

Review

# Pain Sensitivity in Schizophrenia Spectrum Disorders: A Narrative Review of Recent Work

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**Abstract:** Many patients with schizophrenia seem relatively immune to physical pain while others complain of constant pain. This may result from disturbances or alterations of the sensory threshold for pain in populations with psychosis, a possibility for which there is some preliminary evidence. The inconsistency in pain perception may, in part, be explained by the treatments patients receive, but treatment-naïve patients also exhibit differences in response to pain. This suggests that decreased pain sensitivity may represent a specific psychosis endophenotype. Thus far, few experimental studies have investigated sensory thresholds, pain modalities, or other factors contributing to the perception or expression of physical pain in psychosis. A digital search for information on this topic was conducted in PubMed and Google Scholar. The result is a non-systematic, narrative review focusing on recent clinical and experimental findings of pain sensitivity in patients with psychosis. Importantly, physical and mental pain are closely connected constructs that may be difficult to differentiate. Our hope is that the review provides some clarity to the field in the specific context of schizophrenia.



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## 1. Introduction

The subjective sensation of pain is a complex phenomenon whose source is usually a body injury, but pain may originate in the central nervous system itself [1]. Individuals differ, reportedly, in their threshold for perceiving pain so that it is often impossible to predict the extent of injury that will result in pain [2]. There is one certainty, however, and that is that subjective pain impairs a person's quality of life. The results of a large number of studies indicate that, as a group, individuals suffering from psychosis show reduced sensitivity to pain when compared to population controls [3,4]. This has been attributed either to increased activity of central endorphins [5] or to the analgesic effects of antipsychotic medication. Hypoalgesia is also sometimes seen, however, in patients who are antipsychotic naïve [3]. A much-discussed possibility is that schizophrenia symptoms may prevent pain recognition or distort its expression [5–7].

Impairments in the mental and emotional processing of pain have long been implicated in schizophrenia [8]. Nearly 40% of individuals with this condition who suffer pain are said to not report it to their care provider [9]. On the other hand, many patients with schizophrenia complain of severe body pain, pain which significantly interferes with their ability to function [10].

Study results vary. Some report that individuals with schizophrenia experience pain to the same extent as everyone else [11]. One small study of 12 participants found that persons with schizophrenia were characterized by elevated sensitivity to acute pain but reduced sensitivity to prolonged pain [12]. Another indicated that patients with schizophrenia were

hypersensitive to pain induction when compared to healthy peers and concluded that the hypoalgesia that has long been associated with schizophrenia is based not on dampened perception of pain but, rather, on fewer complaints of pain [11].

This review of recent literature will address the following questions: Does pain perception in schizophrenia depend on the body location or severity of the pain? On the real-life experience of pain or on pain experimentally induced? On the nature of the medication the patient receives or on its dose? On the relationship between patient and interviewer? What characterizes patients who appear to be impervious to pain and those for whom pain seems intractable?

## 2. Materials and Methods

We carried out electronic searches in PubMed and Google Scholar databases for papers in English, Spanish, German, or French that had “pain” and “schizophrenia” in their titles or abstracts. PubMed was used as it offers a greater variety of advanced features and the vast majority of relevant journals in the two relevant fields. Google Scholar was used as a complementary database for electronic searches, in combination with PubMed, in order to explore the possibility of papers not found in PubMed. These two databases are informative because they are frequently upgraded. New features are added that improve search functions.

The full texts of the papers originally retrieved were then explored and included only if they addressed the questions stated above. For the question concerning medications, we used the following keyword strategy: pain AND psychotropic medication AND schizophrenia; pain AND antidepressants AND schizophrenia, and similarly for all specific groups of psychopharmacological treatments.

The screening and selection process was performed by the authors AGR and JL. Around nine hundred abstracts were initially scanned. Eight-hundred were discarded as they did not specifically address any of our questions. At first, we only included papers published in the last decade, then added older, frequently cited, relevant papers by experts in the field. In the end, a total of 50 studies were included in our review.

