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Psychological Pain, Depression, and Suicide: Recent Evidences and Future Directions

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Abstract

Purpose of Review The definition of psychological pain is complex. It is a lasting unpleasant and unsustainable feeling characterized by a perception of inability or deficiency of the self, as well as frustrated psychological needs and social disconnection. The aim of our review was to summarize the most recent and updated findings supporting the role of psychological pain in the pathophysiology of depression and suicidal behavior. We also explored the relationship between psychological and physical pain in depression and suicide.

Recent Findings Psychological pain is a prominent dimension of depressive disorder and has been associated with higher risk of suicidal ideation and suicidal behavior. Sensitivity to psychological and physical pain is increased in depression. Conversely, higher tolerance to physical pain is associated with suicidal behavior.

Summary A better understanding of the pathophysiology of pain processing in depression and suicide offers new therapeutic options for the treatment of depression through the use of analgesic drugs.

Keywords Psychological pain · Physical pain · Depression · Mood disorders · Suicidal ideation · Suicidal behavior

Introduction

Analysis of the relevant literature on psychological pain provides a picture of the various perspectives and terminologies used to describe this experience. Terms, such as mental pain, psychic pain, psychological pain, psychache, emotional pain, and suffering, have been used to refer to the same construct. Meerwijk et al. (2014) proposed a consensual definition of psychological pain that is based on the common characteristics of these constructs. Specifically, psychological pain can be defined as a lasting, unpleasant, and unsustainable feeling characterized by a perception of inability or deficiency of the self [1].

Depressive disorders are related to a "painful emotional state" in the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) [2]. Moreover, "unbearable" psychological pain is one of the most frequent complaints associated with serious depression, and its presence may lead to suicide (Shneidman, 1993). Although many risk factors of suicidal behavior have been proposed, a body of evidence supports the central role of psychological pain. A common phrase in suicide notes is "I can't stand the (mental) pain any longer" (Shneidman, 1993). This suggests that a person might seek death by suicide as a means of escaping from pain. Moreover, Joiner, in his Interpersonal Theory of Suicide, hypothesized that increased tolerance for physical pain and reduced fear of death might be associated with suicidal behavior (acquired capability) [3]. In this review, we will summarize the most recent and updated findings supporting the role of psychological pain in the pathophysiology of depression and suicidal behavior. We will also investigate the relationship between physical and psychological pain in depression and suicide. Finally, we will focus on new therapeutic targets and propose new topics for future research. Throughout the review, we will use the term of "psychological pain" to describe the concepts of psychache, mental pain, and psychological pain.

This article is part of the Topical Collection on *Mood Disorders*

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Methods

We conducted a narrative review of studies written in English that assessed the role of psychological pain in depression and suicide and the link between psychological and physical pain in depression and suicide. We searched for original studies published in PubMed using the medical subject headings (MeSH) "pain" AND "depression" AND "suicide." We then selected the most relevant articles by reading the titles and, when necessary, the abstract. We also reviewed the list of references to identify other studies of interest. To provide an updated description and a critical evaluation of the most recent findings, we included only the most representative studies (e.g., in terms of article impact factor, sample size, authority of the experts, and type of publication, such as meta-analyses/reviews).

The Complex Definition of Psychological Pain

The definition of psychological pain is complex. Indeed, it relates to a negative feeling linked to frustrated psychological needs but also to a feeling of social disconnection. According to Sandler (1962) and Baummeister et al. (1990), psychological pain originates from the discrepancy between the ideal and the actual self [4, 5]. On the other hand, Shneidman thought that it might result from frustration of one person's psychological needs, such as desire of affiliation, need of love and protection, and need to avoid humiliation, to organize one's life, to avoid blame and criticism, and to understand and resolve problems [6]. Finally, Bolger (1999) related psychological pain to the perception of "feeling broken" [7]. According to Orbach et al. (2003), it may correspond to the unpleasant feeling of negative changes in the self [8]. Furthermore, psychological pain should be distinguished from the affective part of physical pain. It is known that physical pain induces negative psychological consequences, and has emotional aspects that have been included in the definition of physical pain by the Association for the Study of Pain [9].

More recently, Eisenberger proposed the concept of social pain. This could be considered as a subtype of psychological pain caused by a frustrated need of affiliation and connection with others. Social pain has been defined as the unpleasant experience associated with the actual or potential damage to one's sense of social connection or social value (due to social rejection, exclusion, negative social evaluation, or loss). Interestingly, it has been shown that a common neural network that involves the anterior insula, anterior cingulate cortex, and the prefrontal cortex underlies both social and physical pain [10, 11].

