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### Title

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## Effect of Psychiatric Disorders on Pain Perception: A Literature Review

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### **Abstract**

Our paper discusses findings on the correlation between pain perception and psychiatric disorders. The psychiatric disorders we chose to study are Bipolar Disorder, Schizophrenia, Anxiety, Major Depression, and Parkinson's Disease. We performed a literature review on 30 articles, with at least 6 studies per illness. We hypothesized that pain perception is altered by psychiatric disorders. Whether pain perception was increased or decreased depended on the type of mental illness. We reviewed research articles that induced pain in healthy controls and patients and recorded the difference in pain tolerance and threshold. The pain stimulus varied from electrical, emotional (photo), thermal, and ischemic. Our findings showed that for schizophrenia and bipolar depression there is a very strong case for a decreased pain sensitivity on account of the disorder. Depression had more of a nuanced result as thermal pain decreased pain sensitivity, ischemic pain increased pain sensitivity, and electrical stimulation was inconclusive. Parkinson's Disease showed a generalized increase in pain sensitivity on account of the disorder itself, but the correlation was not very concrete. Finally, anxiety did not have any significant differences in general but PTSD specifically had an increase in pain sensitivity. As a result of our research, we found that our hypothesis was correct: pain perception was altered across all psychiatric disorders surveyed. Bipolar Disorder, Major Depression, and Schizophrenia resulted in general decreases in pain perception while Anxiety and Parkinson's disease showed increases in pain perception.

## **Introduction**

As we transition out of the 2020 COVID-19 pandemic, many people felt the effects of the pandemic on their mental health. With more awareness surrounding the subject, we wanted to perform a research study relating mental illnesses and the possible correlation to brain structure. To do this, we studied the effects of mental illnesses on patients' pain perception. By studying the relationship between pain perception and mental illness, health professionals can gain a better understanding of symptomatology and be better equipped to create drug treatments that will target the areas of the brain that are affected by the disease. We studied pain perception relating to Bipolar Disorder, Schizophrenia, Anxiety, Major Depression, and Parkinson's Disease in order to get a clear understanding of how these common disorders affect pain and to determine any differences between them. We performed a literature review on 30 articles, with at least six articles per illness, to create a comprehensive understanding of pain perception in diagnosed individuals. Previous literature reviews examined outdated methods and experiments and only described one type of pain stimuli. We presented an explicit insight and mechanism for each disorder by conducting an updated literature review. We generated recent literature and studies evaluating the pain in patients with different disorders that integrate different pain stimuli such as electrical, thermal, ischemic, and emotional. Furthermore, the papers analyzed in our review use recent technology to further explain the abnormal pain perception of patients with such psychiatric disorders. With the rationales of disorders, the connections between pain and disorders are more comprehensive. We eliminated some potential variables that may influence pain perception with the literature data; thus, even though more research is needed to finalize the connection and treatment, we provided an organized view of each disorder for future research.

## **Methods**

In compiling our literature review, we searched Pubmed and ScienceDirect databases for studies published between 1993 and 2022 with the keywords “anxiety,” or “depression,” or “bipolar disorder,” or “Parkinson's Disease,” or “Schizophrenia AND “pain,” or “pain perception,” or “pain tolerance.” This approach allowed for searches to remain relevant in material while leaving room for a broadened understanding of the subject.

Each report was manually reviewed, and reference lists from identified papers were also scanned to check for eligibility. The search results in this literature review were limited to: i) English language and ii) peer-reviewed journal publications. In cases where the eligibility of an article could not be determined simply by the title or abstract, the full text was examined. To be eligible for our literature review, the article must have the following study inclusion criteria: i) examination of experimental pain, ii) primary data reports, iii) presence of clinical and healthy control samples, iv) determination of verified clinical diagnosis.

This search strategy yielded a total of 30 publications, evenly divided into each of the five categories of Bipolar Disorder, Schizophrenia, Anxiety, Major Depression, and Parkinson’s Disease.

## **Results**

### ***Bipolar Disorder***

In total, 6 studies were identified through electronic searches and reviewed pertaining to the perception of pain in individuals with bipolar disorder (BP). The six studies examining how

individuals with BP (n=1,163) perceive pain compared to the healthy individuals (n=64) met our criteria for pain perception assessments and were included in the review.

