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GUEST EDITORIAL

Advancing psychiatric care through neuromodulation: From translational research to clinical practice

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Neuromodulation has been one of the most rapidly growing areas of interest in psychiatry over the past decades. In some sense, one might argue that "all psychiatry is neuromodulation." After all, psychiatric treatments alter brain function, even when the brain is not their direct target (1). For example, changes in stimulus-response associations induced by behavioral therapy are almost certainly mediated by the remodeling of neural circuits. However, when referring to neuromodulation in a narrower sense, we generally mean interventions that directly and purposefully target the brain or specific brain regions. These approaches may have a global scope, such as treatments affecting the whole brain (e.g., most psychopharmacological interventions), or they may target a specific cortical region, such as the prefrontal cortex (transcranial magnetic stimulation or transcranial electrical stimulation), or even a discrete nucleus within the basal ganglia, such as the subthalamic nucleus (deep brain stimulation [DBS]). These brain stimulation techniques, whether noninvasive or invasive, can be classified as "exogenous." In contrast, neural activity can also be modulated endogenously through neurofeedback, whereby individuals receive real-time information about specific patterns of brain activity and learn to modify them toward a predefined target (2). Neurofeedback may rely on noninvasive signals (e.g., functional magnetic resonance imaging [fMRI] and electroencephalography [EEG]) or invasive recordings (e.g., local field potentials [LFPs]).

Deep brain stimulation is of particular interest in (neuro)psychiatry due to its spatial precision and capacity to modulate specific anatomical targets and circuits. To date, most studies have focused on depression, obsessive-compulsive disorder (OCD), and Tourette syndrome (TS). In depression, primary targets include the subgenual cingulate cortex (SCC), the ventral capsule/ventral striatum (VC/VS), and the medial forebrain bundle (MFB) at its origin in the ventral tegmental area. Reports across these targets describe substantial clinical improvement, although results from placebo-controlled trials have been mixed (3). In TS, studies have demonstrated up to a 50% reduction in tic severity (4). In OCD, the literature reports improvements of approximately 40% in both obsessions and compulsions, as well as significant differences between real and sham stimulation (5, 6). It is important to remember that for all psychiatric indications, symptoms need to be refractory to standard treatments, and a careful multidisciplinary screening process must be applied. There are also strict regulations (which vary across jurisdictions) regarding the certification of medical devices and oversight, of which psychiatrists need to be aware. Moreover, because this is still a relatively new field and the available evidence from randomized controlled trials is based on small patient samples, psychiatric DBS programs should be accompanied by data collection for research and auditing purposes.

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Another area of neuromodulation that can potentially achieve high neuroanatomical precision is neurofeedback training. During neurofeedback, information about brain activity is provided in (almost) real time to the patient, who can then attempt to modify the brain activity parameter that is being fed back (7). For example, in EEG neurofeedback, the target signal might be the ratio between alpha and theta rhythms measured at a particular electrode. In fMRI-based neurofeedback, the target signal might be the average activation of the left amygdala or the functional connectivity between different cortical areas. Examples of clinical applications—still at the investigational stage—include depression (8, 9), Parkinson's disease, (10) and phobia (11).

Although conceptually very promising, fMRI neurofeedback has not yet been established as a routine treatment technique. Challenges include the standardization of protocols (12) and target signals, as well as reliance on high-end magnetic resonance imaging (MRI) systems. Translation into ambulatory neurofeedback systems, such as EEG fingerprinting of fMRI signals, (13) holds considerable potential. Another limitation, common to all neuromodulation techniques in psychiatry, is the limited understanding of underlying disease mechanisms. Without clear neurophysiological markers of pathology, it is difficult to determine what exactly should be "corrected" through psychiatric neuromodulation. A better understanding of the neural substrates of psychopathology, for example, through symptom provocation techniques (within ethical and safety limits, of course), may provide one avenue for identifying more refined (and personalized) treatment targets. Another approach would be to learn from the neural effects of treatments that are already effective and attempt to replicate them using neuromodulation, ideally with less invasive and/or better tolerated interventions. One example is the ongoing effort to develop neurofeedback protocols inspired by the network effects of deep brain stimulation (14).

Along similar lines, there is considerable interest in identifying biomarkers that can track the therapeutic effects of DBS and guide adjustments in stimulation delivery. Such "closed-loop" adaptive DBS is currently available only for Parkinson's disease, (14) although proof of concept has also been demonstrated for Tourette syndrome (15). For other neuropsychiatric conditions, particularly those in which symptoms and their improvement evolve over longer time scales (hours to days), identifying suitable electrophysiological DBS targets may be even more challenging. The continued refinement of neuromodulation techniques, whether invasive or non-invasive, therefore requires close collaboration between clinicians, neuroscientists, and engineers, as well as careful attention to the perspectives and needs of patients (16) (https://www.diepresearchproject.com/).

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RESEARCH ARTICLE

The psychometric validity and reliability of the DSM-5 Severity Measure for Social Anxiety Disorder in a Turkish adult clinical population

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ABSTRACT

Objective: This study aimed to examine the psychometric properties of the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) Severity Measure for Social Anxiety Disorder—Adult (DSM-5 SAD-S) in a Turkish-speaking clinical population. Specifically, we assessed its factorial structure, internal consistency, and convergent and known-group validity.

Method: The sample included 146 participants (73 diagnosed with social anxiety disorder and 73 healthy controls). All participants completed the DSM-5 SAD-S and the Liebowitz Social Anxiety Scale (LSAS). Exploratory factor analysis (EFA) was conducted using minimum residual extraction with oblimin rotation. Confirmatory factor analysis (CFA), using diagonally weighted least squares (DWLS) estimation, was performed to evaluate model fit. Internal consistency was assessed using Cronbach's alpha. Convergent validity was examined through Pearson correlation with LSAS scores. Known-group validity was evaluated using the Mann–Whitney U test.

Results: EFA supported a unidimensional structure with strong factor loadings (0.561–0.849). CFA indicated acceptable model fit (Comparative Fit Index [CFI]=0.990; Tucker–Lewis Index [TLI]=0.988; Root Mean Square Error of Approximation [RMSEA]=0.106; Standardized Root Mean Square Residual [SRMR]=0.084). Internal consistency was high (α=0.91). The DSM-5 SAD-S score showed a moderate and statistically significant correlation with the LSAS total score (r=0.39, p<0.001). Patients scored significantly higher than controls (t=18.4, p<0.001), supporting known-group validity.

Conclusion: The Turkish adult version of the DSM-5 SAD-S demonstrates strong psychometric properties and is suitable for use in both clinical practice and research to assess the severity of social anxiety symptoms.

Keywords: Anxiety, reliability, social anxiety disorder, social phobia, validation

INTRODUCTION

Social anxiety disorder (SAD) is a common psychiatric condition characterized by a persistent and intense fear of social or performance situations in which individuals may be exposed to possible scrutiny by others. The core fear often involves acting in a way that will be embarrassing or lead to negative evaluation,

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resulting in either avoidance of such situations or enduring them with significant distress (1). Onset typically occurs in childhood or early adolescence, and the disorder frequently disrupts educational, occupational, and interpersonal functioning. Studies have shown that SAD is one of the most prevalent anxiety disorders, with lifetime prevalence rates approaching 10%, and that it is associated with early school dropout and long-term psychosocial impairment (2).

In recognition of the limitations of categorical diagnosis, the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), introduced dimensional severity measures to enhance clinical assessment (3). These tools are presented in Section III of the manual and are organized into two main types: (a) Cross-Cutting Symptom Measures and (b) Severity Measures. The latter include disorder-specific instruments developed by expert panels to quantify symptom severity across a spectrum of internalizing conditions, including SAD, generalized anxiety disorder, panic disorder, and others. These self-report scales, each consisting of 10 items, are designed for rapid assessment and are freely available for clinical and research use.