Psychological Pain and Depression

The models proposed by Klein (1974) and Caroll (1994) to explain depression include disinhibition of the central pain regulatory system together with inhibition of the central pleasure system and of the psychomotor facilitatory system [12, 13]. During depression, non-aversive stimuli become aversive, and central pain dysregulation is associated with lower self-esteem, feeling of devaluation, and guilt. In bipolar disorders, the central pain regulatory system fluctuates between disinhibition during depression and inhibition during manic episodes [13] when patients do not perceive the negative qualities of the self and of the environment and do not anticipate the painful consequences of their acts.

Psychological pain is present in depression, especially through dysfunctional cognitions. Lester (2000) showed that in a small sample of students, current and highest ever psychological pain levels were associated with the depression severity [14]. Orbach et al. (2003) assessed psychological pain and dysfunctional cognitions related to anxiety and depression in a group of students between 18 and 47 years of age. To evaluate psychological pain, they used the Orbach & Mikulincer Mental Pain scale (OMMP), a 44-item questionnaire on nine mental pain dimensions (irreversibility of pain, loss of control, narcissistic wounds, emotional flooding, emotional freezing, self-estrangement, cognitive confusion, social distancing, and emptiness). They found that all dimensions (except for social distancing) were associated with dysfunctional cognition [8], suggesting that cognition during depression is strongly linked to psychological pain. In addition, these dimensions were inversely correlated with cognitive-focused coping (i.e., problem-focused coping strategy, support seeking, and distancing), but not with emotion-focused strategies [8]. Mee and Bunney (2011) developed the Mee-Bunney Psychological Pain Assessment Scale (MBPPAS), a brief 10-item self-report rating scale to assess psychological pain in depressed subjects, and showed that the MBPPAS score was positively correlated with depressive symptomatology [15].

Although, psychological pain is a prominent symptom in people with depression, few studies have explored its relation with biological measures. At the neuroanatomical level, activation of the dorsolateral prefrontal and inferior frontal cortices at rest is higher in depressed patients with high level of psychological pain than in those with low level of psychological pain. Activation of the right occipital cortex and of the left inferior temporal gyrus also is increased [16]. Importantly, in this study, the level of psychological pain was not correlated with the severity of depression. This suggests that psychological pain could be a specific construct with proper neurobiological substrates. For example, the role of the dorsolateral prefrontal cortex in the depressive disorder pathophysiology remains unclear. Conversely, the dorsolateral prefrontal cortex

has been implicated in emotion regulation [17]. Changes in its activity could affect the process of emotion control. Therefore, psychological pain in the context of depression could be the consequence, or at least could be maintained by a deficit of affective control. In a systematic review, Meerjwick et al. described a potential neural network for psychological pain that included the prefrontal and cingulate cortices, and also thalamus, cerebellum, and parahippocampal gyrus [11].

Furthermore, assessment of the heart rate at rest and psychological pain level (OMMP and Psychache Scale) in 35 volunteer outpatients with history of depression showed that high psychological pain was associated with decreased low frequency heart variability. This suggests higher sympathetic activity and altered ability to regulate negative affects and pain [18••]. In addition, analysis of resting-state electroencephalography (EEG) recordings for these outpatients [19••] highlighted, after adjustment for depressive symptoms, an association between frontal dysregulation and level of psychological pain and greater deactivation of the brain default mode network during high psychological pain. These heart rate and EEG findings are in line with the hyperarousal theory of psychological pain whereby psychological pain should be more associated with increased autonomic arousal related to dysregulation of the sympathetic system than with decreased vagal control.

Although psychological pain is not a specific manifestation of depressive disorders [1], its assessment in depressed patients is fundamental for several reasons. First psychological pain overlaps with some of the core depressive symptoms, such as overresponse to negative stimuli, feeling of guilt, painful rumination, or self-devaluation [20]. Second, psychological pain could be linked to altered emotional regulation strategies. Third, psychological pain has been associated with suicide risk.

Psychological Pain and Suicide

Shneidman (1993) proposed that psychological pain is at the center of the suicidal process, from suicidal ideation to suicide [6]. Unbearable psychological pain is the most often reported reason for suicide.

