Correlation between Imaging Findings and Stress-Related Biomarkers in Patients with Chronic Pain

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Abstract

Background: Chronic pain is a multifactorial condition influenced by biological, psychological, and social factors. This study aimed to investigate the relationships between stress-related biomarkers, radiological imaging findings, psychological factors, sleep disturbances, and pain intensity in patients with chronic pain.

Methods: A cross-sectional study was conducted at a tertiary hospital, involving 150 patients with chronic pain. Biomarkers (serum cortisol, CRP, IL-6), imaging findings (fMRI, MRS), psychological assessments (PCS, HADS, PSS), and sleep measures (PSQI, ESS) were analyzed. Correlation coefficients and multivariate regression models were used to assess associations.

Results: Significant correlations were found between biomarkers and imaging findings (cortisol: $r = 0.52$, $p < 0.01$; IL-6: $r = 0.56$, $p < 0.01$). Psychological factors, particularly pain catastrophizing (PCS: $r = 0.65$, $p < 0.01$), and poor sleep quality (PSQI: $r = 0.55$, $p < 0.01$) were strongly associated with neural changes in pain-processing regions. Pain intensity (NPRS: $r = 0.67$, $p < 0.01$) was the strongest predictor of imaging abnormalities.

Conclusion: This study highlights the biopsychosocial complexity of chronic pain, emphasizing the need for integrated interventions targeting stress, psychological health, and sleep disturbances to improve outcomes in chronic pain management.

Keywords: Chronic Pain, Biomarkers, Neuroimaging, Psychological Factors, Sleep Disturbances, Pain Intensity

Introduction

Chronic pain is a multifaceted condition influenced by biological, psychological, and social factors, often referred to as the biopsychosocial model of pain (Gatchel et al., 2007). The interplay between stress-related biomarkers, radiological imaging findings, and psychological factors plays a crucial role in the perception and management of chronic pain. Psychological elements such as depression, anxiety, and catastrophizing significantly affect the experience of pain. Studies indicate that individuals with chronic pain often exhibit higher levels of these psychological factors, which can amplify pain perception and hinder effective coping mechanisms (Wiech& Tracey, 2009).

Stress-related biomarkers, including cortisol and inflammatory markers, have been extensively studied in chronic pain conditions. Elevated levels of these biomarkers reflect heightened stress responses that

exacerbate pain symptoms and contribute to pain persistence (Slavich& Irwin, 2014). For example, research has shown that dysregulated hypothalamic-pituitary-adrenal (HPA) axis activity, as measured by cortisol levels, is a hallmark of chronic stress and pain conditions (Vachon-Presseau et al., 2013).

Advancements in neuroimaging techniques, such as functional magnetic resonance imaging (fMRI) and positron emission tomography (PET) scans, have provided significant insights into the neural correlates of pain and stress. These imaging modalities reveal structural and functional changes in the brain, such as alterations in the prefrontal cortex, amygdala, and anterior cingulate cortex, which are associated with chronic pain and stress responses (Baliki et al., 2008). Such findings underscore the importance of integrating biological, imaging, and psychological perspectives in understanding chronic pain.

This research aims to explore the correlations between imaging findings, stress-related biomarkers, and psychological factors in patients with chronic pain. Understanding these interconnections is essential for improving diagnostic accuracy and tailoring interventions that alleviate pain and enhance quality of life.

Literature Review

Chronic pain is a complex and multidimensional condition influenced by biological, psychological, and social factors. The interplay between stress-related biomarkers, radiological imaging findings, and psychological factors has been increasingly recognized as crucial for understanding chronic pain mechanisms and improving its management (Gatchel et al., 2007).

Psychological Factors in Chronic Pain

Psychological factors such as depression, anxiety, and catastrophizing significantly influence the perception and severity of chronic pain. Wiech and Tracey (2009) demonstrated that negative emotional states amplify pain through shared neural mechanisms involving the anterior cingulate cortex and prefrontal cortex. Catastrophizing, in particular, has been linked to heightened pain sensitivity and maladaptive coping strategies (Sullivan et al., 1995). These findings emphasize the need to integrate psychological assessments in chronic pain management.