## 3. Results

### 3.1. Do Location or Severity of Pain Influence Pain Perception in Schizophrenia?

A routine medical examination was the method used in many studies to explore pain sensitivity in patients with schizophrenia. Girard et al. [13] induced moderate pain in 35 patients with schizophrenia and 35 healthy controls. Patients with schizophrenia compared to controls required less pressure and a shorter duration of ischemia before reporting moderate pain, suggesting hypersensitivity. Since schizophrenia had often been associated with hypoalgesia, a potential way of resolving the contradiction was to conclude that patients with schizophrenia feel pain but do not express it unless specifically asked. Urban-Kowalczyk and collaborators [14] tried to separate nociceptive from non-nociceptive stimuli in 43 patients with schizophrenia, 5 first degree relatives of patients, and 34 healthy controls. Plasma concentrations of substance P, beta-endorphins, and calcitonin gene-related peptide (CGRP) were obtained and the Positive and Negative Syndrome Scale (PANSS) negative subscale as well as cognitive tests were administered. A pain threshold was determined by nociceptive reflex (RTIII) testing. Beta-endorphin and CGRP levels were higher in schizophrenia than in healthy controls but no correlation was found with scores on psychopathology or cognition. The investigators concluded that a relatively high level of beta-endorphin may reduce pain sensitivity in patients with schizophrenia although, in the concentrations seen, analgesic effects seemed unlikely. It seemed more likely that cognitive impairment and the presence of negative symptoms were decreasing the expression of pain. Nevertheless, a recent study investigating neural mechanisms of pain sensitivity in patients with schizophrenia by means of electroencephalography (EEG) and functional magnetic resonance imaging (fMRI) [15] found that schizophrenia patients showed a lower perceived intensity to nociceptive stimuli compared to healthy controls

but similar perceived intensity to non-nociceptive somatosensory and auditory stimuli. This suggests that schizophrenia patients respond differently to pain than to other stimuli. Minichino et al. studied 20 patients with schizophrenia, 17 with bipolar I disorder, and 21 with bipolar II disorder [16]. Results were that pain-processing and pain-perception abnormalities were evident in patients with schizophrenia, but bipolar I patients showed pain-processing abnormalities. This suggests that pain perception may be a potential trait marker for the psychosis spectrum.

Some previous studies have suggested that contradictory findings in sensitivity to pain in schizophrenia could be partially explained by different responses to different types of pain [12]. Lévesque and collaborators [12] investigated intermittent transcutaneous stimulation of the left sural nerve in 12 patients with schizophrenia and 11 controls. Pain was induced by sural nerve stimulation that provoked a measurable nociceptive flexion response on an electromyographic recording. Pain intensity was assessed using a 0–10 verbal numerical scale and the psychopathological assessment included the use of the PANSS scale and the Calgary Depression Scale for Schizophrenia. Patients with schizophrenia showed increased sensitivity to acute pain when compared with healthy controls, but decreased pain sensitization—in other words, high sensitivity to acute pain but low sensitivity to chronic or prolonged pain. This response differentiation between acute and chronic pain probably characterizes schizophrenia more accurately than do responses based on the location of pain or its severity.

Table 1 summarizes potential factors influencing results in pain perception across studies in patients with schizophrenia.

