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Structural Equation Modeling of Neuropsychological Functioning and Quality of Life in MS Patients: The Mediating Role of Distress Tolerance

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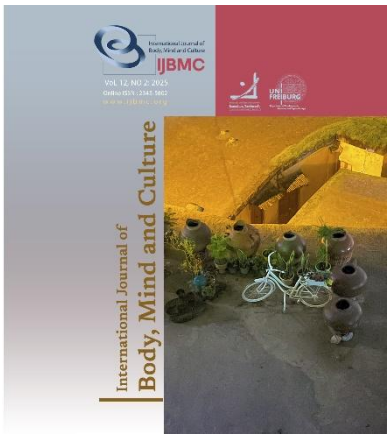

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ABSTRACT

Objective: This study examined the structural relationships between neuropsychological functioning and QoL in MS patients, with distress tolerance as a mediating factor.

Methods and Materials: This descriptive-correlational study utilized structural equation modeling (SEM) to analyze data from 390 MS patients affiliated with the MS Society in Sari, Iran, selected through purposive sampling. Participants completed the Neuropsychological Functioning Questionnaire (Najati, 2013), Multiple Sclerosis Impact Scale (MSIS-29) (McGuigan & Hutchinson, 2004), and Distress Tolerance Scale (Simons & Gaher, 2005). Data were analyzed using SPSS 24 and Amos 22, assessing model fit through CFI, RMSEA, and Chi-square/df indices.

Findings: Neuropsychological functioning had a direct, positive effect on QoL ($\beta = 0.22$, $p < 0.01$), and distress tolerance also had a significant direct effect on QoL ($\beta = 0.39$, $p < 0.001$). Mediation analysis confirmed that distress tolerance partially mediated the relationship between neuropsychological functioning and QoL (Sobel test = 4.58, $p<0.001$). Model fit indices indicated an acceptable fit (CFI = 0.91, RMSEA = 0.066, Chi-square/df = 2.23).

Conclusion: Findings highlight the role of neuropsychological functioning and distress tolerance in predicting QoL in MS patients. Psychological interventions targeting cognitive function and distress regulation may improve patients' well-being. Further research should explore how MS subtypes influence these relationships.

Keywords: Neuropsychological Functioning, Quality of Life, Distress Tolerance, Multiple Sclerosis, Structural.

Introduction

Multiple sclerosis (MS) is a chronic, progressive, and inflammatory disease of the central nervous system, characterized by demyelination and neurodegeneration, leading to motor, sensory, and cognitive impairments (Azizpour et al., 2025). The disease significantly affects patients' daily functioning and independence, leading to physical disability, emotional distress, and reduced quality of life (QoL) (Vaheb, 2024). Research suggests that MS patients experience a lower QoL compared to individuals with other chronic conditions, such as epilepsy and diabetes, due to the combination of physical

disability, neuropsychological dysfunction, and psychological distress (Rostami et al., 2024; Sandesjö et al., 2024; Vagias et al., 2024).

QoL in MS patients is influenced by multiple factors, including disease severity, duration, medication, and psychological variables such as coping mechanisms and resilience (Najafi et al., 2024). Among these, neuropsychological functioning plays a critical role, as MS patients commonly experience deficits in cognitive flexibility, attention, working memory, planning, and problem-solving (Amaslidou et al., 2023). These impairments not only reduce patients' ability to engage in daily activities but also negatively impact their emotional well-being and social interactions (Ow et al., 2022).

One key psychological factor that may mediate the relationship between neuropsychological functioning and QoL is distress tolerance. Distress tolerance refers to the ability to endure and manage negative emotional states, such as stress, anxiety, and frustration (Simons & Gaher, 2005). MS patients with low distress tolerance are more likely to experience heightened psychological distress, leading to poor coping mechanisms, increased symptom severity, and a diminished QoL (Brands et al., 2018). Previous studies have highlighted that distress tolerance plays a crucial role in mental health conditions such as depression and anxiety (Azami et al., 2019), but its mediating role in the neuropsychological functioning-QoL relationship in MS patients remains underexplored.

