

The Mediating Role of Cognitive Avoidance in the Relationship Between Intolerance of Uncertainty and Chronic Pain in Multiple Sclerosis Patients: A Structural Equation Modeling Approach

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1. Round 1

1.1. Reviewer 1

Reviewer:

The third Introduction paragraph, beginning “Among the countless debilitating symptoms associated with MS, chronic pain stands out as a primary and pervasive concern,” contains several claims that need correction or stronger evidence. Specifically, the sentence “A significant portion of this burden is central neuropathic pain, which arises as a direct consequence of a lesion affecting the somatosensory system (Panjwani et al., 2024)” cites a study of intolerance of uncertainty and experiential avoidance in advanced cancer, not MS-related neuropathic pain. Likewise, the statement that central neuropathic pain affects “up to one-third of individuals with MS” should be supported by an MS pain epidemiology source. The authors should revise this paragraph using references that directly address pain prevalence, phenotype, pathophysiology, and functional consequences in MS, particularly Racke et al. (2022), and should avoid attaching references merely because they contain related psychological terminology.

The fourth Introduction paragraph states that “research has demonstrated that higher IU is associated with greater pain intensity and more severe pain-related limitations (Racke et al., 2022).” This assertion appears stronger than the cited evidence

permits. Racke et al. primarily addresses the pathophysiology, diagnosis, and management of pain in MS rather than directly testing intolerance of uncertainty as a predictor of pain intensity. Because the central novelty of the manuscript depends on the IU–pain relationship, the authors should be especially rigorous in distinguishing direct empirical evidence from theoretical extrapolation. Where no prior MS study has directly established this association, the manuscript should state this explicitly and present the proposed relationship as a theoretically derived hypothesis rather than as an already demonstrated empirical association.

The paragraph introducing the Fear-Avoidance Model should be conceptually strengthened. The manuscript currently states that “Within this model, IU functions as a critical dispositional characteristic that amplifies the cycle,” but the cited literature does not establish IU as a formal component of the classical Fear-Avoidance Model. The authors should clarify that IU is being proposed as an extension or antecedent vulnerability factor rather than implying that it is already an established component of the model. A stronger theoretical argument would explain the sequential mechanism more explicitly: intolerance of uncertainty may increase threat appraisal of ambiguous pain or neurological sensations; increased threat appraisal may promote cognitive avoidance; avoidance may prevent corrective learning and increase symptom monitoring; and these processes may contribute to greater perceived pain severity and interference.

The use of principal component analysis to redefine the measurement structures of both the IUS and CAQ requires stronger justification. The manuscript reports a three-component solution for the IUS and a two-component solution for the CAQ and then appears to use these components as indicators in the SEM. Because the study subsequently employs latent-variable modeling, confirmatory factor analysis would be more appropriate than PCA for establishing the measurement structure. The authors should report extraction procedures, rotation method, KMO statistic, Bartlett’s test, eigenvalues, variance explained, loading criteria, cross-loadings, and decisions concerning item retention. More importantly, a separate CFA measurement model should be evaluated before testing the structural mediation model, with standardized factor loadings, composite reliability, and convergent/discriminant validity reported.

The description of the Brief Pain Inventory-Short Form requires clarification because the observed descriptive values do not appear readily interpretable using the standard BPI-SF scoring structure. The manuscript reports mean pain severity of 10.85 and pain interference of 7.05, but it does not explain whether these represent summed scores, mean item scores, or transformed scores. Because standard BPI severity and interference indices are commonly expressed on 0–10 metrics, readers need a precise description of the scoring method used. The authors should specify which BPI-SF items contributed to each latent indicator, how missing responses were handled, the possible range of each score, and whether a validated Persian BPI-SF version was employed.

