Anxiety and Pain: Mental Health is also Physical

Danielle Dalechek

University of Stirling, Scotland

d.e.dalechek@stir.ac.uk

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The primary objective of this retrospective analysis was to investigate the relationship between chronic pain and anxiety diagnosis. The secondary objective was to examine migraine occurrence in those with or without anxiety. It was hypothesized a relationship would be significant for both. The ReCenter database used was the PROMIS Profiles-HUI data, which included the data of 3000 randomly selected adults, age 18 or over. Identifying as female increased the odds of reporting anxiety by 39.9%. Age was negatively correlated with the presence of anxiety. It was found that having anxiety increased the chance of migraine occurrence, particularly for patients identified as female. Overall, there were some significant associations between pain experiences and anxiety, specifically with general health and pain caused by emotional tension. This information could be useful to future research and treatment outcomes when considering the challenges and disparities in treating chronic pain, including gender.

Keywords: Anxiety; pain; migraine; gender; mental health; bias.

Background

During traumatic and intense experiences, the brain is in a heightened state of stress and this stress can have drastic impacts over time. To date, the existing research has focused on behavior, emotional development, mental health, and physical health after stress. However, there has not been enough data to support a direct link between anxiety specifically and the experience of chronic pain without depression acting as a mediator. The long-term impacts of hyperarousal experienced in high anxiety and stress are not fully understood when considering pain, although studies on depression and PTSD have previously been examined in this context.

Clinically and historically, the term *anxiety* is attributed to multiple words; "anxiety" (French: *anxiété*; German: *Angst*) being defined as the anticipation of future threat, distinguished from "fear" (*peur*; *Furcht*) — the emotional response to a real or perceived imminent threat. Further, the term "worry" (*souci*; *Sorge*) in DSM-5 adds an additional nuance by referring to the cognitive aspects of apprehensive expectation (Crocq, 2015). From an evolutionary perspective, anxiety was considered to be biologically adaptive in that it promotes survival by engaging an individual to avoid danger or harmful stimuli.

Despite the common assumption that anxiety is a relatively new disorder, it was mentioned as early as in the *Tusculan Disputations* by Cicero (106 BC to 43 BC). He wrote that "affliction (molestia), worry (sollicitudo), and anxiety (angor) are called disorders (aegritudo)", on account of the connection between a troubled mind and a diseased body. This text also showed that anxious affect is distinguished distinctly from sadness, and that anxiety was defined as a medical illness (*aegritudo*) (Crocq, 2015). It is important to consider how the historical perspectives on these states could influence current perceptions, particularly in healthcare settings.

A difficult feature when considering the societal and public health implications of anxiety and pain is that chronic pain is multifaceted in terms of its socio-psychological effects, and this should be considered when evaluating the issue (Sakamoto et al., 2019). Living with chronic pain requires significant emotional resilience and tends to deplete emotional reserve, and patients often report feelings of stagnancy or having their life on pause as a consequence of their chronic pain. This also corresponds with data from a study showing that it was the pain interference in daily life rather than the pain intensity having the biggest impact on levels of daily functioning for patients (Gentili et al., 2019). In a study to

examine the source of physical guarding behavior, it was found that anxiety, not pain, directly predicted guarding behavior in participants. Pain only predicted guarding indirectly when mediated by anxiety, confirming aspects of the fear and avoidance model (Olugbade et al., 2019). This implies that physical, pain-related guarding should potentially be addressed for anxiety versus attempts aimed exclusively at chronic pain reduction.

Another study examined the potential neuroscience behind pain, depression, and anxiety, concluding that anxiety induced chronic pain by activating astrocytes in the anterior cingulate cortex (ACC) region. The mechanism proposed is that anxiety could actively increase the central sensitivity of pain by regulating corticotropin-releasing and inflammatory factors such as IL-1, IL-6, IL-10, TNF-α, and noradrenaline, which all could play a role in increasing the feeling or experience of pain (Gu et al., 2019).

Additionally, emotional factors, trauma, and infection can trigger both serositis and musculoskeletal pain (Capobianco et al., 2017), which are all important factors in inflammatory conditions where autoimmune dysfunction occurs. Pathogen-associated molecular patterns (PAMPs) released by decayed cells or by invading organisms elicit an inflammatory reaction in the peritoneal cavity, which occurs with conditions such as endometriosis. Furthermore, a sustained inflammation response is also associated with IBS and migraine, so there appears to be a possible link between stress, anxiety, bodily inflammation malfunction, and pain.