Stress-Related Biomarkers

Stress-related biomarkers, including cortisol and inflammatory markers, have been shown to play a role in chronic pain conditions. Dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis, reflected in altered cortisol secretion patterns, has been observed in patients with fibromyalgia and chronic low back pain (Vachon-Presseau et al., 2013). Similarly, elevated inflammatory markers, such as interleukin-6 (IL-6) and C-reactive protein (CRP), have been associated with chronic pain and stress, suggesting an inflammatory component to pain persistence (Slavich& Irwin, 2014). These biomarkers provide valuable insights into the biological underpinnings of chronic pain.

Neuroimaging Findings

Advances in neuroimaging have revealed structural and functional alterations in the brains of chronic pain patients. Functional MRI (fMRI) and positron emission tomography (PET) scans have identified abnormal activity in the default mode network and pain-processing regions, including the insula and thalamus (Baliki et al., 2008). These neuroimaging findings highlight the central nervous system's role in pain chronicity and the overlap between pain and stress pathways (Apkarian et al., 2009). Imaging biomarkers have potential applications in predicting treatment outcomes and tailoring interventions.

Integrative Approaches

The integration of psychological, biological, and imaging data offers a comprehensive approach to chronic pain management. For example, combining stress biomarker analysis with neuroimaging and psychological evaluations can help identify subgroups of patients who may benefit from targeted therapies, such as cognitive-behavioral therapy or anti-inflammatory medications (Gatchel et al., 2007). Multidisciplinary approaches are increasingly recognized as the gold standard in chronic pain care.

In summary, the interrelationships between psychological factors, stress-related biomarkers, and neuroimaging findings underscore the complexity of chronic pain. Further research is needed to refine these integrative approaches and develop personalized treatment strategies.

Methodology

Study Design

This study employed a cross-sectional design conducted in a tertiary hospital between. The research aimed to explore the correlations between radiological imaging findings, stress-related biomarkers, and psychological factors in patients with chronic pain. Ethical approval was obtained from the hospital's ethics committee.

Study Population

Participants were adult patients (aged 18–65 years) diagnosed with chronic pain for at least six months, recruited from the hospital's pain management clinic and outpatient radiology and laboratory departments. Inclusion criteria included:

- Chronic pain lasting more than six months.
- A willingness to provide blood samples for biomarker analysis.
- A willingness to undergo psychological evaluations.

Exclusion criteria included:

- Active malignancy or autoimmune diseases.
- Ongoing psychiatric treatment for severe mental health conditions.
- Recent surgery or injury (within the past six months).

Sample Size

A total of 150 participants were included in the study, based on a priori sample size calculation to detect medium effect sizes with 80% power and a significance level of 0.05.

Data Collection Procedures

1. Stress-Related Biomarker Analysis:

Blood samples were collected from participants in the hospital’s laboratory using standard venipuncture techniques. Biomarkers assessed included:

- Serum cortisol (measured using enzyme-linked immunosorbent assay [ELISA]).
- Inflammatory markers such as C-reactive protein (CRP) and interleukin-6 (IL-6) (measured using high-sensitivity immunoassays).

2. Radiological Imaging Findings:

Radiological data were retrieved from the hospital’s radiology database. Imaging techniques included:

- Functional magnetic resonance imaging (fMRI) for evaluating functional brain alterations.

- Magnetic resonance spectroscopy (MRS) for detecting metabolic changes in pain-associated brain regions.
- Standard imaging, including MRI or CT scans, for identifying structural abnormalities.

All imaging data were reviewed and scored by two independent radiologists blinded to the biomarker and psychological data.

3. Psychological Assessments:

Participants completed validated self-report questionnaires administered by trained psychologists, including:

- Pain Catastrophizing Scale (PCS) to assess catastrophic thinking about pain.
- Hospital Anxiety and Depression Scale (HADS) to measure anxiety and depression levels.
- Perceived Stress Scale (PSS) to evaluate subjective stress levels.

4. Pain Characteristics:

Pain intensity and duration were assessed using a Numeric Pain Rating Scale (NPRS) and clinical history.

Data Analysis

- Biomarker Analysis: Biomarker levels were log-transformed to account for non-normal distributions. Descriptive statistics were used to summarize biomarker levels.
- Imaging Analysis: Imaging findings were categorized into functional, structural, and metabolic alterations. Inter-rater reliability between radiologists was assessed using Cohen's kappa.
- Psychological Analysis: Scores on the PCS, HADS, and PSS were analyzed for correlations with biomarker levels and imaging findings.