### *Methodological Characteristics*

The total number of individuals assessed was 1,228; 64 were healthy controls and 1,163 were subjects with BP. The healthy controls and patients with BP had a mean age of 32.65 years and 40.77 years. Of the 1,163 subjects diagnosed with BP, 87.36 took some form of medication, such as antipsychotics, antidepressants, benzodiazepines, mood stabilizers, neuroleptics, medication for insomnia, and analgesics. One of the studies was not accounted for as the results categorized participants by medication. For instance, if a participant was on three forms of medication, they would be accounted for three separate times (Risch et. al., 2022). For 37 patients, the medication status was not reported in the study.

### *Pain Measures*

Out of the six studies, five arrived at their results using at least two assessments each. Three studies recorded measures through questionnaires and numerical scales (Risch et. al., 2022, Rosa and Leão, 2021, Karling et. al., 2016). One collected data through picture assessments, pain sensitivity sessions, and fMRI scans (Han et. al., 2018). One used pictures assessments and sLORETA (Yang et. al., 2017), and another study used a heat sensitivity experiment (Dworkin et. al., 1995).

Two studies used a pain stimulus experiment to examine pain sensitivity in patients with bipolar disorder. One used a heat stimulus (Dworkin et. al., 1995), and the other induced subjects with hypertonic saline (5% NaCl) during a pain session (Han et. al., 2018). Both studies found that subjects with BP had a higher pain threshold and tolerance. The individuals were able to

endure a high amount of saline and also reported more stoical results for painfulness for higher-intensity stimuli.

Three studies gathered their results with questionnaires and numerical scale tests (Risch et. al., 2022, Rosa and Leão, 2021, Karling et. al., 2016). The tests used across these three studies include the McGill-Reduced Pain Questionnaire, Body Diagram, Visual Numerical Scale, and Suicidal Ideation Scale, Hospital Anxiety and Depression Scale- Anxiety (HADS-A) and Hospital Anxiety and Depression Scale- Depression (HADS-D), Perceived Stress Questionnaire (PSQ), and a self-evaluated pain questionnaire. All the tests in the studies concluded that patients with bipolar disorder were more likely to experience chronic pain and are at high risk of depression. This is due to factors such as emotional reactivity, sleep quality, and depression levels.

In two studies, picture assessments were used to gather additional results (Han et. al., 2018, Yang et. al., 2017). Individuals were shown positive, negative, and neutral images, and their reaction was measured. Individuals with BP showed little fluctuation in their responses to the three types of images being shown. This indicates that emotion and pain interaction in patients with BP is abnormal.

Two studies used imaging techniques such as fMRIs (Han et. al., 2018) and standardized low-resolution electromagnetic tomography (sLORETA) (Yang et. al., 2017). Both were used to acquire information about which parts of the brain were active during pain empathy processing. The fMRI scans showed that there was a decrease in blood oxygen level-dependent (BOLD) signaling in various areas of the brain for individuals with BP. The sLORETA images showed higher levels of activation in areas of the brain involved in pain sensation in the healthy controls compared to the subjects with bipolar disorder.

In summary, the results of the 6 studies conclude that patients with BP have decreased pain perception and pain empathy processing compared to healthy individuals. However, many patients with BP also experience much pain throughout their body indicating that they are at risk of developing chronic pain as they get older.

### Schizophrenia

In total 6 studies were identified as relevant research pieces for our topic, out of the six one was ignored due to the nature of their research being more specific and oriented on the biochemistry of pain, rather than a general concept of pain (Potvin et al., 2007). Of the five there were a total of 528 individuals diagnosed with schizophrenia and 207 healthy controls. These studies assessed experimental pain sensitivity in schizophrenic patients versus those of the control. All of them met our criteria and were used to determine our understanding of this group.

### *Methodological Characteristics*

The mean age for the schizophrenic patients was roughly 35 years old and the mean age for the control was approximately 32. For the most part, all the studies that were reviewed had a certain gauge of the medication which the patients were consuming. Four of the studies required a period of time in which said patients did not consume their medication. Ranging from a month of no medication to 8 weeks. However, one study (May et al., 1947) did not have any data in regards to the medication or treatment and how the test subjects were influenced.

