality disorder. Further, addressing mental pain may be an important pathway to prevent and diminish the opioid epidemic. The data summarized here indicate that mental pain can be incorporated into current psychiatric assessment and included as a PRO measure in treatment outcome studies.

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Introduction

There has been growing emphasis on patient-reported outcomes (PROs) – any report coming directly from patients about how they function or feel in relation to a health condition or its therapy [1]. Patients' perspective

may support analyses of efficacy and effectiveness, examinations of quality of care, and pharmacovigilance. Some PROs focus on self-rated evaluation of specific disease-related conditions, such as cancer, pain, or depression. Other indices are focused on more general perceptions, such as quality of life. PROs are also clinically useful for detecting the burden and impact of symptoms on quality of life and psychological well-being of patients [2]. Physical pain is frequently assessed, generally for determining what type of intervention is likely to affect subjective perception of pain best. Self-report scales and procedures for assessing physical pain in adults have been developed and used in clinical trials [3]. PROs are part of the general psychosomatic approach [4] that considers how a patient perceives symptoms and how this appraisal affects his/her functioning and relationships with others as part of the disease process [5–7]. The need to include consideration of functioning in daily life, productivity, performance of social roles, intellectual capacity, emotional stability, and well-being has emerged as a crucial part of clinical investigation and patient care [5]. Psychosomatic medicine pioneered the self-rated evaluation of psychological status in medical conditions. In psychiatry, self-rating scales, long before the appearance of PROs, have been part of assessment tools for clinical trials [8, 9]. A number of sensitive and valid instruments have been developed for assessing mood, anxiety, and other psychological symptoms [9, 10]. However, assessment of mental pain has been neglected by clinical studies in psychiatry [11, 12]. For instance, the comprehensive Handbook of Psychiatric Measures [13] did not include a specific instrument for mental pain.

The aim of this paper is to outline the clinical implications that assessment of mental pain may entail in psychiatry and medicine, with particular reference to a clinimetric index that may have considerable potential in pursuing such a goal.

Clinical Characterization of Mental Pain

There have been various definitions of mental pain in the literature, where, in addition to mental pain, terms such as psychic pain, emotional pain, psychological pain, social pain, emptiness, psychache, internal perturbation, and psychological quality of life have been used to refer to this construct [11, 14, 15].

Sometimes, according to such definitions the concept is placed in a specific context. Shneidman [16] defined it as “psychache,” an acute state of intense psychological

pain associated with feelings of guilt, anguish, fear, panic, loneliness, and helplessness, which is at the core of the suicidal process. Orbach et al. [17] defined mental pain as “a wide range of subjective experiences characterized as a perception of negative changes in the self and its function that is accompanied by strong negative feelings,” and completed suicide can be viewed as a means of alleviating a painful internal state. Indeed, higher levels of psychological pain were found to be associated with suicidal ideations and acts [18].

Other definitions are broader. According to Cassel [19], suffering can be defined as a state of severe distress that occurs when an impending destruction of the person is perceived. “Suffering is experienced by persons, not merely by bodies, and has its source in challenges that threaten the intactness of the person as a complex social and psychological entity” [19]. As Sensky [20] noted, the term “suffering”, however, may have different meanings to different people. Expressions such as “suffering from intense pain,” “suffering from a terminal illness,” or even “suffering a hangover” are indicative of these ambiguities.

Meerwijk and Weiss [21] attempted to identify some common characteristics of psychological pain (they preferred this term to mental pain), that were identified in unpleasant feelings, appraisal of an inability or deficiency, and its features of unsustainability. They advocated an operational and consensus definition beyond the various conceptualizations of psychological pain [21].

Engel [22] pointed out that grief is a cause of mental pain, produces a variety of bodily and psychological symptoms, and interferes with our ability to function effectively. Grief may occur after the loss of a valued object, being it a loved person, a cherished possession, a job, status, home, country, an ideal, or a part of the body. Schmale [23] underscored that grieving, as with other forms of loss and life change, is a highly personal reaction, which is based on individual past experiences, current life circumstances, and future aspirations. Medical illness may constitute a significant loss, particularly with regard to the state of good health and/or well-being [23].

Engel [22] wondered whether grief could be considered as a disease and challenged its traditional conceptualization, which tends to be restricted to what can be understood or recognized by the physician [22, 24]. Similarly, mental pain may be a universal experience that has a natural course and may become the source of positive insights that prelude to adaptive changes.

