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ORIGINAL RESEARCH

Anxiety as a Psychological Modulator of Endogenous Pain Inhibition in Chronic Neck Pain: Implications for Precision Rehabilitation

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Objective: Chronic neck pain (CNP) is a highly prevalent musculoskeletal disorder with significant personal and socioeconomic impact. In conjunction with low back pain, CNP accounts for the highest healthcare expenditures in the United States and contributes to 3551 disability-adjusted life years per 100,000 population globally. This study explores the relationship between psychological factors and pain processing mechanisms, assessed through Quantitative Sensory Testing (QST), in individuals with CNP.

Design: Cohort study.

Setting: Hospital-based comprehensive outpatient rehabilitation center.

Participants: Forty-one adults diagnosed with nonspecific CNP who presented to physical therapy for initial examination.

Interventions: Not applicable.

Main Outcome Measures: Primary predictors were anxiety and pain catastrophizing; secondary predictors included demographics and self-reported pain and disability. Primary outcomes were central pain processing assessed via Quantitative Sensory Tests (QST) through measures of mechanical Pressure Pain Threshold (PPT) and Conditioned Pain Modulation (CPM).

Results: Generalized additive model analysis revealed a significant nonlinear association between anxiety and PPT (edf = 3.56, F = 3.25, p = 0.030), suggesting possible threshold effects. For CPM, the model explained 26.5% of deviance (adjusted R^2 = 0.155), with anxiety showing a significant linear association (edf = 1.00, F = 4.93, p = 0.036), indicating its role in altered pain modulation.

Conclusion: Our findings highlight anxiety as a key psychological factor influencing pain modulation in chronic neck pain. Targeting anxiety may enhance endogenous pain control, informing both preventive and therapeutic strategies. Early identification of anxiety in patient care may influence clinical decision-making, inform patient education and counseling strategies, as well as influence decisions regarding targeted preventive strategies, advanced imaging, procedural interventions, or referrals to specialty care.

Keywords: chronic neck pain, precision rehabilitation, quantitative sensory testing, conditioned pain modulation, pain processing, anxiety, pain catastrophizing

Introduction

Chronic neck pain (CNP) is defined as pain localized to the posterior cervical spine, with or without radiation to the head, trunk, or upper extremities, persisting for a minimum duration of three months.[1–3] Its pathogenesis involves a complex interplay of diverse contributory mechanisms, with its etiology further influenced by a combination of modifiable and nonmodifiable risk factors.[2,4] Extensive evidence has identified numerous risk factors for CNP, yet its incidence and prevalence continue to rise. This trend underscores persistent gaps in preventive, precision, and early-intervention strategies, with direct implications for both public health and patient outcomes.

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CNP is the most common adult musculoskeletal condition, affecting approximately 50% of the United States (US) population annually.[2,5,6] Individuals reporting more severe neck pain at initial onset demonstrate reduced recovery over time, with 62% of those initially classified as having moderate to severe symptoms continuing to report at least moderate pain after 30 months.[2,6–8] In 2016, neck and low back pain incurred the highest healthcare expenditure in the US, estimated at $134.5 billion.[3] Globally, it contributes to 3551 disability-adjusted life years per 100,000 population, with 25.5 million Americans absent from work by an average of 11.4 days.[5,7] These data highlight the persistent and recurrent nature of neck pain and its substantial impact on modern society, including diminished quality of life, increased healthcare utilization, and significant economic burden.[8–10] They further underscore the need for effective prevention, early intervention, proactive management, and community-based strategies to address modifiable risk factors in both public health and clinical contexts.

Because CNP presents a complex, multifactorial challenge, research has yet to sufficiently elucidate the neuropsychological mechanisms that contribute to both its etiology and treatment responsiveness. Previous meta-analyses have demonstrated that individuals with chronic pain frequently exhibit impaired conditioned pain modulation (CPM) compared with healthy controls, indicating consistent deficits in descending inhibitory function across pain populations.[11,12] Conditioned pain modulation is an endogenous analgesic mechanism in which one painful stimulus is inhibited by a second, spatially distinct noxious stimulus, mediated by descending modulatory circuits originating in supraspinal regions and projecting to the dorsal horn to suppress nociceptive transmission.[13–15] As a result, CPM reflects the balance of inhibitory and facilitatory processes in the descending pain pathway and serves as a clinically relevant biomarker of pain modulation capacity.[15–18] Emerging evidence suggests that psychological factors—particularly anxiety—modulate central pain processing by altering cortical excitability, monoaminergic tone, and autonomic/attentional states.[19,20] Furthermore, Lewis et al (2012) reported moderate to large effect sizes showing reduced CPM efficiency in chronic pain cohorts,[15,16] underscoring the relevance of psychological factors that interact with these inhibitory pathways. These neurobiological changes can weaken descending inhibitory control and manifest as reduced CPM in experimental and clinical samples.[15–20]