Unfortunately, these issues are compounded by disparities in healthcare settings and how different patients may be treated depending on gender identity. In a study examining the experiences of women seeking care for pain, when providers did not give any diagnoses, women typically reported feeling that their bodily self-knowledge was dismissed and their symptoms were attributed to psychosomatic causes (Braksmajer 2018). In a study that examined trends in cardiovascular health over time by race and sex, there were consistent disparities in cardiovascular health for non-Hispanic Black and Mexican-American women as compared with non-Hispanic White women, showing more than just gender discrimination (Pool et al. 2017). These highlight a gap in acknowledging the pain experiences of those who identify as women.

Men also experience bias in the healthcare setting for symptom acknowledgement, such as with fibromyalgia (FM), a serious condition that affects approximately four million people in the United States, and remains historically underdiagnosed in men. In a study

seeking to understand the multiple impacts of fibromyalgia on men in regard to interactions in society and the U.S. health system, thematic analyses showed that men with FM have negative experiences with their physical and mental health, quality of life, relationships, and careers as a result of FM (Muraleetharan et al. 2018). Thus, the first step to acknowledging this gap in evaluating every patient more comprehensively should initially include a validation of the patient's pain and associated mental health (Braksmajer 2018).

Rationale

In terms of financial impact, pain is a major factor affecting psychological stress in workers, and the cost of pain-related lost productivity ranged from an estimated $299 billion to $335 billion in the United States alone (Sakamoto et al., 2019). This makes the annual cost of pain greater than lifestyle diseases (such as heart disease, cancer, diabetes), which are more commonly perceived to have larger economic losses. Chronic pain treatments and opiate abuse have been a topic for decades, but until the underlying mechanisms of pain are understood, outcomes and patient experiences are unlikely to change.

For this project in particular, it could be informative for health care providers and educators to better understand how deeply imbedded into general health and quality of life the impact of anxiety and chronic pain can be and why they should not be treated independently. Patients who are in chronic pain often struggle with daily life and social activity, which are often attributed to anxiety. The two have a complex relationship, and considerations of health disparities and biases further confound this. Hopefully, data obtained by this study could lead to better patient treatment options and experiences, higher quality of life despite the chronic pain, and lower costs annually.

Objectives

The objective of this project is to investigate the relationship between chronic pain and anxiety diagnosis. Without the insight into the underlying permanent changes and dysfunction that may occur biologically, treatment options and success of treatment will continue to be lacking. The secondary objective is to look at whether or not these factors influence migraine occurrence. It was hypothesized that a relationship would exist between anxiety and migraine. Gender differences were also examined.

Methods

This study was completed in an online, electronic setting as a retrospective analysis utilizing existing literature and data. Article screening criteria focused on adversity, trauma outcomes, comorbidities, chronic illness, and neuroanatomical changes due to trauma, anxiety, and stress. The primary database used for this analysis was the PROMIS Profiles-HUI. The published literature was collected via PubMed, the CDC, and the PROMIS database. Primary studies, in English, which investigated patients with a history of anxiety as well as papers exploring the outcomes of trauma, stress, and chronic pain, were included. Publication bias was evaluated, and sensitivity analyses were conducted to ensure data quality.

This study aimed to confirm a relationship between anxiety and chronic pain. Prior research results confirm similar correlations, such as between trauma and emotional issues, or stress and hippocampal volume changes in the brain. In addition, a further relationship between anxiety and migraine was examined. The target project population specifics included:

- Adults who experience chronic pain (with or without anxiety)
- Subjects for inclusion were adults 18 years of age and older
- Exclusion Criteria were subjects less than 18 years of age

Data Collection

The dataset used for this retrospective study was the "ReCenter Patient-Reported Outcomes Measurement Information System (PROMIS®)", a data source compiled using the Health Utilities Index, PROMIS Global items, and the PROMIS profiles, which assessed fatigue, physical function, depression, anxiety, ability to participate in social roles and activities, sleep disturbance, pain interference, and pain intensity. Additional PROMIS items from each bank were also included (Hays et al., 2016). PROMIS data was collected between 2015-2016, with a recruitment sample of 3000 randomly selected adults (18 or older) who completed an online survey on a diverse range of health measures.