The borderland between mental pain and pain referred to the body is of difficult definition, since pain always involves a psychological component [25]. Engel [25]

defined pain “as a psychological experience involving the concepts of injury and suffering, but not contingent on actual physical injury. The idea of injury as well as the need to suffer may lead to pain, just as a real lesion or injury may do. Similarly, the need not to suffer or not to accept the fact that an injury is painful may render a “painful” injury “painless.”

The Link between Mental and Physical Pain

According to the definition of the International Association for the Study of Pain (IASP), “pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage” [26]. This definition clearly determines that in addition to nociceptive activation of the brain, pain is an individual and internal experience, which is consciously perceived, modulated, and transformed according to its emotional context [27]. Moreover, the clinical manifestations of pain can be seen as the result of the complex interplay between biological factors, psychological processes, and social influences. Pain-related neural brain networks fluctuate spontaneously, therefore the pain experience is a result of dynamic communication of networks shaping cognition and behavior, called the “pain connectome” [28]. When acute pain arises, the etiology can be defined in most cases. However, chronic pain may occur in the absence of prior tissue injury and may be the result of dyssynchrony and disruption of the pain connectome [29].

Recent neuroimaging studies have shown that physical pain evoked by nociceptive stimuli involves similar brain regions activated by various emotional and behavioral states [27]. This hierarchical, multilevel neural network is responsible for the process of experiencing physical pain (spinothalamic tract to posterior thalamus – 1st level). This information is further processed and enriched with conscious perception and attentive and cognitive modulation (anterior cingulate cortex, insula, prefrontal cortex, posterior parietal cortex – 2nd level), leading to somatic or vegetative responses. Finally, pain perception and modulation are enriched by the emotional context and individual psychological factors (orbitofrontal cortex, perigenual anterior cingulate cortex, anterolateral prefrontal cortex – 3rd level) to formulate individual pain memory; 2nd and 3rd level brain regions modulate the incoming nociceptive stimuli as either inhibitory or facilitatory through interactions with descending tracts in the spinal cord [27].

In many cases pain awareness in chronic pain (“chronic pain phenotype”) is the result of ongoing subconscious changes in brain function modulated by internal (e.g., genetic, inflammatory, repeated nociceptive events) and external (e.g., environment, socioeconomic levels) processes [29]. In healthy populations, intrinsic brain activity organizes brain networks to interpret, respond, and predict environmental stimuli [30, 31]. This intrinsic activity shows similar networks across populations and over time and does not have a pain phenotype, although there are differences in relation to sex and certain psychological factors (substance use disorders and mood disorders) [29]. Early development injuries (e.g., early child amputation) and acute pain attacks (e.g., migraine) may result in delayed onset of chronic pain, which is related to the underlying alterations in brain network efficiency, connectivity, and strength [29]. Psychological factors, particularly depression, may reorder the neural network, producing a chronic pain phenotype without a history of prior pain [29]. Environmental factors may also play an important role in the development of pain. Chronic therapeutic use of opioids (e.g., in migraine or in chronic pain) may lead to hyperalgesia and further pain chronicity [29]. Physical and psychological trauma accompanied by negative emotions (sexual abuse, torture) may contribute to chronic dysfunction in the brain, resulting in generalized dysfunctional pain modulation with consequent chronic pain at nearly the same level as at the time of the initiating event [29, 32, 33]. When the structural and chemical changes in the brain and the dyssynchrony and disruption of networks reach a tipping point, then conscious pain develops [29].

Patient-Reported Outcome Measures

Engel [25] acknowledges that a limiting factor in patient description during an interview is the patient’s verbal capacity: “one must accept the fact that some persons simply lack the vocabulary and fluency to report much beyond the fact that they are in pain.” This particularly applies to the description of mental pain by patients who present with alexithymic features [5]. There are two methods for assessing mental pain that may be subsumed under the rubric of PRO measures and may complement clinical interviewing.