The statistical analysis subsection is currently inadequate for a structural equation modeling study because it consists only of the sentence “Data were analyzed using structural equation modeling (SEM).” The authors should identify the software and version, estimation method, treatment of missing data, normality assessment criteria, handling of outliers, multicollinearity criteria, model identification strategy, goodness-of-fit thresholds, bootstrapping procedure, confidence-interval method, and significance level. They should also explain whether a two-step SEM procedure was employed in which the measurement model was first validated and the structural model subsequently tested. These details are necessary for reproducibility and for readers to judge the appropriateness of the analysis.

Authors revised the manuscript and uploaded the document.

1.2. Reviewer 2

Reviewer:

In the fifth Introduction paragraph, cognitive avoidance is described as encompassing “distraction, thought suppression, and worry,” while worry is then described as an avoidance strategy that can reduce immediate cognitive and physiological symptoms of anxiety. The conceptual boundaries between cognitive avoidance, worry, thought suppression, and experiential avoidance are insufficiently differentiated. This is important because the Cognitive Avoidance Questionnaire used in the study operationalizes a particular set of strategies, whereas several cited studies address broader experiential avoidance or worry

constructs. The authors should define cognitive avoidance according to the instrument and theoretical framework actually employed, distinguish it from experiential avoidance and behavioral avoidance, and explain why cognitive avoidance specifically—rather than catastrophizing, experiential avoidance, worry, or negative problem orientation—was selected as the mediator.

The final paragraph of the Introduction contains the central causal sequence but would benefit from explicit hypotheses. The sentence “it is hypothesized that the fluctuating course of MS induces high levels of IU in patients, which in turn leads to an increased experience of chronic pain through lower-order mechanisms such as cognitive avoidance” implies a causal temporal process that cannot be established with the study’s cross-sectional design. The wording should be revised to describe expected statistical associations rather than causal effects. In addition, the authors should conclude the Introduction with explicit hypotheses regarding the IU→cognitive avoidance path, cognitive avoidance→chronic pain path, direct IU→chronic pain path, and indirect IU→cognitive avoidance→chronic pain pathway.

The “Method” paragraph reports that 339 patients were recruited from the Kowsar Imaging Center and Iran MS Society using convenience sampling, but essential eligibility information is missing. The manuscript should specify inclusion criteria such as confirmed MS diagnosis, diagnostic criteria used, minimum age, ability to read Persian, duration since diagnosis, presence or duration of chronic pain, and neurological status. Exclusion criteria should also be reported, including major psychiatric disorders, severe cognitive impairment, other neurological disorders, acute relapse, recent corticosteroid treatment, and chronic pain attributable primarily to another medical condition. Without these criteria, it is difficult to determine whether the sampled participants appropriately represent the target population of patients with MS-related chronic pain.

The sample-size justification requires substantial revision. The manuscript states that “a sample size of 339 was chosen to ensure a ratio of more than 20 participants for each of the 15 estimated parameters in the model.” This calculation is unclear because the presented SEM appears to contain substantially more than 15 freely estimated parameters when factor loadings, residual variances, latent variances/covariances, and structural paths are considered. Contemporary SEM sample-size justification should preferably be based on model complexity, anticipated effect sizes, statistical power, estimator, and distributional characteristics rather than a simple observations-per-parameter rule. The authors should either provide an a priori Monte Carlo/power-based justification or explain exactly which 15 parameters were counted and why.

A major methodological concern appears in the Intolerance of Uncertainty Scale description. The authors state that the original 5-point response format was modified to an 11-point scale “to enhance response precision.” Such a substantial alteration changes the measurement properties of an established instrument and cannot be assumed to preserve its validity. The same modification was also made to the Cognitive Avoidance Questionnaire. The authors should provide a methodological rationale and evidence supporting this change, identify whether the modified versions underwent translation/back-translation and content validation, and discuss the consequences for comparability with previous studies. If these modifications were developed specifically for this study, the instruments should not simply be described as established Persian versions without additional validation evidence.

Authors revised the manuscript and uploaded the document.

2. Revised

Editor’s decision: Accepted.

Editor in Chief’s decision: Accepted.