A recent meta-analysis by Ducasse et al. (2017) showed that the level of psychological pain is higher in suicide attempters than non-attempters [21••] and in suicide ideators than in non-ideators. Interestingly, these results remained significant even when subgroups with similar level of depression were analyzed. This is in agreement with the finding that the risk of suicide is positively associated with the level of psychological pain, independently of depression [22]. Similarly, the systematic review by Verrocchio et al. (2016) highlighted the strong relationship between psychological pain and suicidal ideation, suicide attempt, and suicide. Psychological pain could contribute to increase the risk of suicidal ideation and suicidal behavior in different clinical groups (i.e., adult inpatients and outpatients, teenagers, students, prisoners, homeless people, and military populations). Although the severity and lethality of suicide attempts cannot be predicted only on the basis of the level of psychological pain, it could result from the interaction between pain and the feeling of social isolation, difficulties to communicate with others, difficulties in social problem solving, alexithymia, and schizoid personality traits [22]. Furthermore, the suicide attempt severity has been linked to different mental pain dimensions (OMMP factors) [23]. Specifically, comparison of medically serious suicide attempters (MSSAs) (according to Beautrais's criteria [24]: admission for longer than 24 h and being treated in a specialized unit or with surgery under general anesthesia), medically non-serious suicide attempters (MNSSAs) and psychiatric controls (no suicide attempters) showed that the "irreversibility of pain" score was significantly higher in MSSAs than in MNSSAs and controls. Moreover, feelings of emptiness predicted suicide lethality, while cognitive confusion negatively predicted the suicide intent level, probably by hindering the individual planning abilities.

Psychological pain could also interact with environmental factors to trigger suicide. For instance, the levels of suicidality (according to the Suicide Behaviors Questionnaire-Revised) and of psychological pain are higher in individuals exposed to suicide in their family than in non-exposed individuals [25•]. The interaction between exposure to suicide of a family member and psychological pain potentiates the risk of suicide. These results suggest that psychological pain could interact with stressful life events to increase the risk of suicidal behavior in people vulnerable to suicide. Beyond the interaction effect, psychological pain is also a mediating factor between depression and suicide risk [26].

People may seek death by suicide as a way to be relieved of a painful internal state [8]. Clinical experience suggests that suicidal ideation can function as a coping mechanism whereby some people can tolerate high levels of pain and/or disability by telling themselves that if their psychological pain becomes unbearable, they have the option of ending the pain through suicide. In other words, suicidal behavior becomes a problem-solving behavior in order to "stop the painful flow of consciousness" [6]. According to Shneidman's theory of suicide, unbearable psychological pain precedes suicide, and is necessary for suicide to occur. In agreement, the role of positive future expectancies as a predictor for suicidal ideation was emphasized by O'Connor et al. (2008) [27], and motivations to escape from painful self-awareness were mentioned in the *escape theory* of suicide [5].

Several studies have focused on the relationship between social pain, which could be considered as an example of psychological pain and suicidal behavior, particularly since the pioneering study by Durkheim. According to Durkheim, *egoistic suicide* occurs when a subject is insufficiently integrated

within a specific group and has few social bonds. Conversely, *altruistic suicide* takes place when a subject identifies with a social group for whom he or she is willing to sacrifice his/her own life. Both suicide types highlight the influence of social forces on suicidal behavior. More recently, Joiner proposed in his Interpersonal Theory of Suicide that suicidal ideation emerges in people who experience simultaneously thwarted belongingness (e.g., poor social support, loneliness, interpersonal conflict) and perceived burdensomeness (e.g., self-hate, liability to others) [3]. In agreement, these dimensions have been associated with suicidal ideation [28] and low distress tolerance (defined as the capacity to experience, accept and function in the context of negative psychological states) [29]. A meta-analysis of 122 published and unpublished studies found that the interaction between perceived burdensomeness and thwarted belongingness was significantly associated with suicidal ideation. Moreover, the interaction between thwarted belongingness, perceived burdensomeness, and capability for suicide was associated with higher number of past suicide attempts [30••]. Pain is associated with social exclusion because belonging to a group is crucial for survival in social animals. Being excluded or rejected modulates a reflexive painful response (social pain) that is adaptive for survival [31]. Psychological pain serves to draw attention to significant social events that have a negative effect on human desires and aspirations, in order to promote the correction of the events that caused the pain.