QST is a set of psychophysical measures, including CPM assessment, commonly used under clinical or experimental environment to directly evaluate the integrity of individual pain processing mechanisms.[14–16,21–23] Processing of pain input and experience is mediated at the anterolateral quadrant of the spinal cord, the thalamus, and the medial reticular formation of the brainstem through the direct lateral spinothalamic and the indirect medial spinoreticulothalamic pathways.[14,21,23] Although QST remains uncommon in routine clinical management due to its time-intensive nature and the need for trained personnel, its value for prognostication and outcome evaluation in chronic pain populations is increasingly recognized.[21,24–26]

The combined influence of psychological characteristics—such as anxiety and pain catastrophizing—and central pain processing mechanisms on health service needs in individuals with CNP remains poorly defined. Given these mechanistic links, we examined whether anxiety levels predict CPM efficiency in adults with CNP. Establishing this association is essential for integrating psychological assessment and pain processing metrics into mechanism-level evaluation and clinical decision making aimed at restoring efficient endogenous pain control. Our findings will further reinforce the rationale for focusing specifically on anxiety and pain catastrophizing, as these constructs demonstrate stronger and more consistent associations with CPM impairment than other psychosocial variables.[17,27–30]

Symptom driven interventions, coupled with the absence of consistently reliable and effective treatment strategies for nonspecific CNP, underscore the critical need for robust prevention and early intervention approaches. Prioritizing these strategies is essential to advance precision rehabilitation through individualized, patient-centered care and to mitigate the substantial socioeconomic burden associated with this prevalent public health condition. Bridging this gap is essential for developing holistic, evidence-informed clinical frameworks that enhance the precision and responsiveness of patient--centered care. The objective of this study is to investigate the role of psychological profile on pain processing mechanisms using QST in patients with CNP. We hypothesize that higher levels of anxiety are associated with reduced endogenous pain inhibition, as indexed by attenuated CPM, in adults under 65 years with CNP. Demonstrating this relationship will clarify how specific psychological characteristics relate to central pain-processing mechanisms and inform mechanism-informed rehabilitation strategies.

Methods

Participants

A cross-sectional cohort study was conducted using a convenience sample of 41 nonconsecutive patients with chronic neck pain (CNP) who presented for an initial physical therapy evaluation at the Cooperman Barnabas Medical Center (CBMC) Comprehensive Outpatient Rehabilitation Center. Participants were included if they presented with non-specific chronic neck pain, defined as pain persisting for more than 3 months without particular oncologic, immunologic, or metabolic attributes. Individuals were excluded if they had myelopathy, prior cervical surgery, inflammatory or autoimmune disease, fracture, malignancy, burn injuries, or progressive neuromuscular conditions that could account for their neck symptoms through a specific pathological mechanism. The study was conducted in accordance with the Helsinki Declaration. Patients who met the inclusion criteria and agreed to participate in the study provided written consent approved by the Cooperman Barnabas Medical Center (CBMC) Institutional Review Board (IRB ID #: 17–20; FWA00003433).

Assessment

The primary predictors were anxiety and pain catastrophizing profiles, selected based on prior evidence demonstrating their stronger and more consistent associations with CPM and descending inhibitory function compared with other psychosocial variables.[31,32] Meta-analytic findings, including Lewis et al (2012), support the relevance of these constructs in populations with impaired CPM.[15–17] Demographic and health-related characteristics, including self-reported pain and disability scores hypothesized to influence pain processing mechanisms, were included as secondary predictor variables. Primary outcome measures were indices of central pain processing mechanisms using QST through measures of mechanical Pressure Pain Threshold (PPT) and Conditioned Pain Modulation (CPM).

Data Collection

Eligibility screening and study enrollment were conducted by the Principal Investigator (PI) who is a licensed Physical Therapist in the States of New York/New Jersey with clinical training and research expertise in QST. Demographic and health-related information was collected via an intake form, including self-reported pain and disability scores using the Numeric Pain Rating Scale (NPRS) and the Neck Disability Index (NDI), respectively. Psychosocial variables involving anxiety and pain catastrophizing behaviors were assessed using the State–Trait Anxiety Inventory (STAI) Y-1 and the Pain Catastrophizing Scale (PCS), respectively. QST was used to evaluate individual pain processing mechanisms, consisting of mechanical PPT to quantify pain threshold and CPM to evaluate endogenous pain inhibition that reflects the analgesic integrity of the endogenous inhibitory pain modulation.