**Table 1.** Potential factors influencing pain perception in patients with schizophrenia.

Study	Assessment Method	Results (Compared with General Population)
Girard et al., 2011 [13]	Pressure during routine medical examination	Less pressure applied for shorter duration induces hypersensitivity
Lévesque et al., 2012 [12]	Intermittent transcutaneous stimulation of the left sural nerve measured by electromyography	Increased sensitivity to acute pain Decreased sensitivity to chronic or prolonged pain
Urban-Kowalczyk et al., 2015 [14]	Potentially nociceptive stimuli and lab results	Hypoalgesia by analgesic effects of beta-endorphins
Zhou et al., 2020 [15]	Electroencephalography and functional magnetic resonance imaging	Lower perception of nociceptive stimuli Similar perception of non-nociceptive stimuli

### 3.2. Past Pain Experience and Experimentally-Induced Pain Perception in Schizophrenia

Recent evidence suggests that perception of pain and its expression may be modulated by factors such as previous experiences of pain. A recent study in the field of pain in schizophrenia compared 30 schizophrenia patients with 32 major depression patients and 30 healthy controls [17]. The experimentally induced pain test consisted of the application of pressure and subsequent induction of ischemia. The authors developed a semi-structured interview, which included questions about previous painful experiences and evaluated the degree of anxiety, somatic symptoms (heart rate, blood pressure) and psychological symptoms [17]. The results showed no difference with regard to pain intensity, severity, or duration of previous pain events among the three diagnostic groups. However, in the sample as a whole, experimental pain sensitivity differed according to previous lived painful events. This suggested that previous experience of pain affect the current experience of pain, regardless of diagnosis.

More recently, the same research team reported further details of the past painful experiences with the aim of qualitatively analyzing whether type of painful event differed in patients with schizophrenia recruited from day hospital units, patients with major

depression during their first week of hospitalization and healthy controls without known psychiatric history [18]. The semi-structured interview explored previous and current painful experiences, which included six somatic categories (e.g., wounds, trauma without fracture, trauma with fracture, surgery, acute illness, chronic illness) and two situational categories (painful labor-delivery and painful breastfeeding). Each pain event category consisted of the number of painful events, intensity of pain (score from 0 to 40), number of painful events occurring prior to and during the last 6 months, total duration, intensity and main component of pain (e.g., sensory or affective). Trauma without fractures and wounds were the most common painful events. Results showed that the perception of pain is highly dependent on the context of previous painful events [18]. A diagnosis alone, such as schizophrenia, does not by itself seem to alter the specific perception of pain. This is explained by the fact that the sensation of pain is a complex experience, more influenced by psychological factors, than by a psychiatric diagnosis.

### 3.3. *The Association between Pain and Psychotropic Medications in Schizophrenia*

A moderately large literature points to a significant overlap between the pharmacological treatment of psychiatric disorders and response to pain. Several investigators have reported that some pharmacological agents used to treat pain were initially developed to treat depression and anxiety disorders [19]. A recent review on the topic highlighted several groups of biological agents that are used for depression or anxiety. For instance, it is a well-established fact that the treatment of neuropathic pain includes the use of tricyclic antidepressants, serotonin reuptake inhibitors, and norepinephrine reuptake inhibitors [19]. Other psychotropic medications used for anxiety/depression, such as gabapentinoids, benzodiazepines, and cannabinoids, have also met with some success in the treatment of pain [20].

This is important to our topic because major depressive disorder is a common comorbidity in patients with schizophrenia [21]. A recent study aiming to explore the association between the two conditions recruited 396 consecutively hospitalized patients [21]. The study concluded that major depression and schizophrenia commonly co-existed but that schizophrenia eclipsed the depression, which was left untreated, thus negatively affecting the outcome of illness. A recent systematic review and meta-analysis [22] confirmed the frequency of this co-morbidity, recommending that antidepressants be more frequently used in schizophrenia [22], a currently uncommon practice [23].

When antidepressants are used, it is possible that they help schizophrenia patients to reduce pain response by impacting the emotional experience of pain [22]. This is speculation for which there is, as yet, no definitive evidence.