The DSM-5 Severity Measure for Social Anxiety Disorder—Adult (DSM-5 SAD-S) is grounded in well-established models of anxiety that distinguish among cognitive, physiological, and behavioral components of fear (4). The scale items capture these domains using a consistent item template across anxiety disorders, with disorder-specific modifications in wording and context (e.g., "felt anxious, worried, or nervous about social situations"). Responses are rated on a 5-point Likert scale, reflecting the frequency of symptoms over the past seven days.

Psychometric evaluations of the DSM-5 anxiety severity measures—primarily conducted in United States, German, Dutch, Spanish, and Brazilian samples—have demonstrated strong internal consistency, unidimensional factor structures, and convergent validity with both clinician-rated and self-report measures (5-10). Furthermore, studies have reported good test–retest reliability (with the exception of the Specific Phobia scale) and sensitivity to change, supporting their utility for both clinical monitoring and outcome research. However, these findings have not been uniformly replicated across all language adaptations and cultural contexts. Several versions, including the Turkish child adaptation, remain underexplored or only partially validated, particularly in clinical samples (11).

Given that anxiety disorders contribute substantially to chronic disease burden and disability (12, 13), culturally and linguistically validated instruments are essential for accurate diagnosis and effective intervention. Although a Turkish child version of the DSM-5 SAD-S has previously been used in research (11), comprehensive psychometric validation in Turkish adult clinical samples has not yet been published. The present study addresses this gap by evaluating the internal consistency, factor structure, and convergent validity of the Turkish version of the DSM-5 SAD-S in a treatment-seeking sample diagnosed with SAD, alongside a healthy control group. Despite its high prevalence in epidemiological studies, SAD may be underrepresented in psychiatric outpatient settings and, therefore, overlooked in routine clinical practice. As noted by Bandelow and Michaelis (12), even experienced psychiatrists may find it challenging to distinguish mild forms of social anxiety disorder from normative personality traits such as shyness or modesty. This further underscores the importance of reliable dimensional assessment tools in clinical settings.

Accordingly, we aimed to support the use of the DSM-5 SAD-S in Turkish clinical settings as a brief and practical tool for screening social anxiety symptoms, assessing symptom severity, and monitoring patients throughout the treatment. We hypothesized that the Turkish DSM-5 SAD-S would demonstrate high internal consistency and a unidimensional factor structure consistent with the original scale. We further expected DSM-5 SAD-S scores to correlate positively with established measures of social anxiety and related anxiety symptoms, supporting convergent validity. Additionally, we hypothesized that individuals with SAD would score significantly higher than healthy controls, indicating strong discriminative validity. This research contributes to the growing international literature on DSM-5 dimensional assessments and supports their broader application in cross-cultural psychiatric settings.

METHODS

Participants and Procedure

The study sample consisted of 146 Turkish-speaking adults aged between 18 and 45 years (mean [M]=24.86, standard deviation [SD]=5.94), recruited between June 2025 and November 2025 through community outreach and clinical referrals. A total of 110 individuals presenting with suspected social anxiety symptoms were initially evaluated for inclusion in the clinical group. Of these, 31 participants were excluded due to comorbid psychiatric conditions and six were

excluded due to incomplete data. The final SAD group comprised 73 participants who met DSM-5 diagnostic criteria for social anxiety disorder, as determined through a clinical interview using the Structured Clinical Interview for DSM-5 (14). The control group consisted of 73 healthy participants with no current or past psychiatric diagnoses. Participants in the SAD group were recruited from the Psychiatry Outpatient Clinic at the Department of Psychiatry, Faculty of Medicine, Izmir Tinaztepe University, while the control group was recruited from university campuses and the general community.

Inclusion criteria for both groups were Turkish as a native language and completion of at least primary education. Exclusion criteria included the presence of psychotic symptoms, intellectual disability, or a current substance use disorder. Additionally, individuals in the patient group with any comorbid psychiatric disorder were excluded. All participants provided informed consent prior to participation. The study protocol was approved by the International University of Sarajevo Institutional Review Board (Approval No: 01-1810/25), and data collection adhered to the ethical principles outlined in the Declaration of Helsinki. The patient group completed a Sociodemographic Information Form, the Turkish version of the DSM-5 Severity Measure for Social Anxiety Disorder—Adult, and the Liebowitz Social Anxiety Scale (LSAS), all administered in paper-and-pencil format. The healthy control group completed the same questionnaires, with the exception of the LSAS, also in paper-and-pencil format. Clinical participants were additionally asked to provide information regarding age at onset, treatment history, and family psychiatric history.

Measures

Sociodemographic Information Form

A structured Sociodemographic Information Form was developed by the researchers to collect background characteristics of the participants. The form included items assessing age, gender, education level, marital status, psychiatric history, family history of psychiatric illness, and, for clinical participants, age at onset of SAD. Responses were used for descriptive analyses, group comparisons, and examination of known-group differences.

DSM-5 Severity Measure for Social Anxiety Disorder—Adult (DSM-5 SAD-S)

The DSM-5 Severity Measure for Social Anxiety Disorder—Adult is a 10-item self-report scale developed by the American Psychiatric Association (1) to assess the frequency and severity of social anxiety symptoms over the past seven days. Items are rated on a 5-point Likert scale ranging from 0 ("not at all") to 4 ("extremely"), with higher scores indicating greater symptom severity. The scale is designed to be unidimensional and is widely used in both clinical and research settings. In this study, the Turkish-language version of the scale was administered.

A forward–backward translation procedure was employed. The original English version was first translated into Turkish by bilingual professionals and then independently back-translated into English. The back-translated version was reviewed by two bilingual psychiatrists to ensure conceptual and cultural equivalence. Any discrepancies were resolved through consensus.

Liebowitz Social Anxiety Scale

The LSAS is a 24-item clinician-administered or self-report instrument designed to assess fear and avoidance across a range of social interaction and performance situations (15). Each item is rated separately for fear and avoidance on a 4-point scale, yielding subscale scores and a total score. In this study, only the total score was used for the analysis of convergent validity. The validated Turkish version of the LSAS was used (16), which has demonstrated adequate internal consistency and construct validity in previous research.

Statistical Analysis

All statistical analyses were conducted using IBM SPSS Statistics, version 24 (IBM Corp., Armonk, NY, USA) and JASP for structural equation modeling. Descriptive statistics were calculated for all sociodemographic and clinical variables. Continuous variables were summarized using means and standard deviations, whereas categorical variables were reported as frequencies and percentages. Group comparisons between individuals with SAD and healthy controls were performed using the Mann–Whitney U test for non-normally distributed continuous variables, the independent-samples t test for normally distributed continuous variables, and chi-square tests for categorical variables. The internal consistency reliability of the DSM-5 SAD-S was assessed using Cronbach's alpha coefficient, calculated separately for the SAD group and the total sample. Item-level diagnostics, including corrected item–total correlations and Cronbach's alpha if an item was deleted, were also examined. To assess the test–retest reliability, the scale was re-administered two weeks after the initial assessment. A total of 40 participants—20 from the

Table 1: Sociodemographic and clinical characteristics of the study groups

	Social anxiety disorder (n=73)	Control group (n=73)	Statistic	p
Age (years)	26.05 (6.23)	23.68 (5.19)	U=3269.5	**0.011**
DSM-5 SAD-S score	21.50 (8.88)	1.90 (1.96)	t=18.4	**<0.001**
Gender			χ^2=0.030	0.867
Male	34 (46.6%)	32 (43.8%)		
Female	39 (53.4%)	41 (56.2%)		
Education level			χ^2=38.27	**<0.001**
Literate	5 (6.8%)	1 (1.4%)		
Primary school	5 (6.8%)	0 (0%)		
Middle school	4 (5.5%)	1 (1.4%)		
High school	32 (43.8%)	8 (11.0%)		
University	27 (37.0%)	63 (86.3%)		
Marital status			χ^2=10.99	**0.004**
Married	24 (32.9%)	8 (11.0%)		
Single	49 (67.1%)	64 (87.7%)		
Divorced	–	1 (1.4%)		
Psychiatric history			χ^2=35.38	**<0.001**
Present	45 (61.6%)	9 (12.5%)		
Absent	28 (38.4%)	63 (87.5%)		
Family psychiatric history			χ^2=4.52	**0.033**
Present	30 (41.1%)	17 (23.3%)		
Absent	43 (58.9%)	56 (76.7%)		
Age at onset (SAD group only)	20.45 (5.56)	—		