One is provided by self-rating questionnaires. A number of psychometric instruments have been developed: the Psychological Pain Assessment Scale (PPAS) [16], the Multiple Visual Analog Scale (MVAS) [16], the Psych-

Table 1. The Mental Pain Questionnaire (MPQ)

Mental Pain Questionnaire (MPQ)		
Mental or psychological pain is an experience that is part of life. It is different from physical pain. We would like to learn about your experience of mental pain in the past week. There is no right or wrong answer. Please work quickly.		
1.	I feel pain	yes no
2.	My heart is broken	yes no
3.	I will never find again what I have lost	yes no
4.	My pain is everywhere	yes no
5.	My pain is with me all the time	yes no
6.	I cannot understand why I feel this pain	true false
7.	I feel empty	yes no
8.	My life makes no sense	true false
9.	My pain will never go away	true false
10.	The only way to stop my pain is to die	true false

Scoring for each item: yes/true = 1, no/false = 0; total score range: 0–10. From Fava [47].

ache Scale (PAS) [34], the Orbach and Mikulincer Mental Pain Scale (OMMP) [35], the Tolerance for Mental Pain Scale (TMPS) [36], and the Mee-Bunney Psychological Pain Assessment Scale (MBPPAS) [37]. Many of the validation studies have been conducted in relation to suicide attempters.

Another type of measure does not rely on language skills and can be used to rapidly elicit patients' appraisals of their suffering [38, 39]. Büchi et al. [38–41] have devised a measure called the Pictorial Representation of Illness and Self Measure (PRISM), which, in validation studies [41], behaves as expected of a measure of suffering and fits well with Cassel's conceptualization of suffering [19, 42].

At present, however, there is insufficient evidence to indicate that any of these specific instruments satisfies the requirements for inclusion as PROs in clinical trials, according to guidelines [43].

Development of a Clinimetric Index

Clinimetrics, the science of clinical measurements, offers important opportunities for assessing clinical phenomena such as mental pain [10, 44, 45]. Such assessment is generally neglected in standard psychiatric and medical evaluations, where exclusive reliance on the symptoms of the psychiatric diagnostic criteria may not reflect the clinical picture of patients in practice [46].

A simple clinimetric index (a 10-item yes/no questionnaire), the Mental Pain Questionnaire (MPQ) (Table 1), was developed [47, 48]. In psychometrics, homogeneity of

components, measured by statistical tests such as Cronbach's alpha, is often regarded as the most important requirement for a rating scale. However, the same properties that give a scale a high score for homogeneity may obscure its ability to detect changes [44]. In clinimetrics, homogeneity of components is not requested and single items may be weighed in different ways: what matters is the capacity of an index to discriminate between different groups of subjects and to reflect changes in experimental settings such as psychotropic drug or psychotherapy trials [9, 49]. As a result, on the basis of the available literature, some specific features of mental pain in the clinical setting were identified.

- 1 Presence of mental pain. This is the first clinical requirement. Questions such as "Do you feel pain and suffering in your mind that goes beyond what one may experience in life from time to time? How would you describe it? How does it compare with physical pain?" may be a helpful start. In our clinical experience patients are unlikely to spontaneously report mental pain unless they are specifically questioned about it. When they are encouraged, they may provide very vivid descriptions.
- 2 Feeling of being wounded. Mental pain has been characterized as a state of "feeling broken" that involves the experience of being wounded, with loss of self and disconnection from others [14, 23]. Expressions such as "my heart is broken" reflect this state.
- 3 Sense of helplessness and hopelessness. Mental pain may be increased by feelings of helplessness (the perception of being unable to cope with some pressing problems and/or of lack of adequate support from oth-

ers) or hopelessness (the consciousness of having failed to meet expectations associated with the conviction that there are no solutions for current problems and difficulties) [5, 50]. Hopelessness/giving-up may increase the perception of mental pain and thus needs to be distinguished from helplessness [51].

- 4 Pain location. One of the characteristics of mental pain is the fact that it cannot be localized in a part of the body. The term “central pain” has been used, particularly in reference to depression, where the system is disinhibited, with distress arising from stimuli that were previously non-aversive [52–54].
- 5 Duration of pain. It is of crucial importance how mental pain is perceived by the individual as such to get an idea of its duration, persistence, and potential chronicity. Questions such as “Does it hurt all the time or in specific moments? Does it occur every day or less frequently? Is there anything that makes it worse? Is there anything that makes it better?” may provide further helpful specifiers.
- 6 Relation to events and situations. Some patients may date its beginning in relation to a certain event or situation, whereas other people are unable to track a specific time of onset. Lack of understanding the occurrence of mental pain is likely to increase the perception of pain.
- 7 Feelings of emptiness. Feeling numb or empty may be another clinical characteristic of mental pain. Such feelings were found to differentiate major suicide repeaters and non-major suicide repeaters [55].
- 8 Loss of meaning of life. Emptiness may be increased by loss of meaning in life [56]. Frankl [56] suggested that suffering terminates at the moment a meaning is found for it.
- 9 Irreversibility of pain. When mental pain is of long duration it may engender the conviction of its irreversibility, as well as fears and intolerance of suffering.
- 10 Relationships with suicidal ideations. Suicide risk is much higher when the general psychological and emotional pain reaches intolerable intensity [18, 57, 58] in relation to the individual pain tolerance threshold [16], particularly in the context of major mood disorders [59]. Patients may come to believe that the only way to stop pain is to die.