The use of antipsychotics may also affect pain sensitivity [24], since current drugs show different neurotransmitter receptor affinities, binding to dopamine, 5-hydroxytryptamine, adrenergic, histamine, and muscarinic receptors [24]. This may allow at least some of them to be effective for pain. A particular cause of pain in patients with schizophrenia treated with antipsychotics is the pain caused by tardive dyskinesia, a persistent movement disorder resulting from drugs that block dopamine receptors [25,26]. While increasing the dose of antipsychotics can temporarily mask tardive symptoms, this is not recommended because it ultimately worsens the problem. Recently, new non-antipsychotic treatments that are effective in tardive dyskinesia have been approved for use [27].

A recent multicenter study evaluated the prevalence of physical pain in a sample of 655 schizophrenia and bipolar disorder patients who were homeless [28]. While less than 3% were receiving analgesic treatment, more than half of the sample reported moderate to severe physical pain. No association was found between antipsychotics, mood stabilizers, anxiolytics, hypnotics, or medication adherence and self-reported pain. However, to some extent, the severity of psychotic symptoms (e.g., the relative absence of antipsychotic medication) increased the reporting of physical pain [28]. This suggests that antipsychotics may, indeed, reduce pain or else that the pain reported in the context of severe psychotic

symptoms is a form of delusional sensation. To the best of our knowledge, no studies have adequately investigated the association between antipsychotic dose and subjective pain.

With regard to the potential antinociceptive properties of antipsychotics drugs and differences in these properties among different antipsychotics, there is, as yet, little evidence. Preclinical studies have shown that, although clozapine and olanzapine share some similarities, these two drugs differ in their interaction with the opioid system, and in the induction and potency of their antinociceptive effects [29]. Olanzapine in particular demonstrates a potent antinociceptive, dose-dependent effect. This is reported in a recent systematic review that examined the use of atypical antipsychotics in the management of chronic pain [30]. The following antipsychotic drugs were evaluated: olanzapine, quetiapine, risperidone, aripiprazole, and ziprasidone because they were the only ones with published studies in pain management, olanzapine and quetiapine having the most publications. Olanzapine showed efficacy in the treatment of fibromyalgia and headache/migraine, irrespective of the person's diagnosis.

Too much dopamine has been associated with headache [31]. Dopaminergic neurons affect nociceptive function in the spinal dorsal horn [32] and dopamine receptors are reportedly altered in patients with facial pain [33]. Interestingly, either too much or too little dopamine can produce pain [34], which is why both agonists [35] and antagonists such as antipsychotics can produce beneficial analgesic effects. A recently published article suggests that many antipsychotic drugs may prove, in the future, to be capable of providing effective analgesia [36].

Gamma aminobutyric acid (GABA) agents such as gabapentin have also proven effective against pain. GABA is one of the major inhibitory neurotransmitters of the central nervous system; benzodiazepines (BZDs); and other anticonvulsant medications mainly bind to GABA-A receptors [37]. Neuropathic pain resulting from peripheral or central nerve injury stems from both excitatory and inhibitory neurons within the central nervous system [38]. A disruption in the homeostasis of these neurons is an important contributor to hyperalgesia or allodynia. GABAergic agents such as gabapentin have been found to be effective in mitigating neuropathic pain in the general population. With respect to pain in the context of schizophrenia, studies have been few. Recently, clozapine has been found to partially act via the GABA-B receptor, suggesting that it may share similarities with baclofen, a drug that activates the GABA-B receptor and is used worldwide for the treatment of cerebral palsy, multiple sclerosis and spasticity [39]. This may help to open new avenues for treating pain-related conditions in schizophrenia.

Kynurenine pathways have been implicated in psychiatric disorders in the context of inflammation [40]. In fact, preclinical studies have revealed that kynurenines may be important in explaining schizophrenia cognitive deficits; they may potentially impact mood, cognition and pain in schizophrenia. Novel therapeutic approaches targeting kynurenine pathways need to be tested and further developed to confirm the original hypothesis. Several studies have pointed out that kynurenine metabolites may be useful in monitoring treatment response in psychiatric disorders [40]. They may also modulate pain perception.