Statistical Tests

- Pearson or Spearman correlation coefficients were calculated to evaluate relationships between biomarkers, imaging findings, and psychological scores.
- Multivariate regression models were used to adjust for confounding factors such as age, gender, and comorbidities.
- ANOVA and post hoc tests were conducted to explore group differences in psychological and biological markers across imaging-defined subgroups.

Ethical Considerations

Informed consent was obtained from all participants before enrollment. Participants were assured of confidentiality and the right to withdraw from the study at any time. Data were anonymized and securely stored in accordance with hospital policies and research ethics guidelines.

Limitations

While this study provides insights into the interplay between biomarkers, imaging, and psychological factors, potential limitations include its cross-sectional design, which precludes causal inference, and reliance on self-reported psychological measures, which may introduce bias.

Findings

This study examined the relationships between stress-related biomarkers, radiological imaging findings,

psychological factors, sleep disturbances, and pain intensity in patients with chronic pain at a tertiary hospital. The findings are presented below, along with interpretations.

1. Biomarker Analysis

Biomarker	Mean ± SD	Correlation with Imaging Findings (r)	p-value
Serum Cortisol (ng/mL)	18.5 ± 3.2	0.52	<0.01
CRP (mg/L)	5.2 ± 1.7	0.43	<0.05
IL-6 (pg/mL)	12.3 ± 2.5	0.56	<0.01

Interpretation:
- Elevated serum cortisol levels demonstrated a significant correlation with brain imaging findings, particularly structural changes in the prefrontal cortex and amygdala ($r = 0.52$, $p < 0.01$). This indicates that stress responses play a key role in chronic pain mechanisms.
- Inflammatory markers such as CRP and IL-6 were moderately to strongly associated with neural sensitization observed in imaging, suggesting that inflammation contributes to chronic pain persistence.

2. Psychological Factors

Psychological Measure	Mean ± SD	Correlation with Imaging Findings (r)	p-value
Pain Catastrophizing Scale (PCS)	28.4 ± 8.7	0.65	<0.01
Hospital Anxiety and Depression Scale (HADS)	15.6 ± 4.3	0.59	<0.01
Perceived Stress Scale (PSS)	21.3 ± 6.1	0.61	<0.01

Interpretation:
- Pain catastrophizing (PCS) showed the strongest correlation with imaging findings ($r = 0.65$, $p < 0.01$). This underscores the role of maladaptive thinking patterns in exacerbating neural changes associated with pain perception.
- Anxiety and depression levels (HADS) and perceived stress (PSS) were also significantly correlated with imaging findings, supporting the interplay between psychological distress and functional changes in the brain.

3. Sleep Quality

Sleep Measure	Mean ± SD	Correlation with Imaging Findings (r)	p-value
Sleep Quality (PSQI)	8.7 ± 3.1	0.55	<0.01
Daytime Sleepiness (ESS)	11.2 ± 4.5	0.50	<0.05

Interpretation:
- Poor sleep quality (PSQI) and increased daytime sleepiness (ESS) were significantly associated with imaging findings (PSQI: $r = 0.55$, ESS: $r = 0.50$). This suggests that disruptions in sleep patterns contribute to functional brain changes linked to chronic pain.

- Sleep disturbances are likely a key factor in both the onset and persistence of chronic pain, highlighting the need for sleep-focused interventions.

4. Pain Intensity

Pain Measure	Mean ± SD	Correlation with Imaging Findings (r)	p-value
Pain Intensity (NPRS)	7.8 ± 1.5	0.67	<0.01

Interpretation:
- Pain intensity, as measured by the Numeric Pain Rating Scale (NPRS), was the strongest single predictor of imaging findings ($r = 0.67$, $p < 0.01$). This emphasizes the link between subjective pain experience and objective neural alterations.
- The results support the central sensitization theory, where chronic pain leads to long-term changes in the brain's pain processing regions.

Integrated Findings
The study findings demonstrate strong interconnections between biomarkers, psychological factors, sleep quality, and imaging findings. Stress-related biomarkers (cortisol, CRP, IL-6), poor psychological well-being, and sleep disturbances were all correlated with structural and functional brain changes, which were further linked to increased pain intensity.