These 10 characteristics were translated into 10 simple self-rated formulations. The MPQ has shown good clinimetric properties when administered in a clinical population of 200 migraine patients [60], particularly sensitivity in discriminating between patients with or without psychological distress, and incremental validity (according

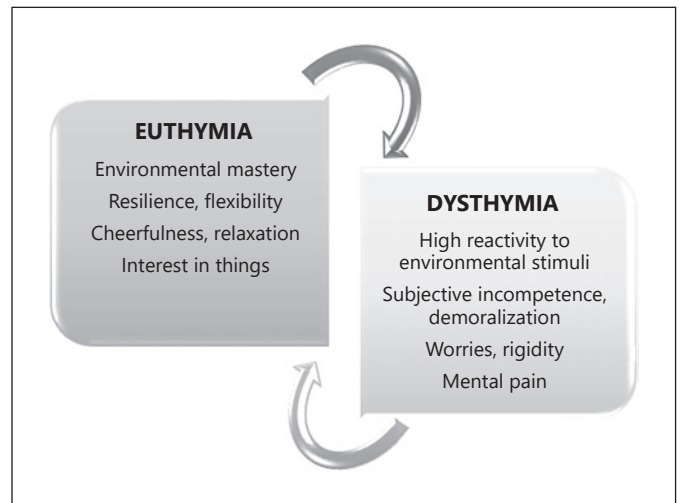


Fig. 1. Transdiagnostic balance between euthymia and dysthymia.

to which each distinct aspect of psychological measurement should deliver a unique increase in information in order to qualify for inclusion). In another investigation on 200 primary care patients [61], the MPQ significantly discriminated between patients presenting with at least one DSM-5 [62] or Diagnostic Criteria for Psychosomatic Research (DCPR) [5] diagnosis and those who had no diagnosis, displaying good sensitivity and discriminating between different patient subgroups. There were highly significant correlations between the MPQ and both observer- and self-rated scales of psychological distress [60, 61], such as the Clinical Interview for Depression [63] and the Psychosocial Index [64]. The MPQ was also significantly negatively correlated with the Euthymia Scale [65, 66]. These preliminary data suggest that the MPQ may satisfy the clinimetric requirements to qualify as a PRO measure.

The Transdiagnostic Features of Mental Pain

In 1967, Eysenck [67] referred to neuroticism and introversion by the term “dysthymia.” The term then became synonymous with chronic depression, but its original definition [67] provides the conceptual ground for the clinical transdiagnostic balance between euthymia (characterized by environmental mastery, resilience, flexibility, cheerfulness, relaxation, interest in things) and dysthymia (encompassing high reactivity to environmental stimuli, subjective incompetence, demoralization, rigidity, worries, and mental pain) [68, 69] (Fig. 1).

The transdiagnostic features of mental pain are supported by its association with a number of psychiatric disorders. Mental pain can be considered as a specifier for DSM-5 “clinically significant distress” caused by the symptoms of a psychiatric disorder [62]. Depression is inextricably linked to its experience: patients may present with a uniquely aversive, anguished, or uncomfortable experience that is characterized by painful tension and torment [52–54, 70]. They may become suicidal when they perceive their emotional state as painful and incapable of change.

However, mental pain can also occur independently from depression. It may be associated with anxiety disorders [61], such as in the perception of invalidism in agoraphobia or social barrier in social anxiety. In anorexia nervosa, the select mental focus on food and eating has been found to be related with emotional avoidance [71] and patients often report feeling emotionally “numb.” When qualitative assessment methods were applied [72], anorexic patients reported that their illness helped them to avoid or control aversive emotions and high sensitivity to emotional pain.

Patients with borderline personality disorder have a range of intense dysphoric affects, sometimes experienced as aversive tension, including rage, sorrow, shame, panic, terror, and chronic feelings of emptiness and loneliness. These individuals can be distinguished from other groups by the overall degree of their multifaceted mental pain [73, 74], which has been associated with a high prevalence of reported childhood maltreatment [75]. Deliberate self-harm may serve to shift attentional focus away from emotional pain and toward physical pain [76].