Few studies have investigated the neural correlates of psychological pain in people with vulnerability to suicidal behavior. Reisch et al. (2010) measured (by functional magnetic resonance imaging) brain activation in recent suicide attempters during three recalled conditions (psychological pain, suicide action, and neutral activity). Compared with neutral activity, suicide recall (psychological pain and suicide action) was associated with decreased activation of the left dorsolateral prefrontal, right anterior prefrontal, and left medial prefrontal cortices, and with increased activity of the right parahippocampus, left middle temporal gyrus, and cerebellum [32]. The authors hypothesized that the concomitant recall of suicidal behavior and psychological pain is associated with deficient emotional regulation linked to prefrontal cortex dysfunction.

Furthermore, quantification by proton magnetic resonance spectroscopy of the at-rest levels of nine metabolites in the right dorsal prefrontal cortex of 10 depressed patients, 15 suicide attempters and 33 healthy controls [33••] showed that N-acetylaspartate levels are negatively correlated with current psychological pain, independently from group, sex, age, or depression level. Moreover, in secondary analyses, psychological pain mediated the relationship between cognitive measures (previously associated with suicidal behavior) and suicidal ideation.

The Link between Psychological and Physical Pain in Depression and Suicide

People frequently use similar pain-related expressions, such as "I am hurt," to refer to physical and psychological pain. Indeed, there is increasing evidence that physical and psychological pains overlap not only in colloquial language, but also in the clinic and neuro-anatomically. Both states involve suffering and activation of the "pain matrix." For instance, experiencing social exclusion activates the insular and cingulate cortices that are also involved in physical pain [34]. Recently, some authors have suggested that both pain experiences activate the pain matrix because they trigger multimodal cognitive processes involved in the reaction to salient events. This activation should lead to focus the attention toward potentially threatening environmental stimuli [35, 36]. Therefore, for human beings, a threat to social bond integrity is as salient as a threat to physical integrity.

Recently, a correlation between self-reported level of social exclusion and perception of physical pain has been found among participants using Cyberball, a virtual ball-toss game to assess social exclusion [36]. This correlation was present also among participants who were included in the game. Thus, individuals could become more sensitive to physical pain due to social exclusion. As previously discussed, intense psychological pain could be involved in the suicidal process. The potential interaction between psychological pain (as a result of social rejection) and physical pain raises the question of the involvement of pain perception in the suicidal process. While physical pain could be related to suicidal phenotypes (from suicidal ideation to suicide) [37], the association between physical pain intensity and suicidal ideation and behavior has not been widely studied.

Emotions are bodily expressed through physical sensations [38], leading to physical pain inner tension when dysregulated [39]. Suicidal and non-suicidal self-injurious behaviors can be understood as a way to escape from an aversive internal state or psychological pain [40]. Some studies highlighted the positive association between physical pain intensity and suicidal ideation in patients with chronic pain, even after controlling for the depression severity [41, 42]. Pain intensity is a predictive factor for suicidal ideation [43] whereas common mental disorders (such as depression or anxiety) could be mediating factors in the relationship between physical pain and suicide [42]. Moreover, pain catastrophizing (i.e., the tendency to magnify or exaggerate the threat value or seriousness of pain sensations [44]) has been associated with increased suicidal ideation and behavior in patients suffering from headaches [45].

However, increased pain tolerance (i.e., the highest intensity or longest duration of pain that can be supported) has been related to suicidal behaviors. Healthy subjects reporting fearlessness of lethal self-injury have a higher tolerance to