The participant eligibility screening and full QST testing protocol were conducted solely by the PI, a clinician and researcher with established expertise in QST. All procedures adhered to the standardized protocol developed by the German Research Network on Neuropathic Pain (Deutscher Forschungsverbund Neuropathischer Schmerz, DFNS).[10,11,15,23,33] The CPM assessment followed a temporal-summation–based paradigm consistent with DFNS methodological principles, incorporating controlled stimulus application, repeated measurements, and anatomical sites commonly used in CPM research to ensure methodological rigor.[10,11,23,27,33]

Experimental pain induction was performed with a calibrated digital pressure algometer seen in Figure 1 (Wagner Pain Test™ FPX 50, Pain Diagnostic Gage, Greenwich, CT, USA), consisting of a 1-cm^2 round rubber disk attached to a digital pressure gauge displaying values from 0 to 100 lb/cm^2. As seen in Figure 2, the PPT and CPM test site was the right upper trapezius muscle belly, halfway between its origin on the spinous process of the seventh cervical vertebra and its insertion on the acromion. Commonly applied for somatosensory characterization in diverse pain conditions, this test site demonstrates high reliability in neck pain populations, with a reported minimum detectable change of 0.48 kg/cm.[11,16,23,33] Figure 3 shows the Conditioned Pain Modulation (CPM) testing process using a digital pressure algometer and ischemic compression with a blood pressure cuff. The PPT and CPM assessments have excellent interrater reliability and high test–retest reliability.[11,16,26,27,33–35]

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Figure 1 Electronic pressure algometer used for experimental pain induction in pressure pain threshold and conditioned pain modulation testing.

Pressure Pain Threshold Assessment

The QST process started with mechanical PPT assessment to determine individual-level mechanical pain threshold. The test site was marked with an "X" using a skin marker to ensure consistency of experimental pain induction, with a one-minute rest period provided between each PPT measurement to avoid cutaneous sensitization. Subjects were instructed to say "STOP!" immediately after the pressure application becomes painful, indicating the pain threshold level was reached and at which point the pressure was removed and recorded. The average of three recorded measurements was calculated to derive the PPT score, which served as the applied pressure magnitude for the CPM protocol. To avoid sensitization from preceding pressure pain stimuli, the CPM protocol was administered five minutes following completion of PPT assessment.

Conditioned Pain Modulation (CPM) Assessment

Conditioned pain modulation (CPM) typically involves comparing responses to a standardized test stimulus before and during (or after) the application of a conditioning stimulus.[11,14,15,27,33] In this study, we used ischemic compression as the conditioning stimulus and mechanical pressure as the test stimulus. To induce ischemic pressure pain, a 14.5-cm inflatable cuff was placed on the left upper arm and inflated at 20 mmHg/s until reaching 200–240 mmHg or until the participant reported at least 4/10 pain on the NPRS. The ischemic compression was maintained for 60 seconds before full deflation. Immediately afterward, ten temporal-summation–based pressure pulses at each participant's pain-threshold level were delivered at a constant rate to the marked right trapezius site using a digital algometer.

Participants verbally rated the pain intensity of the first and tenth pulses. The absolute CPM value was calculated as the difference between the tenth and first pain ratings, as reported in Table 1. This temporal-summation–based approach is widely used in ischemic-compression CPM paradigms because it captures both the initial response and the facilitated response under identical stimulus conditions, thereby enhancing the reliability of inhibitory estimates.[10,11,15,16,23,33]