Mental pain has also been described in the setting of post-traumatic stress disorder [77], obsessive-compulsive disorder [78], schizophrenia [79], and grief [22]. There may be considerable overlaps, even in brain networks, with pain of somatic origin [11, 12, 80]. The characteristics of mental pain associated with medical disease, however, have not been sufficiently explored. Engel [81] observed that some individuals are more prone than others to use physical pain as a psychic regulator, whether the pain includes a peripheral source of stimulation or not. These patients have been defined as “pain-prone” [81, 82].

Finally, the subjective experience of mental pain may be influenced by spiritual and religious factors. According to Wachholtz and Fitch [83], chronic pain conditions may be influenced by religious beliefs and active use of prayer may be a primary form of coping. Religious/spiritual beliefs, however, may have powerful negative impact

on the perception of pain. The Italian scholar of biblical studies Ortensio da Spinetoli [84] underscored how a certain interpretation of the Catholic religion may link suffering to guilt and expiation as a well-deserved punishment, despite lack of any biblical evidence to support such a stance.

Treatment of Mental Pain

Assessment of mental pain may have important implications in intervention research, particularly in psychopharmacology and psychotherapy, and yet it has been ignored. For instance, depressed patients frequently report that treatment with antidepressant drugs yields substantial relief of their mental pain. This would be consistent with the decrease in reactivity to social environment that has been found in placebo-controlled trials with antidepressant drugs using Paykel’s Clinical Interview for Depression [63]. It would also be consistent with Carroll’s neurobiological model of central pain [54]. In the depressed phase, the central nervous system is seen as disinhibited, so that stimuli that previously were non-aversive are experienced as distressing and lead to agitation, pathological guilt, and hopelessness [54]. The findings of van Heeringen et al. [85] indicate that dorsolateral hyperactivity is associated with increased levels of mental pain in depression. It is a common clinical experience to observe relief of mental pain by the use of other psychotropic drugs, such as benzodiazepines [86, 87] or antipsychotics [88]. Since improvement in variables associated with mental pain may also occur with placebo [89], one may wonder what is the specific role of psychopharmacology. We need to test and compare psychotropic drugs in randomized placebo-controlled trials, with mental pain as a PRO.

With regard to psychotherapy, relief of mental pain has been associated with non-specific therapeutic ingredients such as attention and opportunities for disclosure in a high arousal state [5, 49]. In recent years, there has been increasing interest in the role of positive affects in pain and its treatment [90, 91]. Since positive affects have been found to attenuate both the perception of physical pain and its psychological responses [90], it is conceivable, and yet to be tested, that a specific psychotherapeutic strategy for modulating well-being, Well-Being Therapy (WBT), may counteract the manifestations of mental pain [47]. It is also conceivable that appropriately using spiritual resources [92] may lead to clinical improvement.

Mental Pain and the Opioid Epidemic

In recent years, the opioid abuse epidemic has gained increasing visibility [93]. In the USA, in 2016 more than 11 million Americans misused prescription opioids, and opioid-related death has claimed more than 300,000 lives since 2000. The majority of people started with painkillers, and problematic prescription of opioids is often cited as a primary contributor to the current epidemic [94]. Individuals with chronic pain are commonly prescribed opioids for its treatment and are at risk for developing opioid abuse [94]. The role of mental pain in such a population has been insufficiently explored, even though it can be inferred by the use of antidepressant drugs or related substances in the management of somatic pain [12]. Addressing mental pain, whether accompanied or not by somatic manifestations, may be an important pathway to prevent and diminish the opioid epidemic. Garland et al. [95] conducted a randomized controlled trial involving a psychotherapeutic protocol geared to mindfulness and positive emotions compared to a support group in chronic pain patients who abused opioids. The intervention significantly reduced opioid misuse and craving while decreasing pain syndromes.

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Conclusions

The data we summarized indicate that there is a pressing need for research assessing mental pain in medical and psychiatric settings. According to the clinimetric approach, mental pain should be incorporated, among other important psychological variables, into current psychiatric assessment and may yield specific clinical features of patients' psychological distress. Further, mental pain should be included as a PRO measure in treatment outcome studies and may become a very important indicator of the effectiveness and usefulness of interventions, particularly with regard to psychopharmacology and psychotherapy.

Disclosure Statement

All authors have no conflicts of interest to declare.

Author Contributions

G.A.F. wrote the first draft of the manuscript, with the support of E.T. and J.G. All authors contributed to the final version of the manuscript.

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