DSM-5 SAD-S: Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition Severity Measure for Social Anxiety Disorder; SAD: Social anxiety disorder.

patient group and 20 from the healthy control group—completed both administrations. Reliability was evaluated by calculating the correlation coefficient between the two sets of total scores. To examine the underlying factor structure, an exploratory factor analysis (EFA) was conducted in the SAD group using the minimum residual (MINRES) extraction method with oblimin rotation. The number of factors to retain was determined using parallel analysis. Subsequently, a single-factor model was extracted and evaluated in terms of interpretability and item loadings. A confirmatory factor analysis (CFA) was then conducted in the SAD group to test the unidimensional structure of the scale, using the diagonally weighted least squares (DWLS) estimator due to the ordinal nature of the item responses and the moderate sample size (17). Model fit was evaluated using standard fit indices, including the Comparative Fit Index (CFI), Tucker–Lewis Index (TLI), Root Mean Square Error of Approximation (RMSEA) with 95% confidence intervals, and the Standardized Root Mean Square Residual (SRMR). Convergent validity was examined using Pearson bivariate correlations between total scores on the DSM-5 SAD-S and the LSAS. All significance tests were two-tailed, and $p<0.05$ was considered statistically significant.

RESULTS

Sample Characteristics

The two groups differed significantly on several key sociodemographic and clinical variables. Participants in the SAD group were significantly older than healthy controls and reported markedly higher severity scores on the DSM-5 SAD-S, indicating a clear distinction between groups. No significant difference in gender distribution was observed, suggesting comparable male-to-female ratios across groups. In terms of education, a significant disparity was observed: the control group had a substantially higher proportion of university graduates, whereas the SAD group exhibited a broader distribution across lower educational levels. This pattern aligns with previous findings linking social anxiety to educational impairment (18). Marital status also differed significantly between groups. Individuals with SAD were more likely to be married or divorced, whereas the majority of controls were single.

Table 2: Item-level reliability statistics

	Item-total correlation	Cronbach's α if item deleted
Item 1	0.794	0.889
Item 2	0.743	0.893
Item 3	0.744	0.892
Item 4	0.676	0.897
Item 5	0.749	0.892
Item 6	0.661	0.898
Item 7	0.581	0.902
Item 8	0.544	0.904
Item 9	0.566	0.903
Item 10	0.598	0.902

Furthermore, psychiatric history, including both personal and familial history, was significantly more prevalent in the SAD group, supporting the validity of group classification based on diagnostic status. The mean age at onset of social anxiety symptoms in the clinical group was early adulthood, consistent with established epidemiological data (19). Together, these findings underscore the clinical distinctiveness of the SAD group and support the relevance of known-groups validity in the subsequent psychometric analyses (Table 1).

Internal Consistency

The internal consistency of the DSM-5 SAD-S was evaluated using Cronbach's alpha. The scale demonstrated excellent reliability in the total sample (α=0.967). When analyzed separately, internal consistency remained high within the clinical group diagnosed with SAD (α=0.907), indicating that the scale reliably measures symptom severity among individuals with clinically significant social anxiety.

Item–Total Correlations

Item–total correlations for the DSM-5 SAD-S were examined within the clinical sample. Corrected item–total correlations ranged from 0.544 (Item 8) to 0.794 (Item 1), indicating moderate to strong associations between individual items and the overall scale score. Cronbach's alpha values if individual items were deleted ranged from 0.889 to 0.904, suggesting that each item contributes meaningfully to internal consistency and that none warrant exclusion (Table 2).

Test–Retest Correlation Coefficients

The test–retest correlation coefficient for the DSM-5 SAD-S total score was r=0.976. Correlation coefficients for the individual items are presented in Table 3.

Table 3: Test-retest correlation coefficients

	r*
DSM-5 SAD-S	
Item 1	0.939
Item 2	0.932
Item 3	0.994
Item 4	0.975
Item 5	0.956
Item 6	0.956
Item 7	0.960
Item 8	0.963
Item 9	0.949
Item 10	0.877
Total Score	0.976

DSM-5 SAD-S: Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition Severity Measure for Social Anxiety Disorder—Adult, r*: Pearson correlation coefficient.

Table 4: Exploratory factor analysis of the DSM-5 Social Anxiety Disorder—Adult (unidimensional model; minimum residual extraction, SAD group, n=73)

	Factor 1	Uniqueness
Item 1	0.849	0.279
Item 2	0.798	0.364
Item 3	0.788	0.380
Item 4	0.720	0.481
Item 5	0.799	0.362
Item 6	0.688	0.527
Item 7	0.595	0.647
Item 8	0.561	0.685
Item 9	0.591	0.651
Item 10	0.624	0.611

The minimum residual extraction method was used in combination with oblimin rotation.

Exploratory and Confirmatory Factor Analysis

To evaluate the structural validity of the DSM-5 SAD-S, an EFA was conducted using data from the clinical group (n=73). The analysis employed the MINRES method with oblimin rotation. Initially, eigenvalue-based criteria suggested a potential two-factor solution. However, parallel analysis indicated that only the first factor had an eigenvalue exceeding the corresponding simulated value, supporting a unidimensional structure.

The EFA was subsequently re-run with the number of factors fixed at one. All 10 items loaded positively onto the single factor, with standardized loadings ranging from 0.561 (Item 8) to 0.849 (Item 1). Most

Table 5: Standardized factor loadings for the DSM-5 Social Anxiety Disorder Scale (CFA – DWLS; SAD group, n=73)

Latent factor	Observed item	Estimate	SE	95% CI		β	z	p
				Lower	Upper			
DSM-5 SAD-S	Item 1	1.000	0.0000	1.000	1.000	0.903		
	Item 2	0.976	0.0440	0.889	1.062	0.881	22.20	<0.001
	Item 3	0.906	0.0533	0.801	1.010	0.818	16.99	<0.001
	Item 4	0.836	0.0564	0.725	0.947	0.755	14.82	<0.001
	Item 5	0.958	0.0492	0.862	1.055	0.866	19.50	<0.001
	Item 6	0.828	0.0668	0.697	0.959	0.748	12.40	<0.001
	Item 7	0.750	0.0640	0.625	0.876	0.678	11.71	<0.001
	Item 8	0.653	0.0832	0.490	0.817	0.590	7.85	<0.001
	Item 9	0.681	0.0830	0.519	0.844	0.615	8.21	<0.001
	Item 10	0.742	0.0779	0.589	0.895	0.670	9.52	<0.001

CI: Confidence intervals; SE: Standard error; DSM-5 SAD-S: DSM-5 Severity Measure for Social Anxiety Disorder—Adult. Confirmatory factor analysis (CFA) was estimated using diagonally weighted least squares (DWLS) with robust standard errors. All items were treated as ordered categorical variables.

items demonstrated strong loadings above 0.60, and all exceeded the conventional threshold of 0.40, indicating adequate representation of the underlying construct of social anxiety severity. The majority of items also showed acceptable uniqueness values, suggesting that the common factor accounted for a substantial proportion of item variance. These findings support the use of a single total score on the DSM-5 SAD-S as a valid indicator of symptom severity in clinical populations (Table 4). A CFA was conducted using the DWLS estimator, which is appropriate for ordinal data. The 10 items of the DSM-5 SAD-S, rated on a 5-point Likert-type scale, were treated as ordered categorical variables. DWLS was selected due to its robustness in handling non-normal ordinal indicators and its suitability for small to moderate sample sizes. Robust standard errors and mean- and variance-adjusted chi-square statistics were used to evaluate model fit. The model specified a single latent factor underlying the 10 observed items. The one-factor CFA demonstrated excellent incremental fit (CFI=0.990; TLI=0.988) and marginally acceptable residual-based fit (SRMR=0.084). However, the RMSEA was elevated (0.106; 95% confidence interval [CI]=0.062–0.147), indicating that absolute model fit should be interpreted with caution. We therefore interpret model fit using multiple indices in conjunction with the pattern of strong and statistically significant factor loadings. All items loaded significantly onto the latent factor, with standardized factor loadings ranging from 0.590 (Item 8) to 0.903 (Item 1), further supporting the unidimensional structure of the scale (Table 5). These findings are consistent with theoretical expectations and provide additional evidence for the structural validity of the DSM-5 SAD-S in a clinical population.