### *Pain Measures*

In terms of quantifying the pain each study had its unique system, but essentially all of them boiled down to pain tolerance and physical response in terms of gauging the pain an individual is experiencing. Of the five, three used electric stimulation (Guieu, R., et al, 2018; M

Lévesque et al., 2012; Jochum, et al., 2006). Specific measures of pain were measured by verbal questionnaires in two of the studies, Lévesque and Jochum, whereas R. GUIEU looked for the amount of physical response in the measurement of muscle flexion and movement. One study used direct physical pain in terms of pinching the face (MAY et al., 1947) and had a measurement of pupillary dilation as a means of understanding the patient's pain. Finally, one study looked at thermal pain (Urban-Kowalczyk et al., 2015) this pain was measured in terms of how long the patient was able to handle the increased amount of heat.

Ultimately the studies reviewed showed a consistent level of decreased pain perception amongst schizophrenic patients. Although the distinction between reduced sensitivity and impaired ability to respond to pain is not properly realized. As well, there was one study that did not have a difference in their findings, however, it did have a very small sample size and was an outlier to the other studies (Guieu, R., et al, 2018). For the most part, it is clear that schizophrenic patients have some sort of deficient pain perception and it can be an important area of study to recognize the exact mechanism in which this holds true.

### Anxiety

In total, 10 studies were identified for review by electronic searching. These studies examined pain perception levels in either patients diagnosed with an anxiety disorder or those who scored high on a pain-related anxiety scale, as well as healthy controls. Papers with little or no experimental data were rejected in order to meet the review criteria.

### *Methodological characteristics*

Of the combined 446 subjects, 324 were healthy controls. The age of subjects varied from 10 to 48 years old, with a mean age of 27 among the 6 studies that reported this information. The



gender of subjects was generally not given. Across all studies, anxiety subjects were medication-free or the number of medicated patients was not reported. 8 of the 9 studies examined adults with anxiety-related responses compared to healthy adults, while one study examined anxious youth with healthy youth and healthy adults as controls (Michalska et al., 2020). In 3 of the studies, subjects were scored using the Pain Catastrophizing Scale (PCS) and/or the Fear of Pain Questionnaire (FPQ-III) rather than the sole metric of a clinical diagnosis.

### *Pain Measures*

Three experiments in one study examined pain tolerance after watching an anxiety-inducing video (Lautenbacher and Krieg, 1994). Pain threshold was measured using a pressure algometer. In one of these experiments, subjects had diagnosed PTSD as well as anxiety, while the other two experiments involved subjects with generalized anxiety disorder. Two of these experiments found that subjects had decreased pain tolerance after watching the video, including the PTSD experiment, while one experiment found no significant difference when other factors (gender, age) were considered. Two of the three experiments had small sample sizes ( $n < 20$ ) and none of the three included negative controls.

Two studies used electrical stimulation as the pain response metric. Both studies examined pain threshold, with one study examining the minimum intensity needed to induce pain (Lautenbacher and Krieg, 1994), while the other examined the maximum pain tolerance of the subject (Lautenbacher and Krieg, 1994). There was determined to be no difference in pain threshold or tolerance between the clinically diagnosed patients or the healthy controls when the age and gender of the patients were considered. Instead, only patients classified as

“electrodermally labile ” (low electrodermal habituation rate) exhibited significantly lower pain thresholds.

One study conducted a cold-pressor test in a water bath, and subjects were scored based on PCS and FPQ-III results. The study established that subjects passed the test if they could keep their hand in the bath for a 3-minute duration. It was found that subjects with higher questionnaire scores, indicative of increased negative thoughts associated with pain, exhibited a significantly lower pain tolerance than those with lower scores. However, it was also found that gender and race played a significant role in pain tolerance as well (Patanwala et al., 2020).