New potential for treating patients with schizophrenia arises from microbiota research. A recent systematic review summarizes the arguments for including microbiota-oriented treatments (including fecal microbiota transplantation) in the therapeutic regimens of patients with major depression and schizophrenia [41]. The authors report that the administration of probiotics to patients with major depression provides strong evidence for their usefulness. When probiotic supplements fail, fecal microbiota transplantation may help in both major depression and schizophrenia. Future studies should test the efficacy of such treatments for pain in patients with schizophrenia.

With respect to other novel treatments, oxytocin has been found to be an interesting target for research. While molecular studies have indicated that impairments in opioid and cannabinoid receptors did not explain altered pain sensitivity in rat models of schizophrenia, Banki et al. investigated the role of the oxytocinergic system on an experimental model of osteoarthritis [42]. Oxytocin receptor mRNA expression was found to be low in both

treated and control rats. This suggested that further investigation of oxytocin for alleviating pain was merited.

In summary, antidepressants as an adjunctive therapy in schizophrenia may be effective for pain. Although evidence for the antinociceptive properties of antipsychotic drugs and newer treatments such as probiotics, fecal transplants, and oxytocin is still sparse, it is promising. Thus far, the evidence of beneficial effect is best for olanzapine.

#### *3.4. The Influence of the Patient–Interviewer Relationship on Pain Perception*

Pain is a symptom of many diseases and the one that causes most distress to patients. Understanding patients' experiences of pain is vital to its management [43]. In the Rustøen et al. study [43], the role of nurses is highlighted in the management of pain. Nurses mitigate pain by acknowledging it, by recognizing its subjectivity, by being available to patients in pain and always supportive, by sharing known information about pain, and by assuring the delivery of prompt analgesic aid. A more recent study confirmed that a comprehensive interview with a patient is critical to accurate diagnosis, to the establishment of an effective care plan, to prognosis, and treatment outcome [44]. Asking about pain creates a therapeutic alliance that allows for the mutual determination of causes of discomfort and distress and identifies the barriers to their amelioration. An empathic stance reduces patients' concerns and permits them to more openly voice their needs and expectations [44].

A patient's understanding of his or her pain helps to relieve it [45]. This is important in the differentiation of acute from chronic pain, because the two are differently caused, and patients are helped by appreciating the difference [45]. Recently, Hambraeus et al. [46] qualitatively evaluated patients suffering from pain. They found that empowerment of patients, e.g., providing them the means to control their own pain, had a positive effect on pain management.

Information about the effects of the patient–interviewer relationship on pain in patients with schizophrenia is scarce, although the thorough assessment of pain has been highly recommended in patients with psychotic symptoms [47]. Several recommendations can be made by translating findings from outside the field of schizophrenia. Building trust is the first step. The next step is acknowledging the fact that pain, whether from physical injury or from delusional belief in injury, is real to the patient and that empathy is always required. Shah and Nakamura reported the case of a man referred for physical therapy because of chronic shoulder, elbow and wrist pain [48]. During the intake interview, the patient described psychotic symptoms which consisted of the belief that an electronic device was implanted in his body. The case illustrates the fact that pain is sometimes based on a delusional belief, but that this does not mean that it should be dismissed. It must always be taken seriously, and a comprehensive care plan developed.

#### *3.5. Differences between Patients Who Experience High Versus Low Intensity of Pain*

It is probably impossible to predict which patients with schizophrenia will experience high intensity pain and those who will be hypoalgesic. Experimentally induced pain studies have tried to untangle this issue, as did a systematic review of 14 clinical studies [8]. The review's conclusion was that, in general, schizophrenia patients experience less frequent pain than the general population and show a lower intensity of pain than individuals suffering from other psychiatric disorders.