Information on participants who selected yes or no for anxiety diagnosis were included, as well as variables for chronic pain measurement (pain interference, pain interfered with social life, are any of your activities inhibited by migraine, rate of pain on average, pain level now to pain level at worst). Demographics on reported gender were also

considered. Information on other conditions will not be included, since the focus is on anxiety and pain and this study is limited in its scope and time.

The time range of this study was roughly 4 months (August 2019 to December 2019). Data extraction was completed by the first week of October, and the data was synthesized at the end of October. Results and conclusions were summarized by November, and the final report was done by mid-December of 2019.

Analysis Methods

Variables

Primary:

- Dependent variable: Diagnosed with anxiety, not diagnosed with anxiety (Qclinic01a, 16)
- Independent variables include the following 5 pain measures:
    - How intense is your average pain? (QPAINQU8, scale is 1-5, no pain to severe)
    - In the last 7 days, how much did pain interfere with your enjoyment of life? (QPAININ3, scale is 1-5, not at all to very much)
    - In the past 7 days, how often did you feel emotionally tense because of your pain? (QPAININ11r1, scale 1-5, never to always)
    - In the past 7 days, how much did pain interfere with your ability to participate in social activities? (QPAININ31, 1-5, not at all to very much)
    - In the past week, how would you rate your overall health? (QHUI16, 1-5, poor to excellent)

Secondary:

- For those with/without anxiety, how many experienced migraines (Qclinic01a_16), and does it compare to primary results when including additional factors?

An additional comparison of reported gender (Qsocio03) and age (Qsocio02) was included for both.

Sample size

3000 randomly selected adults, age 18 or over. Target amounts for diversity in the sample were met, both for race and age. 1458 participants were male, 1542 were female.

Data Analyses

A logistic regression model was performed for the primary objective due to its binary dependent variable and multiple (5) independent variables. Some of the independent variables are 1 to 5 in terms of least to worst, and others were coded as least to great. Additional covariates were examined to confirm these associations and show potential differences. SAS statistical software was used. The independent variable was anxiety/no anxiety, and the dependent variables were five different pain measures.

Data Protection

Databases from the CDC are protected by Public Law 107-174 (No FEAR Act). All data relevant to this project is stored on a password protected laptop that is locked up when not in use, and is only accessible to myself (as the acting study staff). No personal identifiers are present in the data used.

Results

A total of 3000 randomly selected adults (18 or older) were recruited and completed the PROMIS survey. Of these, a reported 1458 identified as male, 1542 female. It was hypothesized that participants with anxiety would experience more pain measures than participants without anxiety. Additionally, anxiety and migraine were assessed with covariates in mind.

Reporting as female increased the odds of anxiety by 39.9%, holding the rest of the variables constant. Age was negatively correlated with the presence of anxiety; for every unit increase in age there was a corresponding 2.2% decrease in the odds of reporting anxiety.

For examining migraine, women had twice the odds of reporting migraine compared to men. There was no significant relationship to age regarding migraine occurrence.

Table 1: Original logistic regression analysis results

Parameter	Estimate	Standard Error	Chi-Square	Pr > ChiSq	Odds Ratio (95% CI)
Intercept	-0.8156	0.2588	9.9292	0.0016	-
QPAINQU8	-0.0313	0.0640	0.2391	0.6249	0.969 (0.855, 1.099)
QPAININ3	0.0266	0.0636	0.1750	0.6757	1.027 (0.907, 1.163)
QPAININ11r1	0.3214	0.0610	27.7109	<.0001	1.379 (1.223, 1.554)
QPAININ31	-0.0828	0.0607	1.8580	0.1729	0.921 (0.817,1.037)
QHUI16	-0.3233	0.0503	41.2455	<.0001	0.724 (0.656, 0.799)

Of the five dependent variables, only the experience of emotional tension as a result of pain (QPAININ11r1) and overall health (QHUI16) were statistically significant in regard to the dependent variable of anxiety status.

The odds ratio of 1.379 indicates that for every unit increase in the pain scale (emotional tension), there was a corresponding 37.9% increase in odds of having anxiety, with all the other variables held constant. This means that of the 5 independent variables, experiencing pain due to emotional tension was the most significant potential association with having an anxiety diagnosis.

There was a negative association between anxiety and overall health, with the odds ratio estimate being 0.724. The inverse of this odds ratio (1/0.724 = 1.381) means that for every unit increase in overall health there is a corresponding 38.1% increase in odds of not having anxiety, holding the rest of the variables constant.