Two studies used thermal pain as a metric to study the perception, tolerance, and intensity of pain in anxiety-displaying patients. One study used the PCS score to categorize pain-anxiety-prone adults (Chayadi and McConnell, 2019), while one study examined clinically diagnosed youth compared to healthy controls (Michalska et al., 2020). In this case, a high PCS score was found to be an extremely strong indicator of quicker perception and lower tolerance, while having a diagnosed anxiety disorder did not lead to any significant findings. This was stated to be due to the broad characterization of an anxiety disorder, compared to the specificity of the PCS scale.

Lastly, two studies analyzed pain perception following periodontal flap surgery. One study analyzed state anxiety while the other analyzed trait anxiety using results from the Spielberger State-Trait Anxiety Inventory test. Subjects were surveyed for seven days after the procedure and were asked to describe their current level of pain intensity. In the state anxiety study, it was found that subjects with higher anxiety levels exhibited increased pain intensity for the first five days after surgery (Ahmadi et al., 2020). In the trait anxiety study, anxiety subjects had increased pain intensity for the first two days after surgery (Ahmadi et al., 2020).

In sum, six of ten studies found significantly lower pain tolerance in subjects with either a diagnosed anxiety disorder or in those displaying anxiety-like traits. The other four studies found no significant difference compared to control samples or as a result of other variables (gender, age, race). Overall, studies which used a pain-anxiety-related scale generally found a significant trend between anxiety and pain perception, while those that used clinical diagnoses were less likely to find significant results.

### Major Depressive Disorder

#### *Methodological Characteristics*

We analyzed the results of 6 studies related to pain perception and major depressive disorder (MDD). From all 6 studies, we observed a total of 373 patients. 281 were depressed and 92 were healthy. The mean age of all the subjects is about 38.3 years old. 40 were known to be on medication, 16 had not been on medication for at least 2 weeks, and 13 were not on medication for at least 8 weeks. 197 patients are female.

#### *Pain Measures*

Three studies tested pain threshold using electrical stimulation:

Paper 1 (Bar et al., 2005) studied the pain threshold for three different types of pain: ischemic, thermal, and electrical. The study had a total of 60 subjects with 30 healthy subjects in the control and 30 in the experimental group. In the experimental group, 27 subjects are on disorder-related medication. Each group had 23 female subjects. He recorded the pain threshold, which is when subjects begin perceiving stimuli, and pain tolerance, which is when patients can no longer handle the painful stimuli. The mean age of the subjects was 44.9 +/- 10.8 for patients and 44.7 +/- 13.5 for control. Bar found that there were no significant differences in pain

threshold for electrical pain, but patients have increased pain tolerance for electricity, especially on the right side of their body. There's a possibility that antidepressant medication may have biased these results since they do tend to increase pain tolerance.

Paper 2 (Adler et al.,1993) used low-voltage high-frequency electric current as the pain stimulus. There were a total of 32 patients, 16 patients and 16 healthy controls, and 9 female patients in each group. The mean age of all subjects was 33.2 +/- 9.4 years old. None of the patients had been under pharmacological treatment for at least two weeks before the study. Adler recorded the patient's somatosensory perception threshold (SPT) and the pain perception threshold (PPT). Relative pain perception threshold (RPPT) indicates how many times PPT is greater than SPT. The study found that RPPT is significantly decreased in depressed patients, positively correlated with the Hamilton Depression Score subscore of retardation, and negatively correlated with the subscore of anxiety. Adler hypothesized that a decrease in PPT in depressed patients could be regarded as an epiphenomenon of anxiety and impaired stress-coping. The contrast in findings in this study compared to others could also be related to the lower degree of pain induced.

Paper 3 (Marazziti et al.,1998) studied the pain threshold for electrical stimulation delivered by dental testers. There were 26 subjects, 13 healthy controls, 9 female patients, and 5 female controls. The mean age of the subjects was 43.6 +/- 15.8 years old for patients and 30.7 +/- 1.7 years old for controls. 3 subjects were on disorder-related medication. The threshold was measured using arbitrary units from a scale of 1-80 and the range of voltages given is 15-300 V. The results of the study found that the sensory threshold was 52.3 +/- 19.8 and 34.6 +/- 15.4. For the pain threshold, the results were 77.3 +/- 6.9 for patients and 52.4 +/- 20.1 for controls. The

patients had a statistically significant increase in both thresholds. There was no correlation between sensory or pain threshold, and psychological rating scale.