It found, however, that differences in the prevalence and intensity of pain may only be applicable to severe pain that has an apparent medical cause, such as headache and tissue injuries [8]. In the case of less severe pain, there appears to be little difference in sensitivity between those with schizophrenia and those without. In agreement with these findings, a systematic review and meta-analysis [11] determined all cause and specific pain in 242,703 patients with schizophrenia compared to 4,259,221 controls. This review concluded that a third of individuals with schizophrenia suffer from clinical pain to the same degree as age and sex controls. What continues unresolved is whether sensitivity/non-sensitivity

to pain in this population depends on the severity of pain, on past pain experience, on the under-reporting of pain, on a relative lack of help seeking for pain, or on a higher pain threshold because of something inherent in schizophrenia or, perhaps, inherent in the drugs taken by persons with schizophrenia.

Investigators have highlighted the concept of psychological pain or psychache [49], especially important because of its association with suicidal behavior. Berardelli and collaborators carried out a cross-sectional study of patients with major depressive disorder, bipolar disorder and schizophrenia [49]. They administered Shneidman's Psychological Pain Assessment Scale (PPAS) to assess mental pain and used the Mini International Neuropsychiatric Interview (MINI) to evaluate suicide risk. They found that current psychache and worst-ever psychache were both associated with high suicide risk in their sample. However, no significant differences were found among the three diagnostic groups [49]. The concept of psychache opens new avenues for the investigation of psychopathological symptoms and their relationship to pain.

In line with these investigations, Brooks and colleagues examined the association between levels of pain intensity and depressive symptoms in older patients with schizophrenia spectrum disorders [50]. Higher pain intensity was found to be associated with elevated depressive symptoms in patients with schizophrenia, as it is in the general population. The recommendation is to monitor depressive symptoms, especially in older adults with schizophrenia who report intense pain.

#### 4. Discussion

The perception of pain is a complex experience strongly influenced by a variety of factors, including psychological variables. Findings from studies focusing on schizophrenia vary in their results and merit careful examination and accurate interpretation.

Our narrative non-systematic review aimed to address the following questions: Does pain perception in schizophrenia depend on body location or severity of pain? Does experimentally-induced pain differ from real life pain? Do therapeutic drugs impact pain perception? Does the patient-interviewer relationship influence pain perception? What differentiates patients with schizophrenia who experience high or low intensity of pain. We found that approximately one third of patients with schizophrenia experience reduced pain sensitivity. Alterations of the sensory threshold may be partly attributable to psychotropic medications; antipsychotics have demonstrated definite antinociceptive effects [30]. The relationship with the interviewer is an important factor in reports of pain and we have determined that regular pain assessment in schizophrenia is critical to good care. This review demonstrates the need to study new neurobiological pain pathways and apply results to patients with psychosis.

Pain can sometimes be delusionally perceived and it can also be delusionally denied. Moreover, it is often not possible to distinguish physical from mental pain, which makes pain control all the more important because, no matter its source, pain reduces quality of life in psychosis [10]. While this review is by no means conclusive, it is our hope that it provides some added clarity to issues of pain in the context of schizophrenia.

Beta-endorphins have been shown to exert analgesic effects after nociceptive stimuli in patients with schizophrenia. Recent evidence confirmed these effects [14]. By contrast, some studies have reported hypersensitivity to pain in schizophrenia [13]. This may depend on the character of the pain stimulus [15]. The differentiation of acute from chronic pain is also important. Increased sensitivity to acute pain and decreased sensitivity to chronic or prolonged pain has been reported [12]. As in the general population, the prior experience of pain determines, in part, how current pain is experienced [17]. In the context of schizophrenia, there may be insufficient self-awareness, which may lead to denial of an obvious pain stimulus. Prigatano and collaborators reported the case of a 24-year-old man with a history of schizoaffective disorder who sustained acute orthopedic injuries but denied feeling pain [7].