Table 2: Additional covariates (age and gender) analysis results

Parameter	Estimate	Standard Error	Chi-Square	Pr > ChiSq	Odds Ratio (95% CI)
Intercept	-0.4036	0.5238	0.5939	0.4409	-
Qsocio03	-0.1369	0.0489	7.8405	0.0051	0.459 (0.368, 0.571)
Qsocio02	-0.0181	0.00325	31.1730	<.0001	0.993 (0.987, 1.000)

Women had a higher incidence of anxiety, with 362 out of 1541 (or 23.49%) reported to have diagnosed anxiety. Men had 281 out of 1458 (or 19.27%) reported to have anxiety. Adjusting for the covariates in the model, we observed similar results to the primary objective model without the covariates.

Anxiety diagnosis was still statistically associated with two variables in the model at 95% confidence level: the presence of emotional tension because of pain, and overall health.

There was a positive association with anxiety and pain (emotional tension). The odds ratio of 1.346 indicated that for every unit increase in the pain scale (emotional tension), there was a corresponding 34.6% increase in odds of having anxiety, with all the other variables held constant.

There was still a negative association between anxiety and overall health. As with the original model, the remaining 3 independent variables were not statistically significant.

Table 3: Migraine analysis results

Parameter	Estimate	Standard Error	Chi-Square	Pr > ChiSq	Odds Ratio (95% CI)
Intercept	-1.4253	0.1421	100.6566	<.0001	-
Qclinic01a_16	-0.4435	0.0551	64.8484	<.0001	0.412 (0.332, 0.511)
Qsocio03	-0.3981	0.0535	55.4068	<.0001	0.451 (0.366, 0.556)
Qsocio02	-0.00209	0.00294	0.5042	0.4777	0.998 (0.992, 1.004)

Based on the results from this logistic regression model, migraine prevalence (Qclinic01a_16) is significantly associated with anxiety prevalence. In the model, the odds ratio for migraine (yes) vs anxiety (no) is 0.412. Getting the inverse of the odds ratio (1/0.412 = 2.427), suggests the odds of having migraine increased almost 2.5 times among people who suffer from anxiety, versus those who do not, even with age and gender held constant.

The reported gender covariate also emerged significant in the model, with odds ratio of 0.451. Getting the inverse of the odds ratio (1/0.451 = 2.217), and reversing our reference category to women, we can say that women have twice the odds of reporting migraine compared to men, with all the other variables held constant, highlighting a substantial burden for women in healthcare settings and general quality of life.

Discussion

There were some limitations to this study. Weaknesses/issues can occur with:

- Combining the findings of different countries, due to varied and different levels of comprehension across translated questioning, particularly in health-related terminology (such as more nuanced measures of pain)

- Bias from the available literature relevant to this study. This occurs because researchers tend to publish studies that show a significant effect and may not take the time to write up negative findings

For the primary objective, the results were mixed. For overall health and emotional tension caused by pain, there was an association with anxiety diagnosis. However, the remaining three pain variables (Average Pain, Interference on Social Activity, and Interference on Enjoyment) were not statistically associated with anxiety. This was still included in the added covariates analysis, however, because it was deemed important to help contextualize the analysis results and to examine possible gender differences.

When examining migraine prevalence in those with or without anxiety, having migraine could indeed be inferred to have a relationship with concurrent anxiety diagnosis. This was even stronger for patients reported as female. Overall, there were some inferable associations between pain experiences and anxiety, particularly when considering gender.

Based on the logistic regression performed, Anxiety Diagnosis was statistically associated with two variables at the 95% confidence level (Emotional Tension and Overall Health), but not with the other three (Average Pain, Interference on Social Activity, and Interference on Enjoyment). This means that of the 5 independent variables, feeling emotionally tense due to pain had the most significant association with having anxiety. Overall health being better was correlated most strongly with not having anxiety.

For migraine, the odds of having migraine increased almost 2.5 times among people who suffer anxiety compared to those without, even when age and gender were held constant. While each analysis result addressed the research questions and objectives, not every variable was significant. Still, it felt important to include the non-significant variables in the follow-up covariates to further test for possible associations that may have existed when looking exclusively at age or gender.