Given MS's complexity and its cognitive, emotional, and physical burden, understanding how neuropsychological functioning and distress tolerance interact to predict QoL is crucial for developing effective interventions. This study employs structural equation modeling (SEM) to examine the relationships among neuropsychological functioning, distress tolerance, and QoL in MS patients, testing the hypothesis that distress tolerance mediates the impact of neuropsychological functioning on QoL. The findings could inform psychological and cognitive interventions aimed at improving QoL in MS patients.

Methods and Materials

Study Design and Participants

This study employed a descriptive-correlational design and utilized structural equation modeling (SEM) to examine the relationships between neuropsychological functioning, distress tolerance, and quality of life (QoL) in MS patients. The study population comprised all MS patients who were members of the MS Society in Sari, Iran, in 2019.

Participants were selected using purposive sampling, as this method ensured the recruitment of individuals who met the study's specific inclusion criteria. Given that MS manifests with diverse symptoms and varying levels of disability, purposive sampling allowed for the selection of individuals with a range of disease severities, which is critical for examining the impact of neuropsychological functioning and distress tolerance on QoL.

Participants were required to meet the following inclusion criteria: A confirmed diagnosis of MS (any type) by a neurologist, age 18 years or older, Ability to read and complete self-report questionnaires independently, no history of major psychiatric disorders (e.g., schizophrenia, bipolar disorder) that could confound neuropsychological assessments, no history of severe cognitive impairment or neurological conditions other than MS and providing written informed consent to participate.

Patients who failed to complete the questionnaires or had missing data exceeding 10% were excluded from the final analysis.

The required sample size was determined using G*Power 3.1 software, considering an anticipated medium effect size ($f^2 = 0.15$), a power (1-β) of 0.90, and an α level of 0.05. Given that structural equation modeling (SEM) requires at least 15 participants per observed variable (Stevens, 1994), and the study included 26 observed variables, the minimum sample size was set at 390 participants to ensure robust model estimation. Accounting for potential dropout or incomplete responses, the final valid sample consisted of 383 MS patients.

Data collection was conducted in collaboration with the MS Society of Sari, Iran. Participants were informed about the study's objectives, the voluntary nature of participation, and their right to withdraw at any stage. Informed consent was obtained from all individuals prior to their completion of the questionnaires. The survey was administered in a quiet and controlled environment, either in person at the MS Society or online for participants unable to attend in person. A research

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assistant was available to provide clarification when necessary. To minimize response bias, participants were instructed to respond as honestly as possible and were assured that their responses would remain confidential. Given the physical limitations of some MS patients, trained assistants helped with questionnaire completion when required. Each session lasted approximately 30 to 40 minutes, ensuring that participants had ample time to complete the measures. To maintain data quality, incomplete or careless responses were identified and excluded from the final dataset. A total of 390 questionnaires were initially collected; however, seven incomplete responses were excluded, leaving a final sample of 383 valid cases for analysis.

Instruments

The Neuropsychological Functioning Questionnaire (Nejati, 2013) was used to assess cognitive abilities essential for independent living and daily functioning. This 30-item questionnaire measures seven cognitive domains: memory, inhibitory control and selective attention, decision-making, planning, sustained attention, social cognition, and cognitive flexibility. Each item is rated on a 5-point Likert scale, ranging from 1 (strongly disagree) to 5 (strongly agree). The total score reflects an individual's neuropsychological performance, with higher scores indicating better functioning. The questionnaire has demonstrated strong psychometric properties, with Cronbach's alpha values ranging from 0.73 to 0.89 for different subscales (Nejati, 2013). Its construct and convergent validity have been confirmed through correlations with related cognitive measures in prior studies.