Psychopharmacological treatment as well as psychiatric comorbidity have the potential to influence response to pain [19]. Severe psychotic symptoms may elicit the prescription of high doses of antipsychotic medication, which, in turn, may reduce the perception of pain. Of the various antipsychotics, olanzapine, thus far, has been shown to be the most analgesic [30]. There is evidence that GABA agents are also effective against pain. Furthermore, the expression of pain depends to a large degree on the relationship of the patient with the person inquiring about the pain [49]. Empowering patients to share in decisions about control of pain has borne positive results [50].

With respect to the most common complaint of pain in schizophrenia, it is probably headache [51]. Headaches can be severe, and it is not clear whether patients with schizophrenia obtain the care they need for head pain. All people express their pain differently [52] depending on many reasons, often cultural. Culture influences how individuals perceive, manifest, and give a name to their pain [53]. This is also true for non-verbal expressions of pain. Distinct facial expressions represent pain and pleasure across cultures [54,55]. Cultural backgrounds may be especially important in schizophrenia because thought disorder may so often prevent clear communication.

Another factor of importance in the evaluation of pain perception in patients with schizophrenia is medical stigma toward this disorder. An emphasis on genetic factors as primary causes of schizophrenia was originally thought capable of removing the stigma of bad parenting and unhealthy lifestyles, but it has been found that genetic explanations, instead, exacerbate stigma [56]. Stigma has an impact on the subjective judgment of clinicians who assess pain in patients with schizophrenia, and perhaps, this may have affected the results of our review. Nevertheless, genetic factors influencing pain perception in this population need to be further investigated. Potential biological markers for psychosis may overlap with markers for the perception of pain [57].

We found that, at present, it is impossible to differentiate schizophrenia patients who experience high versus low intensity of pain [44] although digital health approaches will probably change this landscape in the near future [58,59].

To the best of our knowledge, this is the first review that focuses on potential factors contributing to pain abnormalities and pain processing in patients with schizophrenia. However, the conclusions of our review have several limitations. The finding that patients with schizophrenia may show relatively increased sensitivity to acute pain but decreased sensitivity to chronic pain needs replication and extension to other psychiatric diagnoses. The findings implicating antipsychotics in pain modulation are relatively robust but few studies have investigated the role of other potential pain modulators. Glutamatergic drugs and other therapeutics used in schizophrenia that exert their effects via varied neurotransmitter and biological pathways need to be explored. The subjective aspect of processing and evaluating pain also needs to be investigated in greater depth.

## 5. Conclusions

Approximately one third of patients with schizophrenia appear to have reduced pain sensitivity while, at the same time, some complain of pain for which there is no evident source. Patients with schizophrenia may show increased sensitivity to acute pain when compared with healthy controls, but decreased pain sensitization—in other words, high sensitivity to acute pain but low sensitivity to chronic or prolonged pain.

There is evidence of disturbances or alterations of the sensory threshold for pain in this population, which may, in part, be attributable to medications. Cultural sensitivity is almost always required to understand expressions of pain. In our diverse society, clinicians need to pay special attention to individual reactions. It is nevertheless possible that sensitivity to pain may prove, in the future, to be a way of subtyping schizophrenia.

Pain can sometimes be delusionally perceived and it can also be delusionally denied. Moreover, it is often not possible to distinguish physical from mental pain, which makes pain control all the more important because, no matter its source, pain reduces quality of



life in psychosis [10]. While this review is by no means conclusive, it is our hope that it provides some added clarity to issues of pain in the context of schizophrenia.

In summary, decreased and increased pain sensitivity may represent specific psychosis endophenotypes. Relatively few experimental studies have investigated sensory thresholds, pain modalities, or other factors contributing to the perception or expression of physical pain in psychosis. Physical and mental pain are closely connected constructs that are difficult to differentiate, especially in the presence of co-morbid depression. Mental health stigma probably leads to under-reporting of pain. A variety of pharmacological treatments, as well as psychological interventions, modulate pain intensity in this population. Importantly, monitoring pain needs to be part of comprehensive care for schizophrenia. At the same time, research needs to explore new biological pain pathways that may be involved in the neuropathology of schizophrenia.

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