Three studies tested thermal pain tolerance in patients with MDD:

For the thermal pain test in paper 1 (Bar et al., 2005), the same control and experimental groups were used. Bar's results were very similar to the electrical pain. He found in both thermal and electrical pain, there were no significant differences in pain threshold and patients have increased pain tolerance on the right side of their body. Once again, there's a possibility that antidepressant medication may have biased these results since they do tend to increase pain tolerance.

Paper 4 (Schwier et al., 2010) tested the cold pain tolerance of depressed patients. There were a total of 40 subjects, 20 patients and 20 healthy controls, and 17 female subjects in each group. The mean age of the subjects was 37.2 +/- 11.5 for patients and 34.8 +/- 10.2 for controls. None of the patients had been on disorder-related medication. The study found that there was a significant difference in pain threshold and tolerance scores in the arms. Depressed patients had significantly increased threshold and tolerance in their right arm compared to healthy controls. The right arm did not have as significant of an increase. The study did not find a correlation between the severity of depression and pain perception. Schwier believes the differences between the results of this study and others could be related to the lack of medication since patients on antidepressants have decreased blood flow to the areas of the brain involved in pain perception.

Paper 5 (Bar et al., 2007) tested thermal pain perception and observed brain activity in subjects. There were a total of 26 subjects, all-female with 13 healthy controls. The mean age of the subjects was 34.3 +/- 10.5 for controls and 35.9 +/- 11.4 for patients. None of the patients had been on disorder-related medication for at least 8 weeks prior to the study. The patients had

significantly increased pain tolerance as expected. As thermal stimulation increased, many areas of the brain were activated. There was an increased BOLD signal in the contralateral, ipsilateral secondary somatosensory cortex, the rostral part of the superior parietal lobe, the right dorsolateral prefrontal cortex, and the right premotor areas or temporal and occipital lobe. Also, activation in the right thalamic, parahippocampal, and bilateral cerebellar are all related to pain increase. For depressed patients, the contralateral primary somatosensory cortex, SII, insula, bilateral premotor, supplementary motor areas, anterior cingulate cortex, right DLPFC, and ventrolateral prefrontal cortex are associated with increasing stimulus intensity. A one-sided t-test revealed significant brain activity in the right temporal lobe, occipital lobe, left cerebellum, and right thalamus and putamen as well as increased prefrontal activation.

One paper (Altok et al., 2016) studied the pain tolerance of shock wave lithotripsy used for the removal of kidney stones. The total number of subjects was 189 with 59 female patients. We are not sure about the number of healthy patients or patients on medication because everyone was tested for their levels of anxiety, stress, and depression. The mean age of all subjects was  $43.92 \pm 13.98$ . The study found that there were no statistically significant differences in terms of VAS (pain perception score) during SWL between patients with and without depression. However, this experiment was conducted observationally, therefore there were no experimental or control groups to compare against. This may have affected the results of the study.

Finally, one study (Bat et al., 2005) also studied ischemic pain in addition to thermal and electrical stimulation. The control and experimental groups were the same ones used in the thermal and electrical trials. For ischemic pain, healthy patients had increased pain threshold and depressed patients have decreased pain tolerance with no side differences. An interesting trend in this study was that patients who had higher thresholds for thermal and electrical pain perceived

painful stimuli in the ischemic pain trial much earlier than the control group, showing that depressed patients may process surface and deep pain differently. We also need to take the effects of antidepressants into consideration, since they do alter pain perception.

In summary, patients with MDD most of the time have increased pain tolerance. Although this depends on the type of pain being induced, thermal pain has increased tolerance, electrical pain has mixed findings, and ischemic pain has decreased tolerance. Paper 2 (Adler et al., 1993) contrasts paper 1 (Bar et al., 2005) and concluded that depressed patients have a lower pain perception threshold for electrical pain, but that could be due to the lower stimulus of pain that was induced. Paper 6 (Marazziti et al., 1998) was also inconclusive, but that could be a result of the study being observational rather than comparing two experimental and control groups with each other. Future research should consider the effect of antidepressants or other medication-related drugs on pain perception because that may have skewed the results of the studies. Some of the patients had taken antidepressants in the past but not during the time period when the studies were conducted, so it is unclear whether their medication altered their pain perception after their prescription stopped.