To assess the quality of life of MS patients, the Multiple Sclerosis Impact Scale (MSIS-29) (McGuigan & Hutchinson, 2004) was employed. This 29-item scale is divided into two subscales: physical impact (20 items) and psychological impact (9 items). Responses are scored on a 5-point scale, with higher scores indicating greater impairment and lower quality of life. The physical impact scores range from 20 (best) to 100 (worst), while the psychological impact scores range from 9 (best) to 45 (worst). The MSIS-29 has been widely used in MS research and has demonstrated high reliability, with Cronbach's alpha coefficients of 0.92 for the physical impact subscale and 0.87 for the psychological impact subscale. Its validity has been supported by significant correlations with disability measures and psychological distress indicators (McGuigan & Hutchinson, 2004). The Persian version of this scale has been validated in Iranian MS populations, showing satisfactory reliability (Ayatollahi et al., 2006).

The Distress Tolerance Scale (DTS) (Simons & Gaher, 2005) was utilized to measure participants' ability to withstand emotional distress. This scale consists of 14 items across four subscales: tolerance (perceived ability to tolerate distress), absorption (preoccupation with negative emotions), appraisal (subjective evaluation of distress), and regulation (efforts to manage distress). Items are rated on a 5-point Likert scale, with higher scores indicating greater distress tolerance. The DTS has been shown to have good internal consistency, with Cronbach's alpha values ranging from 0.67 to 0.79 in previous research. Its construct validity has been confirmed through factor analysis, and its reliability has been established in Iranian populations (Azami et al., 2019).

Data Analysis

The collected data were analyzed using SPSS 24 and AMOS 22. Before conducting statistical analyses, preliminary data screening was performed to identify missing values, outliers, and violations of normality assumptions. Missing data were examined using Little's MCAR test, and cases with more than 10% missing responses were excluded from further analysis. Outliers were identified using the Mahalanobis distance and removed as necessary. To test the assumptions of structural equation modeling (SEM), data normality was assessed through skewness and kurtosis values, as well as the Kolmogorov-Smirnov test. Since the data deviated from normality, maximum likelihood estimation with bootstrapping was used to obtain robust standard errors and confidence intervals.

Structural equation modeling (SEM) was applied to evaluate the proposed model, examining both direct and indirect effects of neuropsychological functioning and distress tolerance on quality of life. Model fit was assessed using several goodness-of-fit indices, including: Chi-square/df ratio (acceptable fit if < 3), Comparative Fit Index (CFI>0.90), Root Mean Square Error of Approximation (RMSEA<0.08), and Standardized Root Mean Square Residual (SRMR<0.08). Mediation analysis was conducted using Sobel's test and bootstrapping

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techniques, with 5,000 resamples to estimate the indirect effects of distress tolerance on the relationship between neuropsychological functioning and quality of life. Statistical significance was set at $p<0.05$ for all analyses.

Findings and Results

A total of 383 MS patients participated in this study. Among them, 193 (50.4%) were women, and 190 (49.6%) were men. Regarding educational levels, 169 participants (44.1%) had a high school diploma, 95 (24.8%) had a bachelor's degree, 68 (17.8%) had an associate degree, 40 (10.4%) had less than a high school diploma, and 11 (2.9%) had a master's degree or higher. The demographic analysis also revealed that 133 participants (34.7%) fell within the 20-30 age range, which had the highest frequency, while 28 participants (7.3%) were over 50 years old, representing the group with the lowest frequency. Descriptive findings indicated that 209 participants (54.6%) had a high quality of life, 133 participants (34.7%) had a moderate quality of life, and 41 participants (10.7%) had a low quality of life. Table 1 presents the descriptive statistics for neuropsychological functioning, distress tolerance, and quality of life.

Table 1

Descriptive Statistics for Study Variables

Variable	Mean (M)	SD	Skewness	Kurtosis
Neuropsychological Functioning	89.83	21.60	-0.12	0.35
Memory	18.32	7.61	-0.45	0.52
Inhibitory Control & Selective Attention	17.82	6.70	-0.31	0.29
Decision-Making	15.18	6.03	-0.22	0.38
Planning	8.78	3.96	-0.51	0.46
Sustained Attention	9.00	3.66	-0.33	0.41
Social Cognition	9.09	3.69	-0.44	0.36
Cognitive Flexibility	11.62	4.82	-0.27	0.31
Distress Tolerance	7.72	3.54	0.15	0.21
Absorption in Negative Emotions	5.21	2.57	0.09	0.18
Subjective Distress Appraisal	15.59	5.95	-0.38	0.29
Regulation Efforts for Distress Relief	7.61	3.30	-0.20	0.34
Quality of Life - Physical Impact	61.36	17.33	-0.19	0.25
Quality of Life - Psychological Impact	28.02	9.05	-0.14	0.28