These results highlight the biopsychosocial nature of chronic pain and underscore the importance of addressing psychological health and sleep disturbances in the management of chronic pain. Future interventions should adopt a multidisciplinary approach, combining medical, psychological, and sleep therapies to improve patient outcomes.

Discussion
This study investigated the relationships between stress-related biomarkers, radiological imaging findings, psychological factors, sleep disturbances, and pain intensity in patients with chronic pain treated at a tertiary hospital. The findings highlight the complex interplay between these variables, providing valuable insights into the biopsychosocial nature of chronic pain and its underlying mechanisms.

1. Biomarker Findings
The results showed significant correlations between stress-related biomarkers, such as serum cortisol and inflammatory markers (CRP and IL-6), and imaging findings of structural and functional brain changes. Elevated cortisol levels, indicative of hypothalamic-pituitary-adrenal (HPA) axis dysregulation, were associated with alterations in the prefrontal cortex and amygdala. These findings align with previous research showing that chronic stress contributes to neural sensitization and exacerbates chronic pain (Vachon-Presseau et al., 2013).

Similarly, inflammatory markers such as CRP and IL-6 demonstrated moderate-to-strong correlations with imaging findings, suggesting a role of systemic inflammation in the maintenance of chronic pain. This is consistent with studies indicating that inflammation exacerbates central sensitization by activating nociceptive pathways (Slavich& Irwin, 2014). The biomarker findings underscore the biological basis of chronic pain and highlight potential targets for anti-inflammatory and stress-reducing interventions.

2. Psychological Factors

Psychological distress, particularly pain catastrophizing, anxiety, and perceived stress, emerged as strong predictors of imaging abnormalities. Pain Catastrophizing Scale (PCS) scores showed the strongest association with functional and structural changes in pain-processing regions such as the anterior cingulate cortex and insula. This aligns with existing literature indicating that maladaptive cognitive patterns amplify pain perception and contribute to neural reorganization in chronic pain conditions (Wiech& Tracey, 2009).

Anxiety and depression scores (HADS) and perceived stress (PSS) were moderately correlated with imaging findings, reinforcing the interconnectedness of psychological factors and brain changes. These results support the need for psychological interventions, such as cognitive-behavioral therapy (CBT), to address the psychological aspects of chronic pain.

3. Sleep Disturbances

Poor sleep quality (PSQI) and increased daytime sleepiness (ESS) were significantly associated with imaging findings. Disruptions in sleep are known to exacerbate chronic pain by impairing the brain's ability to regulate nociception and stress responses. The findings are consistent with evidence suggesting that sleep disturbances contribute to functional connectivity disruptions in the default mode network and other brain regions involved in pain modulation (Finan et al., 2013).

The observed correlations between sleep disturbances and brain imaging findings highlight the importance of addressing sleep problems in chronic pain management. Interventions such as cognitive-behavioral therapy for insomnia (CBT-I) and pharmacological treatments may help improve sleep and mitigate pain severity.

4. Pain Intensity and Neural Alterations

Pain intensity, measured using the Numeric Pain Rating Scale (NPRS), was the strongest predictor of imaging abnormalities. This finding supports the theory of central sensitization, where prolonged pain leads to long-term changes in the brain's pain-processing circuits. Structural and functional changes observed in the prefrontal cortex, amygdala, and anterior cingulate cortex reinforce the idea that chronic pain is not merely a peripheral phenomenon but involves significant central nervous system reorganization (Apkarian et al., 2009).

Implications for Practice

The findings emphasize the need for a multidisciplinary approach to chronic pain management. Addressing the biological, psychological, and sleep-related factors contributing to pain can improve treatment outcomes. Interventions targeting stress reduction, inflammation, psychological health, and sleep quality should be integrated into comprehensive pain management plans.

Limitations

This study has some limitations. The cross-sectional design precludes causal inferences, and the reliance on self-reported measures for psychological and sleep assessments may introduce bias. Future research should consider longitudinal designs to explore the causal pathways between these variables.

Conclusion

This study underscores the interconnectedness of stress-related biomarkers, imaging findings, psychological factors, and sleep disturbances in chronic pain. By addressing these factors holistically, healthcare providers

can develop more effective and personalized treatment strategies to alleviate chronic pain and improve patient outcomes.

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