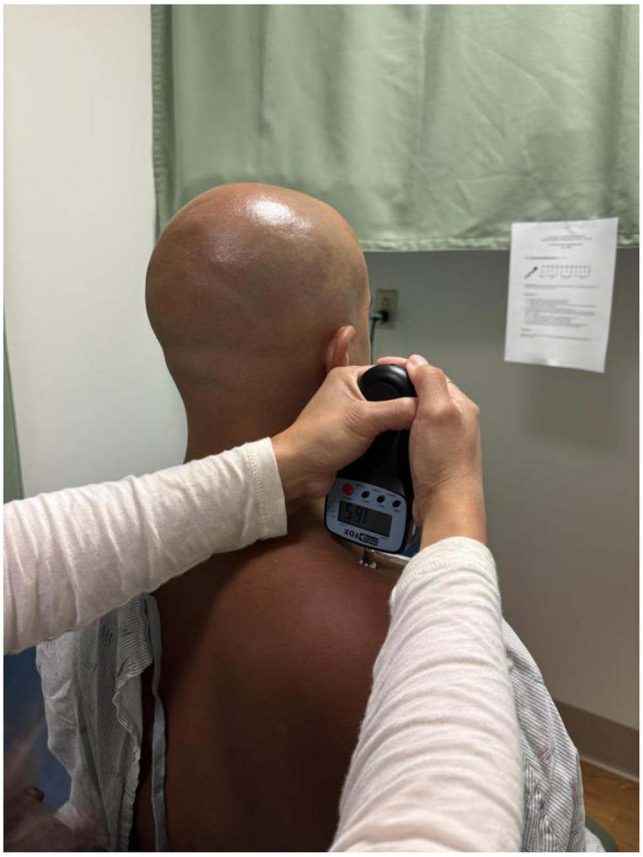

Figure 2 Mechanical pressure pain threshold (PPT) assessment using a digital pressure algometer to identify individual pain threshold as used for conditioned pain modulation testing.

Although the conditioning stimulus was applied before the pressure-pulse sequence, the resulting CPM effect still reflects the change in pain response between conditioned and unconditioned states, consistent with the conceptual definition of CPM.

Our methodology—combining ischemic compression with mechanical pressure testing across contralateral arm and shoulder regions—has demonstrated excellent inter- and intra-session reliability.[11,16,26,27] This is further supported by a recent meta-analysis by Nuwailati et al (2022), which identified this specific combination of test sites and stimulus modalities as producing the most reliable CPM outcomes.[11,27,35,36]

Analytic Approach

We employed a non-probabilistic convenience sampling strategy based on the clinical and logistical accessibility of patients who met the inclusion criteria and agreed to participate. As a result, formal sample size calculations were not performed, given the inability to determine an effect size with clear clinical relevance to support external validity. The final cohort was relatively homogeneous—supported by strict inclusion criteria and the use of a single PI as the sole examiner/rater—which aligns with methodological approaches used in similar studies and helps justify the smaller sample size and reduced variability.[37–39] Sample demographics and health-related outcomes are reported in Table 1. Our analytic approach focused on examining associations between psychological factors and QST outcomes to characterize our sample and align with our overarching study aim. Accordingly, we reported the absolute CPM values derived from the temporal-summation–based calculation rather than conducting statistical comparisons between the 1st and 10th pain ratings. This approach enabled us to replicate the expected pattern of reduced inhibitory capacity in individuals with chronic pain and ensured methodological consistency with prior literature demonstrating diminished functional CPM in chronic pain population.

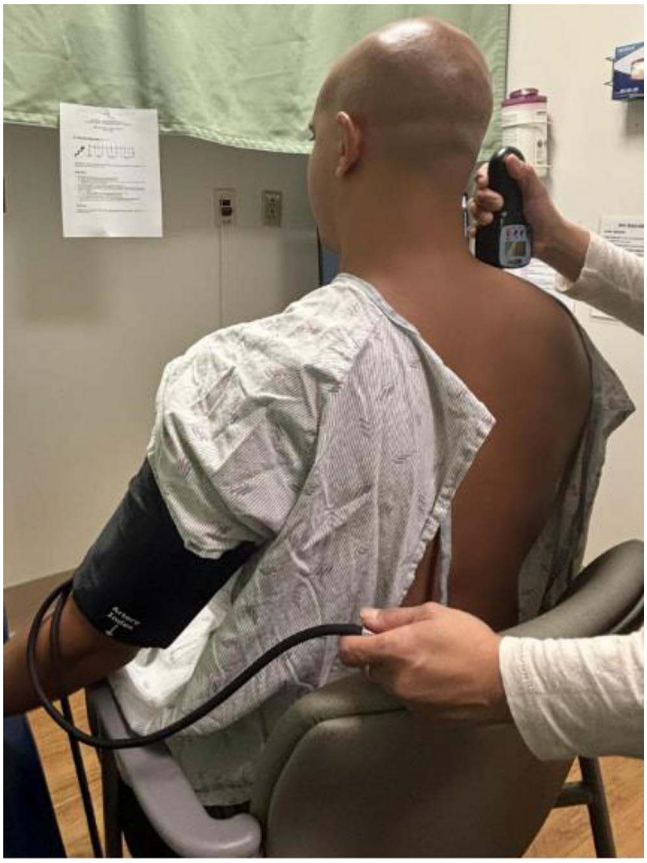

Figure 3 Conditioned pain modulation (CPM) testing using a digital pressure algometer and ischemic compression using a blood pressure cuff.