Convergent Validity

To assess convergent validity, a Pearson bivariate correlation was computed between total scores on the DSM-5 SAD-S and the LSAS within the clinical sample. The observed association between the DSM-5 SAD-S and the LSAS ($r=0.390$, $p<0.001$, $df=71$) indicates moderate convergent validity. This magnitude is consistent with prior evidence demonstrating moderate correlations between the DSM-5 SAD severity scale and the Liebowitz Social Anxiety Scale–Self-Report (LSAS-SR) (e.g., approximately $r\approx0.47$ in a clinical sample) (20). Differences in correlation magnitude across studies may reflect variations in sample composition, restricted score variability within a single diagnostic group, and the fact that the DSM-5 SAD-S is a brief severity measure while the LSAS is a broader inventory of fear and avoidance across multiple social situations.

Statistical Power

For convergent validity, with n=73 (SAD group) and $\alpha=0.05$ (two-tailed), the sample provided ~80% power to detect correlations of $r\approx0.32$ or greater. The observed association with the LSAS ($r=0.39$) therefore falls within a detectably moderate range. For known-groups validity, with n=73 per group and $\alpha=0.05$ (two-tailed), the sample provided ~80% power to detect group differences of approximately $d\approx0.46$. The observed group separation was extremely large (approximately $d\approx3.05$), indicating statistical power effectively exceeding 0.99 (21).

DISCUSSION

The DSM-5 introduced dimensional severity assessments to complement categorical diagnoses and enhance

clinical precision (1). Among these measures, the Anxiety Severity Measures (ASM) were developed to evaluate core anxiety symptoms in a concise and accessible format (1, 3). Although several international validation studies have supported the reliability and structural validity of these tools (7, 8, 10, 11), the Turkish adult version of the DSM-5 SAD-S had not undergone formal psychometric evaluation prior to the present study.

Our findings support the unidimensional structure of the Turkish version of the DSM-5 SAD-S. Both the EFA and CFA yielded a single-factor solution with high factor loadings across all 10 items, consistent with theoretical models of anxiety that distinguish cognitive, physiological, and behavioral components (22). The CFA demonstrated excellent fit based on the CFI and TLI. However, the RMSEA slightly exceeded conventional cutoff values. This elevation is likely attributable to the sample size and the non-normal distribution of the data, a known issue when applying RMSEA to categorical data estimated using DWLS (17). Although incremental indices supported the one-factor model, the RMSEA exceeded commonly cited heuristic cutoffs. Such elevations can occur in relatively simple CFA models, particularly when degrees of freedom are small, where the RMSEA may over-reject even correctly specified models (23). In our study, structural validity was evaluated within a clinical SAD group (n=73) using a simple one-factor model with 10 indicators, all of which demonstrated moderate-to-strong loadings (EFA: 0.56–0.85; CFA: 0.59–0.90). Simulation research indicates that smaller samples can yield adequate factor recovery when loadings are strong and model complexity is limited, whereas even large samples can perform poorly when communalities are low or models are misspecified (24, 25). These findings are consistent with prior validation studies conducted in German, Brazilian, Dutch, and Spanish samples (6, 7, 9, 10), suggesting that the structure of the SAD scale is stable across diverse cultural and linguistic contexts.

The scale also demonstrated excellent internal consistency (α=0.91), consistent with previous studies reporting Cronbach's alpha coefficients above 0.85 (3). Furthermore, the scale demonstrated strong convergent validity with the LSAS, a well-established clinician-administered and self-report instrument. The correlation coefficient between the total SAD severity score and the LSAS score was significant (r=0.390, $p<0.001$), indicating that the two instruments assess overlapping constructs while still capturing potentially distinct dimensions of social anxiety symptomatology.

Sociodemographic comparisons between the clinical and control groups also supported the discriminative utility of the scale. The clinical group reported significantly higher severity scores and differed across relevant clinical variables, including psychiatric history, family psychiatric background, and earlier age at symptom onset. These findings suggest the scale's clinical sensitivity but further underscore the importance of early identification of individuals at risk.

Nevertheless, certain limitations should be acknowledged. First, the sample size was modest, which may limit statistical power and the stability of model fit estimates, particularly in factor-analytic procedures. Second, we did not conduct discriminant validity analyses using external measures of unrelated constructs (e.g., externalizing behaviors), which limited our ability to fully evaluate the construct boundaries of the SAD severity measure. Accordingly, it remains unclear whether the scale uniquely captures the severity of social anxiety symptoms without substantial overlap with related psychological dimensions such as general distress, depression, or trait anxiety. Future research should incorporate measures of unrelated or adjacent constructs to rigorously examine the discriminant validity of the instrument in diverse clinical and community samples.

An additional limitation is that psychiatric comorbidities were excluded from the SAD group to obtain a diagnostically homogeneous sample and reduce potential confounding effects of other disorders on symptom ratings. However, social anxiety disorder commonly co-occurs with other psychiatric conditions, most notably depressive disorders and other anxiety disorders (26). While this approach allowed for a clearer evaluation of the scale's psychometric properties, it may limit the generalizability of the findings, as patients with SAD frequently present with comorbid conditions in routine clinical settings. Future studies should therefore examine the performance of the scale in more heterogeneous clinical samples to better reflect real-world practice.

Another limitation concerns the translation and cultural adaptation process. Although a forward–backward translation procedure was applied and the final version was reviewed by two independent bilingual psychiatrists to ensure conceptual and cultural appropriateness, additional steps, such as formal committee review, pilot testing, or cognitive debriefing, were not undertaken. Consequently, certain linguistic or contextual nuances may not have been fully addressed. Future studies would benefit

from incorporating these procedures to further strengthen the cross-cultural validity of the scale.

Finally, the cross-sectional design of the study did not permit evaluation of sensitivity to treatment-related change, which is an important consideration for longitudinal clinical applications.

Future research should examine the scale in larger samples that better represent the clinical complexity of social anxiety disorder, including individuals with comorbid psychiatric conditions rather than exclusively diagnostically "pure" cases. Research involving different age groups would also be valuable. Moreover, longitudinal designs are needed to assess the instrument's sensitivity to treatment-related change and its utility in tracking symptom progression over time.

CONCLUSION

Despite these limitations, this study provides the first evidence for the structural validity, internal consistency, and convergent validity of the Turkish version of the adult DSM-5 SAD-S. Given the high prevalence of anxiety-related symptoms among Turkish youth and adults (27), the availability of a psychometrically supported, freely accessible, and time-efficient screening tool represents a valuable resource for both clinical practice and research settings in Turkiye. This tool may facilitate the early identification of individuals in need of treatment, streamline intake procedures, and improve the precision of symptom monitoring in routine clinical care.

Ethical Approval: The International University of Sarajevo Ethics Committee granted approval for this study (Date: 26.06.2025 No: IUS-REC-01-1810-25).

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	Data acquisition	F.P.C.
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Category 3	Final approval and accountability	F.P.C., K.A., O.A., E.K., O.Aydemir.
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RESEARCH ARTICLE

Mental health challenges, preventive behaviors, and perspective on telepsychiatry in patients with chronic mental illness during the pandemic

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ABSTRACT

Objective: This study examines the challenges faced by patients with schizophrenia (SCZ) and bipolar disorder (BD) during the coronavirus disease 2019 (COVID-19) pandemic, including healthcare accessibility, treatment adherence, social support, illness course, vegetative symptoms, concerns about COVID-19, protective healthcare behavior, sources of COVID-19-related information, and attitudes toward telepsychiatry.