provoked pain. It has been suggested that one can acquire the fearlessness necessary to enact lethal self-injury only by experiencing a series of painful and provocative events leading to habituation to suicide fear and pain [46]. The acquired suicide capability, mediated by painful events [47], requires higher pain tolerance and lower fear of death. It has been recently reported that, compared with depressed suicidal ideators and controls, depressed suicide attempters have higher levels of fearlessness, higher pain insensitivity, and history of painful and provocative life events [48]. Caceda et al. (2017) found time-related modifications of pain thresholds (i.e., the lowest stimulus intensity perceived as painful) and psychological pain after a suicide attempt. High psychological pain level and elevated physical pain threshold are associated in suicidal patients, but they go back to normal levels after the resolution of a suicidal crisis [49•]. Other studies revealed higher pain tolerance and threshold in patients with history of suicidal behavior. Orbach et al. (2007) found increased pain tolerance in suicidal patients compared with non-suicidal psychiatric and healthy controls, independently of the psychiatric diagnosis and hospitalization length [50]. The role of dissociation in the modification of pain tolerance also has been investigated. For instance, pain tolerance and threshold are increased in adolescents with a history of suicide attempt and are associated with the dissociation level [51]. Comparison of the pain level in two patients' groups admitted to the emergency ward following suicide attempt or accident and in a control group (1996) showed increased pain tolerance in suicide attempters compared with controls. Conversely, pain tolerance was reduced in patients with accident injuries [52]. The higher pain tolerance and threshold in suicidal individuals could be related to a dissociative detachment mechanism [53] to protect against pain. Conversely, the decreased pain threshold in the accident group serves as an alarm to avoid new harmful stimulations and for self-preservation. Interestingly, the meta-analysis by Calati et al. (2017) found greater level of dissociation in psychiatric patients with past suicidal behavior and non-suicidal self-injury than in psychiatric controls without suicide attempts and self-harm [54••]. At the neuroanatomical level, the insula, which participates in the neural network underlying physical pain sensitivity ("the pain matrix"), could play a role in pain tolerance and dissociation in individuals vulnerable to suicidal behavior. The insula is part of the brain network related to Joiner's acquired capability for suicide [55]. This brain region has been associated with physical pain processing [56, 57], and is also implicated in the mechanism of pain tolerance in healthy controls [58]. Ducasse et al. (2014) suggested that insula activation could trigger dissociative states under the control of the dorso-lateral prefrontal cortex [40].

Although they share the same neural networks, the perception of physical pain decreases and that of psychological pain increases in people vulnerable to suicide, whereas they are both increased in patients with depressive disorders. In agreement, Ducasse et al. (2014) reported habituation to painful stimuli and increased psychological pain in patients with borderline personality disorder (BPD), who have high risk of suicidal behavior. In fact, suicidal behavior, self-harm and self-mutilation are observed in nearly 80% of patients with BPD [59]. In patients with BPD, hypoalgesia for acute physical pain has been associated with dissociative states. Ludäscher et al. (2007) assessed the pain threshold in 12 women with BPD and 12 healthy controls by applying electric stimulation. Pain threshold was significantly higher in patients than in controls and was associated with the level of trait and state dissociation assessed with the Dissociative Symptom Questionnaire and the Dissociative State Scale, respectively [60]. The repetition of current self-injurious behavior may also be at the origin of and maintain pain insensitivity [40]. Conversely, patients with BPD show increased sensitivity to psychological/social pain. For instance, analysis of the emotional reactions in an experimental social exclusion task (i.e., the Cyberball game) in 30 patients with BPD and 30 controls showed that patients have a biased perception of social exclusion with higher feelings of social rejection, independently of their inclusion in or exclusion from the game [61]. A recent comparison of the mental pain scores (OMMP scale) in patients with BPD and depression did not find any difference, with the exception of the mental pain subscale of narcissistic wounds (feeling rejected and having low self-worth). Higher scores in this subscale were a specific predictor of BPD and BPD symptoms' severity [62].

Differently from what observed in individuals with history of suicide attempt, pain perception is increased in patients with depressive disorders. A study on a community sample in Michigan (1179 people interviewed by telephone) indicated that nearly 35% of individuals reporting chronic pain had probable depression [63]. Comorbidity between chronic pain and depression was associated with old age, being a woman, part-time employment, and low educational level. Patients with pain symptoms are two times more likely to develop a depressive disorder than patients without pain, and the risk increases by fivefold in those with multiple pain symptoms [64]. Other studies have shown increased sensitivity to pain during depressive episodes. Adler et al. (1993) found decreased relative pain perception threshold (i.e., the pain perception threshold divided by the somatosensory perception threshold) in 16 patients with depressive disorder compared with age- and sex-matched controls [65]. More recently, Klauenberg et al. (2008) compared pain threshold and wind-up ratio (this measure relates to the temporal summation of supra-threshold painful stimuli and reflects enhanced spinal cord excitability) in patients with depressive disorder ($n = 25$), fibromyalgia ($n = 35$), and healthy controls ($n = 25$) [66]. Patients with depressive disorder had a lower cold pain threshold and higher wind-up ratio than patients with

fibromyalgia and healthy controls. This suggests the existence of a pain-related central hyper-excitability in depression. Similarly, Zambito Marsala et al. (2015) found that pain threshold and pain tolerance are lower in patients with depression before treatment ($n = 27$) than in age-matched healthy controls ($n = 27$) [67]. Finally, Thompson et al. (2016) found that in patients with depression, pain threshold, and tolerance vary also according to the pain type, and are lower for exteroceptive stimulation and higher for interoceptive stimuli [68].