All statistical analyses were conducted using the R version (4.2.0) for Generalized Additive Modeling (GAM). Prior to analysis, all continuous predictor variables were centered to reduce multicollinearity and improve interpretability of the model intercepts. GAMs with thin plate regression splines were employed to examine potentially non-linear relationships between

Table 1 Demographic and Health-Related Measures of the Study Sample, Including Age, Sex/Gender, Race/Ethnicity, Average Pain Intensity, and Psychological Measures

Variable	Summary Median (Range)/N (%)
Demographic Factors	
Age (y)	46.7 (13.3)
Sex (Female)	29 (70)
Race	13 (32)
Black	16 (39)
White	12 (29)
Other	8 (20%)
Ethnicity (Hispanic)	
Health-Related Measures	
Pain Catastrophizing Scale (PCS) score	20.9 (13.3)
Neck Disability Index (NDI)	32.4 (16.9)
State Trait Anxiety Inventory (STAI) Form Y1	41.8 (11.6)
Conditioned Pain Modulation (CPM) scores	2.7 (2.4)*
Pain Pressure Threshold (PPT)	7.9 (4.9)*

Note: *unit measurement in lbs.
Abbreviations: NPRS, Numeric Pain Rating Scale; NDI, Neck Disability Index; STAI, State-Trait Anxiety Inventory; PCS, Pain Catastrophizing Scale; PPT, Pressure Pain Threshold; CPM, Conditioned Pain Modulation.

predictor variables and outcomes, allowing for greater flexibility in modeling complex associations. Separate GAMs were constructed for each outcome variable of interest: PPT and CPM. Predictor variables include the Neck Disability Index (NDI), State-Trait Anxiety Inventory (STAI Form Y1), Pain Catastrophizing Scale (PCS), and age. Each model included smooth terms for the continuous predictors, allowing the model to capture both linear and non-linear effects. Model fit was evaluated using adjusted R-squared values, deviance explained, generalized cross-validation (GCV) scores, and visual inspection of residual plots. Significance of smooth terms was assessed using approximate F-tests, with p-values < 0.05 considered statistically significant. Effective degrees of freedom (edf) were used to interpret the complexity of the smooth terms; edf values near 1 indicate approximately linear relationships, while higher values suggest non-linearity. All models were checked for influential outliers, and the results were reported as estimates with standard errors for parametric terms, and F-statistics with p-values for smooth terms.

We did not conduct subgroup analyses comparing participants with and without anxiety because the study was not powered for stratified analyses. Dividing the sample into categorical subgroups would have resulted in very small cell sizes, unstable parameter estimates, and an increased risk of Type II error. To preserve statistical power and retain the full variability of the construct, we modeled anxiety as a continuous variable. This approach avoids arbitrary cut-points, maintains model stability, and aligns with recommended analytic practices for psychological variables in pain-science research.[40–42]

Results

Effect of NDI, STAI, and Age on PPT

GAM was used to examine the nonlinear associations of NDI, STAI, and age on PPT. The overall model accounted for a substantial portion of the variance in PPT (*adjusted* $R^2 = 0.453$; deviance explained = 61.1%), indicating moderate model fit. Among the predictors, a significant nonlinear effect was observed for anxiety (*edf* = 3.56, $F = 3.25$, $p = 0.030$), suggesting that the relationship between anxiety and PPT is not linear and may involve threshold effects. Neither NDI (*edf* = 1.00, $p = 0.200$) nor age (*edf* = 4.13, $p = 0.118$) demonstrated statistically significant associations with PPT.

Effect of NDI, PCS, and Age on PPT

GAM was used to evaluate the nonlinear effect of NDI, PCS, and age on PPT. The model explained a meaningful proportion of variance in PPT (*adjusted* $R^2 = 0.451$; deviance explained = 67.9%), indicating a moderately good fit. However, none of the smooth terms reached statistical significance. Specifically, NDI (*edf* = 3.20, $F = 1.31$, $p = 0.315$), PCS (*edf* = 3.09, $F = 0.96$, $p = 0.577$), and age (*edf* = 6.16, $F = 1.93$, $p = 0.122$) were not significantly associated with PPT in this model. In contrast to anxiety, catastrophizing may have a weaker or more context-dependent role in pain sensitivity within this sample.