Method: A dual-interview method was employed with 200 patients: 100 interviews were conducted by telephone and 100 face-to-face in the outpatient clinic (50 SCZ and 50 BD patients in each group), enabling a comparative analysis of interview modalities.

Results: Among the patients, 22% experienced difficulties reaching their doctors or hospitals, 6.5% were unable to access medications, and 7.5% reported insufficient social support. Avoidance of hospital visits due to COVID-19 concerns was higher in the telephone group than in the outpatient group (61% vs. 31%, p=0.001). Exacerbations occurred in 27% of participants, and treatment nonadherence was observed in 25.5%. Nonadherence, insufficient social support, insomnia, and appetite and weight loss were significantly associated with exacerbations. Nonadherence was highest among patients receiving sodium valproate (40%), whereas clozapine (17.1%) and lithium (20%) were associated with better adherence. Adoption of COVID-19 protective behaviors ranged from 83% to 95%, while only 23% used online resources, with slightly higher use among outpatients. Most patients (92.5%) were unaware of telepsychiatry; however, after receiving an explanation, willingness to use it was higher in the telephone group, except among patients with SCZ or delusional symptoms.

Conclusion: This study highlights the need for tailored healthcare strategies for individuals with chronic mental illnesses. Lack of familiarity with telepsychiatry may contribute to disruptions in the continuity of psychiatric care during crises, underscoring the importance of integrating telehealth services and improving access pathways.

Keywords: COVID-19, schizophrenia, bipolar disorder, telepsychiatry, preventive behavior

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INTRODUCTION

Public health measures and healthcare restrictions during the coronavirus disease 2019 (COVID-19) pandemic disrupted routine outpatient follow-up and access to medications for individuals with severe mental illnesses such as schizophrenia (SCZ) and bipolar disorder (BD).

Pre-pandemic evidence indicates that missed follow-up appointments are associated with worse outcomes in SCZ and BD (1, 2). During the COVID-19 period, service disruptions were accompanied by higher relapse rates and increased rehospitalization or use of acute psychiatric care among individuals with severe mental illness (3). Some settings also reported a shift in inpatient diagnostic case mix toward bipolar and psychosis-related conditions, or a higher proportion of schizophrenia-spectrum diagnoses, suggesting an increased acute-care burden in at least some healthcare systems (4-6). Continuity of treatment was further challenged by procedures requiring in-person contact, including long-acting injectable (LAI) antipsychotic administration and therapeutic drug monitoring (e.g., clozapine, lithium). Prolonged LAI dosing intervals or reduced injection frequency have been associated with relapse (7-11).

Telepsychiatry has been proposed as an alternative strategy to maintain continuity of care (12). However, uptake among patients with schizophrenia-spectrum disorders may be limited by barriers such as low eHealth literacy, limited access to technology, cognitive impairments, and paranoid ideation (13, 14). Administrative and within-system analyses in serious mental illness also suggest heterogeneity across quality-of-care indicators and indicate that increased telemedicine use does not necessarily eliminate treatment interruptions (15, 16). Reports from Turkiye and China similarly demonstrate reduced outpatient contact following the onset of COVID-19 (17, 18). However, individual-level comparisons between patients who continued in-person follow-up and those who avoided it—using multidomain profiling that includes symptom-related outcomes, treatment adherence, social support, and attitudes toward telepsychiatry—remain scarce.

The aim of this study was to explore the clinical and service utilization profiles of individuals with SCZ or BD. Both diagnoses require continuity of outpatient care for relapse prevention and were expected to face similar system-level barriers during the pandemic. We compared patients who continued routine outpatient follow-up with those who avoided in-person visits during the COVID-19 pandemic. We assessed healthcare access, symptom-related outcomes (exacerbations and vegetative symptoms), treatment adherence, social support, and attitudes toward telepsychiatry. We hypothesized that individuals avoiding in-person visits would exhibit higher rates of exacerbation and vegetative symptoms, as well as lower treatment adherence. Lower digital literacy and poorer social support were expected to be negatively associated with both in-person care-seeking and receptiveness to telepsychiatric services.

METHODS

Study Design and Participants

This cross-sectional study was conducted between July and November 2020 at a university hospital outpatient psychiatry clinic. This period was characterized by fluctuating restrictions and frequently revised service arrangements, with measures tightening again as autumn progressed and many clinics operating at reduced in-person capacity. Participants were identified through electronic health records and included adults (≥18 years) with a confirmed diagnosis of schizophrenia (International Classification of Diseases, Tenth Revision [ICD-10]: F20) or bipolar disorder (ICD-10: F31), who had attended at least three outpatient visits in the year preceding the pandemic. Patients with cognitive impairment, dementia, substance-induced psychiatric disorders, or acute psychotic agitation that interfered with interviews were excluded. Acute psychotic agitation was operationally defined as observable agitation or behavioral dyscontrol that prevented completion of the interview and/or required urgent intervention (e.g., rapid tranquilization or restraint), as documented by the treating psychiatrist.

Data Collection and Study Groups

Participants were drawn from a cohort of 672 patients with schizophrenia and 460 with bipolar disorder who had attended regular outpatient visits prior to the pandemic. During the study period, 266 patients with SCZ and 231 with BD continued regular follow-up (defined as ≥3 outpatient visits between January 1, 2019 and March 11, 2020).

Study Groups

Outpatient Group

To represent individuals who maintained access to care, 119 patients attending in-person appointments were approached (balanced 1:1 for SCZ and BD).

Nineteen declined participation, resulting in a final sample of 100 participants (50 with SCZ, 50 with BD).

Phone Group

This group comprised patients who had not accessed psychiatric care during the pandemic. We identified individuals who had missed scheduled appointments and had no hospital visits since the onset of the pandemic. To match the outpatient group, 100 patients were included (50 with SCZ, 50 with BD). The sample size was feasibility-based (no a priori power calculation) within the fixed recruitment period. Of 136 randomly contacted patients, 36 did not participate due to outdated contact information (n=22), unanswered calls (n=7), refusal (n=7), or incomplete interviews (n=2).

The study was explained to all participants (and relatives, when present). Written informed consent was obtained from outpatients, and verbal informed consent was obtained from those interviewed by phone.

Variables and Data Collection Tools

Structured interviews lasting 45-60 minutes were conducted to assess sociodemographic variables (age, gender, education level, employment status, marital status), psychiatric and medical history, current psychiatric symptoms, COVID-19-related concerns, levels of social support, difficulties in healthcare access, treatment adherence, attitudes toward telepsychiatry, and adherence to COVID-19 protective behaviors.

Telephone interviews followed the same structured guide. Symptom-related outcomes were recorded using prespecified standardized probes (presence/absence) in accordance with the study's operational definitions.

Hospital avoidance was operationalized as self-reported avoidance of hospital or outpatient visits due to concerns about COVID-19 infection. System-related access limitations (e.g., inability to reach services, restriction due to public health measures) were recorded separately under healthcare access difficulties.

Definitions and Outcome Measures

All outcomes were specified a priori and operationalized using explicit criteria (thresholds and/or established clinical frameworks), as detailed below. Outcomes were obtained using a structured interview guide (face-to-face or telephone) with predefined response options. Variables were coded according to prespecified decision rules.

Medication Nonadherence (Noncompliance)

Defined as missing prescribed medication for ≥10 consecutive days, taking <75% of the recommended dose in the past month, or missing scheduled doses of long-acting injectables. Nonadherence was coded as present if any criterion was met, based on patient or relative report (and clinical records when available).

Exacerbation

Defined as the presence of depressive, manic, hypomanic, or mixed episodes (BD), or recurrence/worsening of psychotic symptoms (SCZ), based on the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) criteria and assessed using structured DSM-anchored probes. Exacerbation was coded as present if DSM-5 episode or relapse criteria were met during the study period.

Vegetative Symptoms

Defined as self-reported changes in sleep, appetite, or weight compared with the pre-pandemic baseline. Vegetative symptoms were coded as present if a change in any domain was endorsed.