Therapeutic Targets and Future Perspectives

Several neurotransmitter systems have been implicated in the mechanism of psychological pain in mood disorders and suicide, notably the opioid and endocannabinoid systems. In a cohort study on 857 elderly people aged 65 years and older, Olié et al. (2013) showed that opioid consumption was higher in individuals with history of depression than in healthy controls [69], with the highest opioid consumption in patients with a lifetime history of suicide attempt. More recently, our group analyzed 858 elderly people among whom 335 were already included in the study by Olié et al., and found (i) higher consumption of opioids in patients with suicidal ideation during the follow-up or with a lifetime history of suicide attempt compared with healthy controls, (ii) higher presence of physical pain in affective controls (lifetime history of major depression) than in healthy controls, and (iii) higher influence of physical pain on the quality of life in suicidal patients compared with both control groups [70••]. These results led us to hypothesize that in our sample, physical pain was comparable in suicidal patients and controls, differently from psychological pain, which was not assessed in this study. Consequently, they could consume more opioids to get relief from psychological/social pain.

Moreover, analysis of the mu opioidergic system using in vivo positron emission tomography during social rejection and acceptance experimental tasks showed that opioid receptors were activated during the rejection task. This suggests that the opioid system is involved in the regulation of social pain [71]. Interestingly, analysis of the association between the A118G polymorphism in the mu opioid receptor gene (OPRM1, rs1799971) and the occurrence of a major depressive disorder following a targeted social exclusion adverse event in 420 adolescents included in a birth cohort study [72] indicated that the risk to develop a depressive disorder following targeted rejection was twofold higher in carriers of the G allele than in A/A homozygotes. These results confirm the role of the opioidergic system and mu opioid receptors in social pain and in the vulnerability to depressive disorder. Based on these findings, the efficacy and safety of very low dose of buprenorphine for the treatment of suicidal ideation was evaluated in a double-blind placebo-controlled trial [73••]. Compared with the placebo group, patients who received buprenorphine had decreased suicidal ideation and psychological pain.

Besides the opioidergic system, endocannabinoids also are promising potential therapeutic targets in the field of depression and physical pain. Cannabinoid receptors (CB1 and CB2) are present in the central nervous system and in peripheral tissues and regulate ascending nociceptive information in the spinal and supra-spinal regions [74]. CB1 and CB2 gene polymorphisms are associated with bipolar disorder and depression [75, 76]. Animal experiments suggest that cannabinoids have an antidepressant and anti-anxiety effect [77], but clinical studies on the treatment of mood disorders with cannabinoids are still lacking.

Finally, ketamine, which has an analgesic effect and is used in anesthesiology, has a blocking effect on the N-methyl-D-Aspartate (NMDA) receptor and reduces chronic and acute pain efficiently [78]. Moreover, ketamine infusion has a rapid antidepressant efficacy in patients with treatment-resistant depression [79].

Conclusion

In summary, considered both the complexity and the importance of the construct of psychological pain, we suggest its deeper investigation, with the attempt to disentangle psychopathological aspects, from relational and existential ones and to explore its etiology (biology, frustration of essential psychological needs, frustration of pathological needs, etc.).

Psychological pain is present in both depressed patients and patients with suicidal ideation and behaviors but it seems to be higher in suicidal patients, so it has to be further investigated. The same could be said for social pain. Similarly, physical pain is present in depressed patients and in patients with suicidal ideation and behaviors; however, two different sub-types of suicidal patients could be present: individuals with low physical pain tolerance (e.g., depressed patients with suicidal ideation and/or behaviors) and individuals with high physical pain tolerance (e.g., individuals who self-harm, with borderline diagnosis and high dissociation levels).

In conclusion, our review emphasizes the tight link between psychological pain and depressive disorder, and the strong relationship between psychological pain and suicidal behavior. Sensitivity to both psychological and physical pain seems to increase in depression.

Further research is needed to confirm this hypothesis and to develop new analgesic treatments to treat depression.

Compliance with Ethical Standards

Conflict of Interest Ismael Conejero, Emilie Olié, Déborah Ducasse, and Philippe Courtet declare no conflict of interest.

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