### *Parkinson's Disease*

A total of six studies about the relationship between Parkinson's disease (PD) and pain perception were included. 699 subjects were reported, including 107 healthy controls and 592 Parkinson's patients. Additionally, Patients with Progressive Supranuclear Palsy (PSP) and Multiple System Atrophy (MSA) were also assessed in one study for comparison (Avenali et al., 2017).

### *Methodological Characteristics*

Of the subjects with PD, 253 were tested by the Unified Parkinson's Disease Rating Scale (UPDRS). The mean age is  $62\pm 3$  years old. We included 281 female subjects and 311 male subjects. 592 PD patients were on regular PD treatment.

### *Pain Measures*

261 patients were tested by King's PD Pain Scale; 123 subjects were tested by Mini-Mental State Exam (MMSE); 62 subjects were tested for the threshold and temporal summation threshold of nociceptive withdrawal reflex.

All the area-related analyses were reported by the Visual Analogue Scale (VAS). Through VAS, the pain was located mostly in patients' limbs (65.4% of 123 subjects) (Lee et al., 2006). The main types of pain in PD patients are musculoskeletal pain (44.4%) and dystonic pain (19.1%). One patient may report more than one type of pain, the overlapping is common among the subjects. However, the correlation between pain types was not discovered. Instead, the severity of pain exhibited a significant positive association with the number of pain types ( $p=0.001$ ), both of them were unrelated to age, stage of disease, disease duration, MMSE, or self-reported depression. But the dystonic pain was determined to be significantly associated with motor complications (Tinazzi et al., 2006). Patients with different diseases were included in the subjects: 12 Progressive Supranuclear Palsy (PSP) patients, 11 Multiple System Atrophy (MSA) patients, and 15 PD patients. A significant reduction in both threshold and temporal summation threshold of nociceptive withdrawal reflex in PSP, MSA, and PD patients compared with healthy control. L-Dopa induced an increase in the threshold of nociceptive withdrawal



reflex in the PSP group while the temporal summation threshold of nociceptive withdrawal reflex increased in both PSP and PD patients (Avenali et al., 2017).

In conclusion, PD patients generally have an increase in pain perception. The majority of pain comes from their limbs. The pain level in each patient varies, but they are not related to disease duration and disease severity. PD patients also reported multiple types of pain, mainly musculoskeletal pain, the correlation between each type of pain was not found.

## **Discussion**

### *Bipolar Disorder*

Out of the six studies included, three studies concluded that patients with bipolar disorder are at higher risk for chronic pain in areas such as their backs, limbs, heads, necks, and joints (Risch et. al., 2022, Rosa and Leão, 2021, Karling et. al., 2016). One hypothesis as to why chronic pain is highly prevalent in patients with BP is that there may be an impairment in the patient's multisensorial integration (Karling et. al., 2016). This is consistent with two other studies which concluded that patients diagnosed with BP have abnormal brain activity (Han et. al., 2018, Yang et. al., 2017). Compared to healthy control BP patients are slower at processing pain empathy (Yang et. al., 2017). Patients with BP also exhibited various differences compared to healthy control during BOLD imaging and fMRI. Differences can be noticed in the areas of the brain that are active when looking at a positive or negative emotional stimulus and when experiencing tonic pain (Han et. al., 2018). In three of the studies, it was found that patients with BP are at high risk for depression (Risch et. al., 2022, Karling et. al., 2016, Dworkin et. al., 1995). These findings show that pain perception in patients with BP is altered. Understanding these differences can help to expedite the diagnosing process and prevent patients from being

diagnosed with other mental disorders. Furthermore, understanding which parts of the brain are involved in pain processing in BP patients can help researchers to focus on those areas and find treatments.