Social Support

Classified as sufficient, partially sufficient, or insufficient based on reported support across three domains: assistance with daily activities, support for treatment continuity/adherence, and financial support. Support was categorized as sufficient when reported in multiple domains, partially sufficient when limited to a single domain, and insufficient when no support was reported.

COVID-19 Protective Behaviors

Assessed using structured items reflecting contemporaneous World Health Organization (WHO) and Ministry of Health recommendations (mask use, hand hygiene, social distancing, avoiding crowded places). Each behavior was recorded as yes/no.

Telepsychiatry Awareness and Acceptability (Willingness to Use)

Prior knowledge of telepsychiatry was recorded (yes/no). After a brief standardized explanation, willingness to use telepsychiatry in the future was recorded (yes/no).

Statistical Analysis

IBM Statistical Package for the Social Sciences (SPSS), version 22.0, was used for statistical analyses. Chi-square tests were applied to categorical variables,

Table 1: Characteristics of the participants

Diagnosis	BD		SCZ	
Interview (int.) group	**Outpatient n (%)**	**Phone int. n (%)**	**Outpatient n (%)**	**Phone int. n (%)**
Age groups				
18-24	3 (6)	2 (4)	4 (8)	4 (8)
25-34	9 (18)	8 (16)	10 (20)	5 (10)
35-44	13 (26)	15 (30)	13 (26)	11 (22)
45-54	10 (20)	13 (26)	16 (32)	16 (32)
55 and over	15 (30)	12 (24)	7 (14)	14 (28)
Test statistics	χ^2=1.126 (df)=4	p=0.890	χ^2=4.167 (df)=4	p=0.384
Gender				
Female	30 (60)	28 (56)	19 (38)	22 (44)
Male	20 (40)	22 (44)	31 (62)	28 (56)
Test statistics	χ^2=0.041 (df)=1	p=0.839	χ^2=0.372 (df)=1	p=0.0572
Marital status				
Married	26 (52)	29 (58)	17 (34)	23 (46)
Never married	14 (28)	13 (26)	30 (60)	22 (44)
Widowed/separeted	10 (20)	8 (16)	3 (6)	5 (10)
Test statistics	χ^2=0.423(df)=2	p=0.809	χ^2=2.632 (df)=2	p=0.268
Education				
Primary school	14 (28)	17 (34)	16 (32)	18 (36)
High school	23 (46)	16 (32)	24 (48)	23 (46)
University	13 (26)	17 (34)	10 (20)	9 (18)
Test statistics	χ^2=2.080 (df)=2	p=0.353	χ^2=0.192 (df)=2	p= 0.909
Occupation				
Housewife	5 (10)	14 (28)	8 (16)	10 (20)
Employed	31(62)	17 (34)	12 (24)	14 (28)
Retired	12 (24)	7 (14)	9 (18)	10 (20)
Unemployed	12 (14)	12 (24)	21 (42)	16 (31)
Test statistics	χ^2=6.00 (df)=4	p=0.112	χ^2=1.104 (df)=3	p=0.776
Chronic medical illness-present	23 (46.0)	21 (42.0)	15 (30.0)	26 (52.0)
Absent	27(54)	29 (58)	35 (70)	24 (48)
Test statistics	χ^2=0.162 (df)=2	p=0.687	χ^2=5.002 (df)=2	p=0.025
Sufficient social support	29 (58)	26 (52)	33 (66)	27 (54)
Insufficient social support	21 (39)	24 (48)	17 (34)	23 (46)
Test statistics	χ^2=0.412 (df)=2	p=0.812	χ^2=3.001 (df)=2	p=0.212
COVID-19 infection	1 (2)	2 (4)	2 (4)	2 (4)
COVID-19 infection in the family	6 (12)	6 (12)	6 (12)	9 (18)

BD: Bipolar disorder; SCZ: Schizophrenia.

while the Mann–Whitney U test was used for non-normally distributed continuous variables. Statistical significance was set at $p<0.05$.

Ethics Committee Approval

The study was approved by the Gazi University Ethics Committee (July 6, 2020; Approval No: 406) and the Turkish Ministry of Health, COVID-19 Research Evaluation Commission (June 1, 2020; Approval No: T14-37-57). The study adhered to the principles of the Declaration of Helsinki and received no financial support.

Table 2: Psychotropic drugs used by participants and treatment noncompliance

	SCZ (n=100)*	BD (n=100)*	All participants n (%)	Treatment noncompliance n (%)	Lab. testing n (%)**
LAI antipsychotics	20	3	23 (11.5)	6 (26.1)	NA
Lithium	1	19	20 (10.0)	4 (20.0)	(11) 55.5
Clozapine alone or combinations	34	1	35 (17.5)	6 (17.1)	(20) 58.8
VPA	3	42	45 (22.5)	18 (40.0)	(14) 31.0
Oral atypical antipsychotic monotherapy	22	37	59 (29.5)	13 (22.0)	NA
Oral atypical antipsychotic combinations	5	12	17 (8.5)	5 (29.4)	NA
Oral typical antipsychotic monotherapy	4	1	5 (2.5)	0 (0)	NA
Lamotrigine	–	8	8 (4)	0 (0)	NA
Antidepressants	16	26	42 (21)	7 (16.7)	NA

SCZ: Schizophrenia; BD: bipolar disorder; LAI: Long-acting injectable antipsychotic; VPA: valproic acid; NA: Not applicable; * Because each group included 100 patients, n and % are identical; therefore, % is not presented; ** This column represents patients who were able to visit the hospital for a CBC test or blood drug level monitoring during the pandemic.

RESULTS

Sociodemographic Characteristics of Participants

Baseline characteristics were comparable between the telephone and outpatient groups and across diagnoses (mean age: 44.7±12.5 years; p>0.05) (Table 1). Chronic medical conditions were present in 42% of participants, most commonly hypertension (n=26), diabetes (n=23), and hyperlipidemia (n=16). Overall rates were similar between the SCZ and BD groups (44% vs. 41%). However, within the SCZ group, patients in the telephone group had higher comorbidity rates than those in the outpatient group (52% vs. 30%; p=0.025). Confirmed COVID-19 infection was rare (3.5%, n=7). Most participants rated their perceived social support as adequate (57.5%) or partially sufficient (35%), while 7.5% reported insufficient support. No significant differences were observed between groups or diagnoses.

Healthcare Access During the Pandemic and Treatment Compliance

Overall, 63.5% of participants (n=127) missed at least two hospital visits during the pandemic. Missed visits were significantly more common in the telephone group (78%) than in the outpatient group (49%; χ^2=18.143, p=0.001). Fear of COVID-19 infection was the most frequently reported reason for missed visits (61% vs. 31%; χ^2=18.116, p=0.001).

Twenty-two percent of participants (n=44) reported being unable to contact healthcare providers due to pandemic-related restrictions, with no significant difference between the telephone (20.8%) and outpatient (23.2%) groups (p>0.05). Twelve patients who experienced exacerbations requiring hospitalization reported barriers to accessing care, including service closures. Among telephone-group patients, hospital avoidance rates were similarly high in the BD (82%) and SCZ (74%) subgroups (p>0.05).

Treatment Compliance

During the pandemic, 25.5% of participants (n=51) reported treatment noncompliance. Noncompliance was more frequently attributed to side effects or personal refusal (19%, n=38) than to limited access to medications (6.5%, n=13). The remaining 74.5% (n=149) reported no access problems. Noncompliance rates did not differ between the SCZ and BD groups (21% vs. 30%; p>0.05). By medication types, noncompliance was highest among patients receiving valproate and certain antipsychotic regimens and lowest among those receiving clozapine and lithium (Table 2). Half of the sample required therapeutic drug monitoring or complete blood count (CBC) testing (50%, n=97). Monitoring rates were lowest among valproate users (31.0%) compared with lithium (55.5%) and clozapine users (58.8%) (χ^2=7.166, df=2, p=0.028), with testing typically conducted at 2–6-month intervals (Table 2).