The skewness and kurtosis values for all variables were within the acceptable range (-1 to +1), suggesting that the data were approximately normally distributed. However, the Kolmogorov-Smirnov test for normality indicated some deviations from normality ($p < 0.05$). Given this, maximum likelihood estimation with bootstrapping was used to ensure robust parameter estimation. Missing values were analyzed using Little's MCAR test, which indicated that data were missing completely at random ($\chi^2 = 7.12$, $df = 9$, $p = 0.62$). Cases with more than 10% missing data (n = 7) were excluded from further analysis. Outliers were identified using Mahalanobis distance at $p<0.001$, resulting in the removal of 5 additional cases, leaving a final sample of 383 participants. To test the hypothesized model, SEM was conducted using AMOS 22. Table 2 presents the model fit indices.

Table 2

Model Fit Indices

Fit Index	Recommended Threshold	Obtained Value	Interpretation
Chi-Square / Degrees of Freedom (χ^2/df)	< 3.00	2.23	Acceptable Fit
Comparative Fit Index (CFI)	> 0.90	0.91	Acceptable Fit
Tucker-Lewis Index (TLI)	> 0.90	0.90	Acceptable Fit
Root Mean Square Error of Approximation (RMSEA)	< 0.08	0.066	Acceptable Fit
Standardized Root Mean Square Residual (SRMR)	< 0.08	0.057	Good Fit

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All fit indices indicated that the hypothesized model provided an acceptable to good fit to the data.

Table 3

Standardized Regression Coefficients for Direct Effects

Pathway	Standardized β	SE	t-value	p-value
Neuropsychological Functioning → Quality of Life	0.22	0.095	2.61	0.009
Distress Tolerance → Quality of Life	0.39	0.072	5.23	<0.001
Neuropsychological Functioning → Distress Tolerance	0.30	0.084	3.74	<0.001

The results showed a significant direct effect of neuropsychological functioning on quality of life (β = 0.22, p < 0.01) and distress tolerance (β = 0.30, p < 0.001). Additionally, distress tolerance had a substantial direct effect on quality of life (β = 0.39, p < 0.001), supporting its role as a key factor in predicting well-being among MS patients. A mediation analysis was conducted using bootstrapping (5,000 resamples) to test whether distress tolerance mediates the relationship between neuropsychological functioning and quality of life (Table 3).

Table 4

Mediation Analysis Results

Pathway	Direct Effect	Indirect Effect	Total Effect	Sobel Test (Z)	95% Bootstrapped CI
Neuropsychological Functioning → Quality of Life	0.26	0.129	0.389	4.58 (p < 0.001)	[0.08, 0.19]
Distress Tolerance → Quality of Life	0.43	-	-	-	-

The indirect effect of neuropsychological functioning on quality of life, mediated by distress tolerance, was significant (β = 0.129, 95% CI [0.08, 0.19], p < 0.001). This finding confirms that distress tolerance partially mediates the relationship between neuropsychological functioning and quality of life (Table 4).

Discussion and Conclusion

The present study investigated the structural relationships between neuropsychological functioning, distress tolerance, and quality of life (QoL) in MS patients, with a focus on the mediating role of distress tolerance. The findings support a significant direct effect of neuropsychological functioning on both distress tolerance and QoL and a partial mediation effect of distress tolerance in this relationship. These results provide further insight into the cognitive and psychological mechanisms influencing QoL in individuals with MS and highlight potential intervention strategies.

The first significant finding of this study was the direct positive relationship between neuropsychological functioning and QoL in MS patients. This result is consistent with previous research suggesting that cognitive impairments, including deficits in memory, attention, problem-solving, and executive functioning, significantly impact daily activities and overall well-being in patients with MS (Benedict et al., 2005; Fernández-Jiménez & Arnett, 2015). Studies have indicated that MS-related neurocognitive dysfunction not only reduces the ability to manage daily life activities but also exacerbates psychological distress and social isolation (Grech et al., 2015; Lanzillo et al., 2016). Therefore, interventions aimed at improving cognitive flexibility, executive functioning, and memory processing may help enhance QoL in MS patients.