Effect of NDI, STAI, and Age on CPM

GAM was conducted to assess the nonlinear effects of NDI, STAI, and age on CPM. The model accounted for a modest proportion of variance in CPM (*adjusted* $R^2 = 0.155$; deviance explained = 26.5%), indicating a limited overall fit. Among the predictors, a significant effect was observed for anxiety level (*edf* = 1.00, $F = 4.93$, $p = 0.036$), suggesting a linear relationship in which increased anxiety was associated with altered pain modulation. NDI showed a nonlinear trend (*edf* = 1.50, $p = 0.114$), indicating potential curvilinear effects that may emerge with a larger sample. Age was not significantly associated with CPM (*edf* = 1.00, $p = 0.366$). These findings suggest that anxiety is a relevant psychological factor influencing pain inhibitory mechanisms and support further investigation into how neck disability may interact with anxiety in shaping individual pain modulation capacity.

Effect of NDI, PCS, and Age on CPM

GAM was used to examine the nonlinear associations between NDI, PCS, and age on CPM. The model explained a small portion of the variance (*adjusted* $R^2 = 0.083$; deviance explained = 24.6%), indicating a limited fit. None of the predictors demonstrated statistically significant effects: NDI (*edf* = 1.97, $p = 0.200$) and PCS (*edf* = 1.81, $p = 0.572$) both showed nonlinear trends, but these did not reach significance. Similarly, age showed no significant association with CPM (*edf* =

Table 2 Results of Generalized Additive Modeling (GAM) Analysis Across Predictor and Outcome Variables

Outcome Variables	Predictor Variables Included	Significant Predictors	Smooth Term (edf)	F-value	p-value	Adjusted R^2	Deviance Explained (%)	Model Interpretation
PPT	NDI, STAI, Age	STAI	STAI: 3.56	3.25	0.030*	0.453	61.1	Anxiety showed a significant nonlinear association with PPT, NDI and age were not significant.
PPT	NDI, PCS, Age	None	NDI: 3.20 PCS: 3.09 Age: 6.16	1.31 0.96 1.93	0.315 0.577 0.122	0.451	67.9	No predictors demonstrated significant nonlinear associations with PPT.
CPM	NDI, STAI, Age	STAI	STAI: 1.00	4.93	0.036*	0.155	26.5	Anxiety showed a significant (linear) association with CPM, NDI and age were not significant.
CPM	NDI, PCS, Age	None	NDI: 1.97 PCS: 1.81 Age: 1.00	—	0.200 0.572 0.840	0.083	24.6	No significant associations, nonlinear trends observed for NDI and PCS.

Note: *p < 0.05.

Abbreviations: NDI, Neck Disability Index; STAI, State-Trait Anxiety Inventory; PCS, Pain Catastrophizing Scale; PPT, Pressure Pain Threshold; CPM, Conditioned Pain Modulation; GAM, Generalized Additive Model; edf, estimated degrees of freedom.

1.00, $p = 0.840$). These findings suggest that, within the current sample, neither physical disability nor pain-related psychological processes were robust predictors of pain inhibitory function, though the presence of nonlinear trends warrants further investigation with a larger sample.

We assessed model linearity and confirmed substantial multicollinearity between anxiety and pain catastrophizing, consistent with prior literature, which further supported our decision to examine their associations with PPT and CPM in separate models.[40–42] Given our modest sample size and the risk of overfitting, we prioritized model parsimony to ensure more stable and interpretable estimates. Including both constructs in the same model would have reduced interpretability and compromised model stability.[40–42] Furthermore, simpler models—with fewer predictors—are particularly advantageous in non-linear regression frameworks such as GAMs, where multicollinearity can disproportionately inflate variance and obscure individual effects. By analyzing our predictor and outcome variables as separate models, we were able to isolate the unique contribution of each psychological factor to PPT and CPM. A summary of GAM results for each psychological variable is presented in Table 2.

Discussion

The results supported our hypothesis that maladaptive psychological profiles—specifically elevated anxiety—in individuals with CNP are associated with altered pain-processing mechanisms, reflected as impaired pain modulation. Our findings align with prior studies demonstrating a link between anxiety and diminished central pain modulation.[27,39,43] Importantly, this work advances existing literature by showing anxiety-related differences in pain modulation using objective, quantitative pain-processing metrics rather than subjective self-reported pain measures. This methodological shift provides new insight into the contributory pathophysiological mechanisms underlying CNP within a defined age-specific cohort. Clinically, reduced CPM in anxious patients may help explain greater pain sensitivity and poorer analgesic responses in some individuals.[39,43] Recognizing anxiety as a modulator of descending pain inhibition supports integrating psychological assessment and interventions (eg, anxiety-targeted cognitive behavioral training, relaxation, pharmacologic modulation of monoamines) when addressing impaired endogenous pain control.