These results provide useful insight into future research objectives, which could look more closely into the impact of anxious or emotional tension in the body and daily pain issues when making healthcare treatment decisions and in general patient screening. If pain impact has more to do with having anxiety than with the chronic pain itself, treatment approaches could shift dramatically based on this new information and better assessments could be implemented to address the issue more comprehensively—inclusive of anxiety and pain together as opposed to independently. In addition, migraine and anxiety could be

examined for their association to chronic pain and patient quality of life. The noted differences in reported gender also highlight the need for treatment approaches to address the potential gender differences in experiencing and feeling pain.

Conclusion

The results of this study highlight a need to examine the gender differences not only in pain experience, but also in the physical symptoms of anxiety. It is possible that the combination of migraine and anxiety diagnosis influence chronic pain interference in overall quality of life and health of patients presenting with pain.

References

Braksmajer A. (2018) Struggles for medical legitimacy among women experiencing sexual pain: A qualitative study. *Women Health*. Apr;58(4):419-433. doi: 10.1080/03630242.2017.1306606.

Brown, R. C., Plener, P. L., Braehler, E., Fegert, J. M., & Huber-Lang, M. (2018). Associations of adverse childhood experiences and bullying on physical pain in the general population of Germany. *Journal of pain research*, *11*, 3099–3108. doi:10.2147/JPR.S169135

Capobianco, A. , Cottone, L. , Monno, A. , Manfredi, A. A. and Rovere-Querini, P. (2017), The peritoneum: healing, immunity, and diseases. *Journal of Pathology*, 243: 137-147. doi:10.1002/path.4942

Cella, David. (2017) "PROMIS Profiles-HUI data", https://doi.org/10.7910/DVN/P7UKWR, Harvard Dataverse, V1

Crocq M. A. (2015) A history of anxiety: from Hippocrates to DSM. *Dialogues in clinical neuroscience,* 17(3), 319–325.

Diagnostic and Statistical Manual of Mental Disorders (2013). 5th ed. Arlington, VA: *American Psychiatric Association.*

Du, H. X., Chen, X. G., Zhang, L., Liu, Y., Zhan, C. S., Chen, J., … Liang, C. Z. (2019) Microglial activation and neurobiological alterations in experimental autoimmune prostatitis-induced depressive-like behavior in mice. *Neuropsychiatric disease and treatment*, *15*, 2231–2245. doi:10.2147/NDT.S211288

Gentili, C., Rickardsson, J., Zetterqvist, V., Simons, L. E., Lekander, M., & Wicksell, R. K. (2019) Psychological Flexibility as a Resilience Factor in Individuals with Chronic Pain. *Frontiers in psychology*, 10, 2016. doi:10.3389/fpsyg.2019.02016

Gu, Damin, Zhou, Minmin, Han, Chao, Lei, Daoyun, Xie, Songhui, Yuan, Yanbo, & Ma, Tieliang. (2019) Preoperative anxiety induces chronic postoperative pain by activating astrocytes in the anterior cingulate cortex region. *Revista da Associação Médica Brasileira, 65(9), 1174-1180*. Epub October 10, 2019. https://dx.doi.org/10.1590/1806-9282.65.9.1174

Harvie, D., Broeker, M., Smith, R., Meulders, A., Madden, J., & Moseley, G.L. (2014) Bogus visual feedback alters movement-evoked pain onset in people with neck pain. *Psychological science.* 26(4):385-92. https://doi.org/10.1177%2F0956797614563339

Hays, Ron D., et al. (2016) Using Linear Equating to Map PROMIS® Global Health Items and the PROMIS-29 V2.0 Profile Measure to the Health Utilities Index Mark 3. *PharmacoEconomics* 34.10: 1015-1022. doi: 10.1007/s40273-016-0408-x

Muraleetharan D, Fadich A, Stephenson C, Garney W. (2018) Understanding the Impact of Fibromyalgia on Men: Findings From a Nationwide Survey. *American Journal of Men's Health*. Jul;12(4):952-960. doi: 10.1177/1557988317753242.

Olugbade, T., Bianchi-Berthouze, N., & Williams, A. (2019) The relationship between guarding, pain, and emotion. *Pain reports*, *4*(4), e770. doi:10.1097/PR9.0000000000000770

Sakamoto, Y., Oka, T., Amari, T., and Simo, S. (2019) Factors Affecting Psychological Stress in Healthcare Workers with and without Chronic Pain: A Cross-Sectional Study Using Multiple Regression Analysis. *Medicina*, 55(10), 652; https://doi.org/10.3390/medicina55100652