Illness Course

During the pandemic, 27% of participants (n=54) experienced exacerbations, while 73% (n=146) remained clinically stable. Exacerbations were numerically more frequent in the BD group (31%; 19% depressive episodes, 12% manic episodes) than in the SCZ group (23%; 19% psychotic episodes, 4% depressive episodes), approaching statistical significance (p=0.060). Exacerbations were also more

Table 3: The characteristics of patients with and without exacerbations

	Nonexacerbated (n=146)		Exacerbated (n=54)		χ^2 (df)	p
	n	%	n	%		
Interview group						
Outpatient	67	45.9	33	61.1	3.653 (1)	0.050
Phone	79	54.1	21	38.9		
Diagnosis						
SCZ	77	52.7	23	42.6	1.624 (1)	0.203
BD	69	47.3	31	57.4		
Missed regular visits						
Yes	92	63.0	35	64.8	0.055 (1)	0.814
No	54	27.0	19	35.2		
Treatment noncompliance	26	17.8	25	46.3	16.840 (1)	**<0.001**
Treatment compliance	120	82.2	29	53.7		
Sufficient social support	97	66.4	18	33.3		
Insufficient social support*	53	33.6	32	66.3	13.782 (1)	**0.001**
Vegetative symptoms						
Sleep						
No change	115	76.7	7	14.0		
Hypersomnia	8	5.3	5	10.0		
Insomnia	27	18.0	38	76.0	64.214	**<0.001**
Body weight						
No change	105	70.0	31	62.0		
Weight gain	39	26.0	9	18.0		
Weight loss	6	4.0	10	20.0	13.353	**<0.001**
Appetite						
No change	124	82.7	19	38.0		
Increased	18	12.0	6	12.0		
Reduced	8	5.3	25	50.0	55.807	**<0.001**

*At least insufficient in two domains; SCZ: Schizophrenia; BD: Bipolar disorder.

common among outpatients than among those interviewed by telephone (Table 3).

Diagnosis and missed hospital visits were not associated with exacerbations. However, noncompliance, insufficient social support, and vegetative symptoms (insomnia, weight loss, decreased appetite) were more common among patients who experienced exacerbations (Table 3). Suicidal ideation was reported by 3% of participants (n=6), two of whom required emergency care. Treatment regimen was not associated with exacerbation rates (p>0.05). In the overall sample, insomnia (32.5%) and weight gain (24%) were the most common symptoms. Weight gain was more frequent in the telephone group than in the outpatient group (30% vs. 18%; p=0.028). Compared with SCZ patients, those with BD reported higher rates of sleep disturbance (48% vs. 30%; p=0.006) and appetite loss (23% vs. 10%; p=0.047). When analyzed by episode type, insomnia (manic 92.3%, psychotic 72.2%, depressive 65.2% vs. stable 17.1%), weight loss (depressive 34.8%, manic 15.4%, psychotic 11.1%, stable 2.7%), and appetite loss (manic 69.2%, depressive 52.2%, psychotic 33.3%, stable 4.1%) differed significantly across groups (all p<0.001). Active delusions were present in 23% of participants (n=46), including COVID-19-related delusions in 4% (n=8) of SCZ patients.

Compliance with Health Protective Behavior and Its Relationship with COVID-19-Related Concerns

COVID-19-related concerns were most commonly related to fear of infection (60.5% for themselves and 40% for relatives), disruption of psychiatric care (11%), and financial difficulties (4.5%). Depressive symptoms were most frequently associated with social isolation

Table 4: Compliance of participants with preventive measures against COVID-19 infection

Preventive measures	Compliant		Noncompliant	
	n	%	n	%
Staying at home/avoiding social interaction	173	86.5	27	13.5
Avoiding public areas	147	73.5	53	26.5
Minimized contact with family and friends	129	64.5	71	35.5
Washing hands and using hand sanitizer	166	83.0	34	17.0
Wearing face mask	190	95.0	10	5.0
Wearing gloves	31	15.5	169	84.5
Disinfecting items and surfaces	58	29.0	142	71.0

COVID-19: Coronavirus disease 2019.

and inactivity (34%), COVID-19-related losses (4.5%), and financial problems (4%). Overall compliance with core preventive measures was high, whereas glove use and surface disinfection were relatively uncommon (Table 4). Between-group comparisons showed greater avoidance of family and friends in the telephone group, but higher rates of mask use and surface disinfection in the outpatient group. Patients with SCZ were more likely than those with BD to use gloves, and patients who experienced exacerbations demonstrated lower compliance with mask use and handwashing (Table 4). Participants reporting infection-related concerns showed greater adherence to several core preventive behaviors (e.g., staying at home and hand hygiene) compared to those without such concerns (Table 4), while other preventive behaviors did not differ across subgroups.

Information Sources About the Pandemic

Television was the primary source of COVID-19 information for 94% of participants (n=188). Internet use was reported by 23% of participants and was slightly higher among BD patients (25%) than SCZ patients (21%; p>0.05). Internet use was also more common among outpatients than among those interviewed by telephone (28% vs. 18%; p>0.05).

Internet use varied significantly by age (p<0.001), being lowest among participants older than 55 years (4%, n=2) and highest among younger age groups (23.6%–50%).

Knowledge and Attitudes Toward Telepsychiatry Practices

Most participants had no prior knowledge of telepsychiatry (92.5%, n=185), and only 7.5% reported any familiarity (limited knowledge: 6.5%, n=13; familiar: 1%, n=2). After receiving a brief explanation, 71% (n=142) indicated willingness to use telepsychiatry services. Acceptance was higher in the telephone group compared to the outpatient group (82% vs. 60%; p=0.001) and higher among BD patients than SCZ patients (80% vs. 62%; p=0.005). COVID-19-related concerns were associated with greater acceptance (p<0.001), whereas the presence of active delusions was associated with lower willingness to use telepsychiatry (p=0.019). Recent exacerbations were not significantly associated with attitudes toward telepsychiatry.

DISCUSSION

In this cross-sectional observational study, we investigated the challenges faced by individuals with bipolar disorder and schizophrenia during the COVID-19 pandemic. Gender, education level, marital status, and occupation were comparable across groups. However, our findings indicate that patients who were unable to access healthcare for routine psychiatric follow-up differed in characteristics and needs from those who maintained access.

We found that 63.5% of participants experienced difficulties accessing healthcare. The primary reason (72%) was fear of infection, and 22% reported being unable to contact their doctors or hospitals due to pandemic-related restrictions. These findings indicate that participants experienced significant challenges in accessing healthcare during the COVID-19 period, most commonly related to curfews, appointment restrictions, and infection-related fears among individuals with chronic mental illnesses (19-22).

Avoidance of hospital visits due to COVID-19 concerns differed significantly between the telephone and outpatient groups (61% vs. 31%), suggesting higher infection-related anxiety in the telephone group. In contrast, the outpatient group reported lower levels of infection-related concern. However, given the cross-sectional design and the small number

of confirmed COVID-19 cases, causal inferences regarding subsequent exposure risk cannot be made (23-25). Additionally, a higher proportion of patients in the SCZ telephone group had chronic medical conditions such as diabetes and hypertension. This clinically meaningful comorbidity burden may have contributed to differences in COVID-19 risk perception and healthcare-seeking behavior. These patients may have been more aware of their vulnerability to COVID-19 infection, potentially leading to greater avoidance of hospital visits. At the same time, these findings underscore the need to improve medical care accessibility for high-risk populations (20, 21, 24).

Psychiatric services were also disrupted, with hospital wards repurposed for COVID-19 care, contributing to a decline in psychiatric hospitalizations overall (21, 22, 26). In our study, 9.4% of participants required hospitalization but encountered difficulties accessing inpatient services. These results highlight the importance of ensuring continuity of mental health services during public health crises.

Medication disruptions were reported by 25.5% of participants, with 19% attributable to noncompliance. These rates are consistent with both pre-pandemic and during-pandemic findings, which indicate that medication noncompliance among individuals with serious mental illnesses averages approximately 20%-30%. Notably, only 6.5% of participants reported difficulties accessing medication, likely reflecting government measures implemented to support individuals with chronic mental illnesses during the pandemic (27-29).