The limitations in this review include that many studies had patients that were on various forms of medication and some studies had a relatively small sample size compared to others. Taking medication at the time of the study can result in inaccurate results, as medication acts as a confounding factor. For example, in the studies that collected data from questionnaires, the medication may have played a part in how the subjects may have answered regarding their current levels of pain (Rosa and Leão, 2021, Risch et. al., 2022, Karling et. al., 2016). Additionally, smaller sample sizes can lead to the overgeneralization of results being applied to the population. For instance, one of the studies had only 20 subjects (Han et. al., 2018). Thus any conclusions made from the study are at risk of overgeneralization since the sample size is not a good parameter for the overall population.

### Schizophrenia

Generally, patients with schizophrenia have shown clear signs of not experiencing the same level of pain as the general population. In a lot of ways the sensitivity they experience is reduced, even when the type of pain and administration of said pain is properly varied. The only point of contention can be introduced in regards to the medication the patients took and the long-term effect said the medication would have. Although the studies had some control for medication use, none of them were larger than three months.

All of this is rather important because it introduces ways in which other researchers can understand the different conditions of schizophrenia and look into why the decreased pain

sensitivity even exists. Perhaps this research can reveal a new aspect of schizophrenia and overall increase the academic understanding of the disease. Specifically, it can lead to different neurophysical mechanisms and how this interplays with neural linkages that are askew on account of schizophrenia. Furthermore, the discussion on how medication and the illness interact can be further developed as many medications that are currently used are limited in their understanding.

In a lot of ways, new research needs to be done on this topic as the current research is relatively limited. Pain is a major aspect of an individual's neural pathways and is important for a healthy individual. Understanding how different mental disorders interact with the mechanisms of pain can be vital for developing new methods of treatment. Beyond that it allows caregivers to understand that individuals with schizophrenia might not be able to report/feel crucial pain that is affecting their physical health. Introducing a completely different aspect of this decreased pain sensitivity and how important it can be to an individual's life. Essentially the most fundamental question needs to be addressed, why does pain decrease, and how we can counteract the side effects? Hopefully, this area of research can be looked at more in the future and introduce promising results.

### Anxiety

Due to the differing results found across the ten studies evaluated, caution should be taken in drawing concrete conclusions. Patients with diagnosed anxiety disorders were found to either have an increased perception of pain or no significant difference, depending on the pain stimulation method used for the study. Outside of the experimental procedures, however, it was

determined that patients with anxiety do have an increased awareness of pain in their day-to-day lives. The exact reasoning behind this requires further study.

For most of the studies, the types of anxiety disorders surveyed were very generalized, which may explain the lack of significant results. In the study that examined PTSD, a very specified anxiety disorder, it was found that patients did have an increased pain perception compared to control subjects (Lautenbacher and Krieg, 1994). Further research should be done on similar specified anxiety disorders, such as social anxiety and OCD, to determine whether a correlation exists in these unique populations.

When clinical diagnoses were not used, however, it was clear that a significant correlation exists between pain perception and overall anxiety associated with pain. In five of the ten studies, a sliding scale of anxious tendency was created using a variety of tests and questionnaires. After conducting a range of pain stimulation procedures, it was widely found that a higher score, indicative of increased fear of pain, resulted in increased pain perception. This suggests that while clinical anxiety disorders may be too broad of a metric to determine the effect on pain perception, evaluating pain-related anxiety may be useful to determine relative pain perception.

### Major Depressive Disorder

From these results, we can conclude that the effects of depression on pain perception vary depending on the type of pain stimulation. All thermal pain studies we examined had increased pain tolerances for both heat and cold pain. Electrical pain had mixed findings ranging from increased pain tolerance, no effect, and decreased pain tolerance. These differences may be due to the level of electrical stimulation. Also, the study that concluded electricity had no effect was

conducted observationally and there may have been confounding factors that altered the results of the study, therefore more studies should be examined regarding electrical pain. The one study we read on ischemic pain concluded that pain tolerance is decreased in depressed patients. These differences in results bring up the hypothesis that depressed patients may experience surface level and deep tissue pain differently than healthy controls. There is also medication to take into consideration. Antidepressants are known to alter pain perception, and many of the patients had either taken medication in the past or were currently taking medication.