Catastrophizing did not demonstrate significant associations in our sample despite prior literature reporting such effects. One possible explanation is that catastrophizing may exert task-specific influences that are more pronounced during prolonged or emotionally evocative pain tasks, rather than during brief mechanical stimuli such as PPT.[44] The relatively low variability in PCS scores within our cohort may also have contributed to the absence of significant

associations. In addition, recent work has reported inconsistent or attenuated relationships between catastrophizing and QST outcomes in musculoskeletal pain populations, suggesting that the association may not be uniform across pain modalities or clinical contexts.

Primary Findings

Across our models, anxiety levels (STAI) emerged as the most consistent psychological correlate of pain processing, particularly for mechanical PPT and CPM. In the model with PPT as an outcome measure, anxiety demonstrated a significant nonlinear association, suggesting the presence of threshold or saturation effects, whereby anxiety may exert minimal influence at low-to-moderate levels but markedly impact pain sensitivity once a certain threshold is exceeded. This pattern is consistent with previous work indicating that anxiety can amplify central sensitization processes and heighten pain perception through hypervigilance and attentional bias toward threat-related sensory cues.[43–45] Although prior studies have reported associations between disability, catastrophizing, and altered pain thresholds, recent work demonstrates that these relationships are not consistent across musculoskeletal pain populations.[46,47] Reviews of QST methodology and cross--sectional studies show that neither disability nor catastrophizing reliably correlates with PPT, likely due to high inter-individual variability and modality-specific differences in pain sensitivity.[11,13,14,46] These findings align with our observation that neither NDI nor PCS showed significant associations with PPT in our sample. This lack of significance might be attributable to our small sample size, sample characteristics, or interactions that our models could not fully capture.

In a model including CPM, anxiety further demonstrated a significant linear association, with higher anxiety levels corresponding to reduced pain inhibition capacity. This aligns with literature suggesting that anxiety-related hyperarousal and dysregulation of descending inhibitory pathways can impair endogenous pain modulation.[39,43–46] NDI exhibited a nonsignificant nonlinear trend with CPM, suggesting the possibility of curvilinear effects that might emerge in larger cohorts, while PCS remained nonsignificant across all models. These results collectively point toward *anxiety as a potential key psychological target* for interventions aimed at optimizing both pain sensitivity and inhibitory control.

Comparisons Between Psychological Constructs

Our findings suggest that anxiety and pain catastrophizing affect the neural pain processing differently. Anxiety showed consistent associations with both sensory discriminative (PPT) and modulatory (CPM) outcomes, whereas catastrophizing was unrelated to either measure. One interpretation is that catastrophizing, while often associated with chronic pain, may exert a more pronounced effect on long-term disability and coping strategies rather than on immediate sensory thresholds or inhibitory function. Also, pain catastrophizing's influence may be task-specific, becoming more relevant in scenarios involving sustained pain exposure rather than brief noxious stimuli.

Pain and Its Age-Related Effects

The experience of pain is highly variable and multifaceted. Patient symptomatology may be reported as severe despite relatively benign diagnostic imaging findings. Conversely, a substantial proportion of asymptomatic individuals present with significant imaging abnormalities, the prevalence of which increases with each decade of life. What patients and providers often assume causes pain may be normal age-related changes. Integrating individual neuropsychological and similar contextual factors may lead to more effective patient education, clinical decision-making across patient care, and ultimately better outcomes.

Contrary to prior evidence suggesting that aging is associated with diminished pain inhibitory capacity, age did not significantly influence PPT or CPM in any of our models. The nonlinear smooths for age in the PPT models indicate that any age-related effects may be subtle or obscured by inter-individual variability in psychological or physiological resilience. Notably, our sample excluded patients >65 years old, given the established age-related decline in pain inhibitory capacity. Accordingly, age was controlled for as a confounding factor in QST analyses by restricting the age range for study participation. NDI was not a significant predictor in any model, although its weak nonlinear trends in relation to CPM highlight a need to further explore whether functional impairment contributes to altered central pain processing in clinical neck pain populations. Given the imperfect correlation between imaging findings and patients' pain, alternative approaches to exploring and quantifying clinical symptoms are warranted to minimize the inherent subjectivity of pain assessment.