The second major finding was the significant effect of neuropsychological functioning on distress tolerance. This aligns with prior studies indicating that cognitive impairments in MS patients are associated with lower distress tolerance, which manifests in heightened emotional reactivity, poor coping strategies, and reduced ability to regulate stress (Simons & Gaher, 2005). Since distress tolerance is closely linked to psychological resilience and emotion regulation, cognitive rehabilitation programs focusing on problem-solving skills, self-regulation, and adaptive coping strategies

may strengthen distress tolerance in MS patients, subsequently reducing emotional distress.

Furthermore, distress tolerance exhibited a substantial direct effect on QoL, reinforcing the idea that individuals with higher distress tolerance experience less psychological distress and better emotional adjustment. Prior studies have highlighted that low distress tolerance is associated with greater anxiety, depression, and emotional instability in MS patients, leading to poorer QoL outcomes (Azami et al., 2019). Given these findings, psychological interventions such as cognitive-behavioral therapy (CBT), acceptance and commitment therapy (ACT), and mindfulness-based stress reduction (MBSR) could be beneficial in enhancing distress tolerance, thereby improving emotional well-being and QoL in MS patients.

A key contribution of this study is the confirmation of distress tolerance as a partial mediator in the relationship between neuropsychological functioning and QoL. This result suggests that neuropsychological impairments do not affect QoL solely through cognitive limitations but also via their impact on emotional regulation and coping mechanisms. This aligns with previous findings emphasizing the interplay between cognitive deficits, emotional dysregulation, and psychosocial adjustment in MS (Gromisch et al., 2016). Given this mediating role, integrated rehabilitation programs that simultaneously address cognitive impairments and emotional regulation difficulties may be more effective in improving QoL in MS patients.

Despite its strengths, this study has several limitations. First, the use of self-report questionnaires may have introduced response bias, as participants might have over- or under-reported their cognitive and emotional difficulties. Future studies should incorporate objective cognitive assessments such as neuropsychological tests and functional MRI scans to validate self-reported measures. Second, the study utilized purposive sampling, which may limit the generalizability of the findings. Future research should employ randomized sampling methods to ensure a more representative sample of MS patients. Finally, this study did not account for MS disease subtypes and progression stages, which could influence neuropsychological functioning and QoL. Future research should explore these variables to provide a more nuanced understanding of cognitive-emotional interactions in MS.

This study provides empirical support for the structural relationships between neuropsychological functioning, distress tolerance, and QoL in MS patients, highlighting the mediating role of distress tolerance. The findings suggest that cognitive impairments negatively impact QoL, both directly and indirectly, through reduced distress tolerance. Given these insights, interventions aimed at improving cognitive functioning and distress tolerance should be integrated into MS management strategies. From a clinical perspective, cognitive rehabilitation programs targeting memory, executive functioning, and problem-solving skills may help mitigate the negative impact of neuropsychological impairments on daily life. Additionally, psychological therapies focusing on distress tolerance, emotional regulation, and coping strategies should be considered essential components of MS care plans. Future studies should aim to expand these findings by exploring longitudinal data to assess how cognitive and emotional factors evolve in MS patients. Furthermore, research incorporating biological markers (e.g., neuroinflammation, brain atrophy measures) alongside psychological assessments could provide a comprehensive framework for understanding and improving QoL in individuals with MS.

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Declaration of Interest

The authors of this article declared no conflict of interest.

Ethical Considerations

The study protocol adhered to the principles outlined in the Declaration of Helsinki, which provides guidelines for ethical research involving human participants. This study's ethical considerations included the fact that participation was entirely optional.

Transparency of Data

By the principles of transparency and open research, we declare that all data and materials used in this study are available upon request.

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Authors' Contributions

All authors equally contribute to this study.

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