Examining the relationship between these pain types and depression can provide insight into what areas of the brain are changed in a depressed patient versus a healthy control. One of our papers (Bar et al., 2007) included a discussion about the neural activation of thermal pain. Depressed patients had significant activation in the contralateral primary somatosensory cortex, SII, insula, bilateral premotor, supplementary motor areas, anterior cingulate cortex, right DLPFC, and ventrolateral prefrontal cortex are associated with increasing stimulus intensity. A one-tailed t-test revealed statistically significant brain activity in the right temporal and occipital lobe, left cerebellum, and right thalamus and putamen as well as increased prefrontal activation. Discovering which areas of the brain are affected by depression can help psychiatrists gain insight into how exactly depression affects a patient's neurobiology, and from there prescribe and create medications that target issues specific to depressed patients. We still are unsure whether the differences in the brain are a result of medication or from the disease. More studies should be done with depressed patients who are not on medication to reveal the neurological differences caused solely by the disease and not the medication.

### *Parkinson's Disease*

To find the contribution of Parkinson's disease to pain perception, we summarized six pieces of literature studying in a similar field. The patients with Progressive Supranuclear Palsy and Multiple System Atrophy were included. To determine the connection between PD and pain perception, the physical interaction between them is the emphasis. Thus, the effect of emotional status was excluded by the Mini-Mental State Exam, where patients with a variety of scores reported identical or similar pain levels. King's PD Pain Scale used in Chaudhuri's study provided an insight into the frequency of occurrence and localization of pain types in detail (Chaudhuri et al., 2015). Through further analysis, the pain was proved to not be related to the duration or severity of PD disease. However, the pain was only exhibited in PD patients, so it is still a mystery how PD induces pain in patients. Therefore, we combined the studies using different methods to develop a potential direction for future PD studies. In VAS, 65.4% of the PD patients reported pain in their limbs. Therefore, while studying the connection between PD and pain, we should focus on the nervous system in patients' limbs. The target could be narrowed down with the data reported in Chaudhuri's and Hanagashi's work, 44.4% of 96 PD patients reported musculoskeletal pain (Hanagashi et al., 2011) ; thus, the future study could focus on musculoskeletal pain receptors in limbs. Moreover, Tinazzi's study presented numerical data on the connection between pain and motor complications. The data shows a significant association of pain with motor complications with a p-value of 0.001 (Tinazzi et al., 2006). However, it still did not report the correlation between dystonic and non-dystonic pain. It needed to be confirmed because PD is a disorder in the muscle system, by eliminating the synergy between dystonic and non-dystonic pain, we could emphasize on the dystonic pain induced by PD. To further investigate the connection of pain with PD, we included the patients with Progressive Supranuclear Palsy (PSP) and Multiple System Atrophy (MSA) from Avenali's study. PSP and

MSA are different from PD but result in similar symptoms. Therefore, they were considered to study whether the correlation between pain and PD symptoms exists. Due to the similarity in the result from PSP and PD patients, PSP may be considered as a reference sample while investigating PD patients. However, this is the only study that combined these two disorders and the number of patients in each disorder is less than 20. Thus, further study on the similarity of PSP and PD patients with more measurement is required to cross-compare the disorder for medical treatment in Parkinson's disease.

## **Conclusion**

From the reviewed literature it was noted that schizophrenia, depression, and bipolar disorder showed clear signs of decreased pain sensitivity. In general, schizophrenia and bipolar disorder showed an all-around decrease in pain whereas depression was more nuanced in terms of the type of pain stimulation that was administered to the patients, specifically thermal pain. It was also noted an increased pain sensitivity when it came to ischemic pain for depressed patients. Schizophrenia, bipolar disorder, and depression had important notes that the research did not provide a clear distinction between the disorder itself and the medication administered. Anxiety as a whole did not have any real indication of a correlation between the disorder and pain sensitivity. However, PTSD specifically did have a strong correlation with increased pain sensitivity in the patients. Following that, it is noted that Parkinson's Disease has a strong correlation with increased pain but nothing was definitive. Overall, there was a wide variety of data on the data and it is clear that through all of them that this is a field of important research where the relationship between mental illness and pain sensitivity can be further explored.

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