Study Limitations

Our findings support an association between psychological factors and pain processing, as assessed through QST in patients with CNP. Although the study was exploratory in nature—which informed the analytic approach—the generalizability of these results is limited by methodological constraints. Most notably, the sample size was modest, and demographic characteristics were imbalanced across sex, race, and ethnicity. Although the GAM framework enabled us to model complex nonlinear relationships, the limited sample size precluded subgroup analyses and may have reduced our ability to detect smaller effects—a notable consideration given the flexibility and data demands of GAM models. However, the homogeneity of the sample—ensured by stringent inclusion criteria and a single examiner—reduced variance and partially justified the smaller sample size.[37,38] Future work should consider multivariable GAMs or interaction terms to better capture potential interdependencies among predictors. Longitudinal studies with more diverse and representative samples are needed to examine how psychological factors and pain modulation evolve over time and in response to treatment.

While we recognize that the use of nonprobabilistic convenience sampling and a single-rater assessment may introduce bias, we also note the strength in QST reliability afforded by having a trained clinical and research expert conduct all assessments. In addition, the use of self-reported anxiety and pain-catastrophizing questionnaires prevented the PI/examiner from influencing participant responses, thereby mitigating concerns regarding measurement reliability. Importantly, our sample exceeded those of several comparable studies, supporting the internal validity of our findings.[20,31,39,43,46] While these limitations should be considered when interpreting the results, similar patterns have been reported across pain and rehabilitation literature.[20,31,39,43,46] Thus, the application of our findings should be viewed in the context of both these constraints and the corroborating evidence in the field.

Conclusion

This study demonstrates that higher anxiety levels are associated with diminished conditioned pain modulation in adults under 65 years with CNP, underscoring the role of psychological factors in shaping endogenous pain-inhibitory capacity. These findings directly advance the study's objective of clarifying how specific psychological characteristics relate to pain-processing mechanisms and reinforce the importance of incorporating psychologically informed assessment into clinical evaluation frameworks. Elevated anxiety has been shown to disrupt descending inhibitory pathways through several converging mechanisms, including cortical disinhibition, alterations in monoaminergic signaling, and heightened autonomic and attentional arousal.[19,20,32] Together, these processes provide a coherent neurobiological explanation for the observed anxiety-related reductions in CPM and highlight the clinical relevance of identifying anxiety as a modifiable contributor to impaired pain modulation. Although QST is time-intensive, selective use of CPM assessment in patients with elevated anxiety may be both feasible and clinically valuable. Mechanistic information derived from QST can help inform contextual approaches to chronic pain prevention strategies, clarify complex symptom presentations through patient education, guide clinical decisions regarding imaging and interventional procedures, and support more precise health service delivery and referral pathways. Early recognition of anxiety-related impairments in descending inhibition may also facilitate timely implementation of targeted behavioral and rehabilitative strategies, potentially reducing the risk of symptom persistence, limiting functional decline, and decreasing reliance on high-cost interventions. By grounding these implications in the demonstrated relationship between anxiety and pain modulation, this work strengthens our mechanistic understanding of CNP and supports precision rehabilitation through the development of more individualized, mechanism-informed models of care.

Future research should examine these relationships longitudinally to determine whether anxiety-related impairments in descending inhibition predict symptom persistence, treatment response, or transition to chronicity. Broader psychosocial profiling and exploration of age-related differences in CPM may further refine our understanding of the neuropsychological contributors to CNP and advance prevention and precision rehabilitation approaches.

Abbreviations

CNP, Chronic Neck Pain; QST, Quantitative Sensory Tests; PPT, Pressure Pain Threshold; CPM, Conditioned Pain Modulation; PCS, Pain Catastrophizing Scale; STAI, State-Trait Anxiety Inventory; NDI, Neck Disability Index; NPRS, Numeric Pain Rating Scale.

Data Sharing Statement

Data is accessible but not publicly available pursuant to organizational security and privacy policies including state and federal laws governing protected health information. Data available upon request from the corresponding author. During the preparation of this work, the authors did not use any Generative AI and AI-assisted Technologies in the Writing Process.\.

Ethics Statement

The study was conducted in accordance with the Helsinki Declaration, and all participants were provided with, and completed the informed consent approved by the Cooperman Barnabas Medical Center (CBMC) Institutional Review Board (IRB ID #: 17-20; FWA00003433), member of the Robert Wood Johnson Barnabas Health (RWJBH) Health System, Livingston, New Jersey, United States of America.

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Disclosure

The authors have no conflicts of interest to disclose.

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