Patients receiving clozapine and lithium demonstrated the highest compliance rates, consistent with pre-pandemic evidence (30, 31). These patients also showed greater adherence to laboratory monitoring requirements compared to those receiving valproic acid. This pattern suggests a positive association between routine monitoring and medication adherence, underscoring the importance of regular follow-up in psychiatric care.

Overall, 27% of participants experienced exacerbations during the pandemic (BD: 28%, SCZ: 22%), in line with previous reports (23). Exacerbations were more frequent among outpatients (31%) than among patients interviewed by telephone (19%), possibly reflecting help-seeking behavior during the pandemic, whereby symptom worsening prompted in-person visits despite infection concerns. Medication noncompliance was strongly associated with exacerbations (45.1% vs. 18.1%) (9, 27, 32).

Social support plays a critical role in preventing exacerbations (33, 34). Participants reporting adequate social support had lower exacerbation rates (15.7%) compared to those reporting partial (40%) or inadequate support (26.7%). Insufficient support may contribute to more severe symptom profiles, reduced access to care, and increased stress levels (32-34). These findings emphasize the essential role of social networks in maintaining mental health during public health crises.

All types of exacerbations (psychotic, depressive, and manic) were associated with higher rates of insomnia, weight loss, and reduced appetite compared to stable cases (35, 36). Additionally, 24% of participants reported weight gain, which may contribute to increased health risks (37). These findings underscore the importance of monitoring vegetative symptoms—readily identifiable even by nonpsychiatric clinicians—to help mitigate health complications during crises.

Most participants adhered to pandemic guidelines, with high rates of mask use (95%), staying at home (86.5%), and handwashing (83%). Similar adherence patterns have been reported in the general populations, suggesting that individuals with severe mental illnesses remained aware of preventive recommendations (38-40). These findings indicate that targeted public health messaging and supportive interventions, such as accessible information delivery, may help sustain and further enhance compliance within this population.

Patients interviewed by telephone were more likely to avoid social interactions (73% vs. 56%), possibly reflecting heightened caution. In contrast, outpatients demonstrated greater adherence to measures such as mask use (100% vs. 90%) and surface disinfection (39% vs. 19%), likely due to increased exposure outside the home (40-42). However, these unadjusted group differences may also reflect potential confounding factors, including age, illness severity, medical comorbidity, and differential access to COVID-19-related information.

Patients experiencing exacerbations were less likely to use masks and maintain adequate hand hygiene, consistent with evidence that active mood or psychotic symptoms may increase vulnerability to COVID-19 infection (43-45).

Our study found that 94% of participants, regardless of interview method or psychiatric diagnosis, relied on television as their primary source of COVID-19 information. Despite the increase in internet and social media use among individuals with severe mental illnesses over the past decade, television remained the

dominant information source during the pandemic (46-48). Similarly, research in the general population reported that 80% relied on television and 70% on the internet (including 20% via social media and 12% via websites) (49). Consistent with previous research, older patients reported less frequent use of the internet and social media (47, 48). This limited digital engagement underscores the need for effective strategies to disseminate information and facilitate telepsychiatry participation among older adults.

Although the use of telepsychiatry increased during the pandemic due to public health restrictions, both awareness and accessibility remained low (50). In our sample, 92.5% of participants were unfamiliar with telepsychiatry, and only 1% reported adequate knowledge. However, after receiving a brief explanation, 71% expressed willingness to use telepsychiatry services. Because willingness was assessed immediately following an informational explanation, the observed acceptability may partially reflect an information or priming effect rather than baseline attitudes. Patients interviewed by telephone demonstrated higher acceptance (82%) than outpatients (60%), suggesting a possible association between perceived infection risk and telepsychiatry adoption. Although prior studies indicate that paranoia and referential delusions may reduce telepsychiatry engagement among individuals with schizophrenia (51), 60% of patients in our SCZ group expressed willingness to use these services. This receptivity may be attributable to the long-term, trust-based therapeutic relationships established at our institution.

Future mental health policies should consider integrating telepsychiatry into routine psychiatric care, while addressing issues of accessibility and infrastructure.

This study has several limitations. Its single-center, cross-sectional design limits generalizability and precludes causal or directional inferences. Additionally, because participants were recruited from routine outpatient follow-up visits, the findings may underrepresent individuals without stable access to care. Because no a priori power calculation was performed, some subgroup comparisons may have been underpowered to detect small effects. Missed follow-up visits were recorded dichotomously (≥2 missed visits) rather than as an exact count, precluding analyses based on the total number of missed appointments. Additionally, only a small number of participants had confirmed COVID-19 infection (n=7); therefore, infection-related findings should be interpreted with caution.

Some data were self-reported and are therefore subject to recall and response bias. Moreover, a portion of the sample was assessed via telephone, which may have reduced standardization in symptom probing and quantification and precluded assessment of nonverbal clinical cues. Telephone-based assessments may also reduce granularity and introduce measurement variability, with potential misclassification for certain variables. Nevertheless, key outcomes were specified a priori and operationalized using explicit thresholds and a structured assessment guide (and, where applicable, established clinical frameworks). Future longitudinal studies are needed to evaluate the sustained impact of public health crises on psychiatric populations.

CONCLUSION

This single-center cross-sectional study provides clinically relevant insights into the challenges faced by patients with schizophrenia and bipolar disorder during the COVID-19 pandemic, most commonly limited access to care and infection-related concerns. Importantly, not all patients were severely affected: approximately three-quarters remained clinically stable, whereas about one-quarter experienced symptom exacerbations associated with medication noncompliance and lower perceived social support. These findings underscore the value of structured follow-up and early monitoring of vegetative symptoms to maintain continuity of care during service disruptions. Telepsychiatry was largely unfamiliar to participants, highlighting an opportunity to implement structured remote follow-up pathways and provide practical support to enhance patient engagement during similar crises.

Ethical Approval: The Gazi University Ethics Committee granted approval for this study (Date: 06.07.2020, Number: 406).

Informed Consent: Informed consent was obtained from all participants prior to data collection. Written consent was obtained from outpatients, and verbal consent was obtained for telephone interviews.

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Contribution Categories		Author Initials
Category 1	Concept/Design	B.E.M., R.F.K., M.K.
	Data acquisition	B.E.M.
	Data analysis/Interpretation	B.E.M., R.F.K.
Category 2	Drafting manuscript	B.E.M., R.F.K., M.K.
	Critical revision of manuscript	B.E.M., R.F.K., M.K.
Category 3	Final approval and accountability	B.E.M., R.F.K., M.K.
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RESEARCH ARTICLE

Psychiatric comorbidities in multiple sclerosis patients and their relationship with clinical variables: A university hospital sample

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ABSTRACT

Objective: This study aimed to determine the prevalence of clinically documented psychiatric diagnoses in patients with multiple sclerosis (MS) and to identify demographic and clinical predictors associated with an increased risk of comorbidity.

Method: This study included 382 patients with MS who were followed at a university hospital between January 2022 and June 2025. Medical records were reviewed for demographic characteristics, disease course and duration, disability severity (Expanded Disability Status Scale [EDSS]), comorbid neurological symptoms, disease-modifying therapies, and documented psychiatric diagnoses. Patients were categorized into those with psychiatric comorbidity (PC+) and those without psychiatric comorbidity (PC–). Univariate analyses and binary logistic regression were performed to identify independent predictors.

Results: At least one psychiatric diagnosis was present in 35% of the patients. Depression (20%) and anxiety disorders (10%) were the most common conditions. Overall, 51.8% of patients were using at least one psychotropic medication, prescribed either for psychiatric diagnoses or for MS-related symptoms such as fatigue and neuropathic pain. Comparison of the PC+ and PC- groups revealed significant differences in age, sex, duration of MS, disease severity, presence of urinary incontinence, and fatigue. Logistic regression analysis showed that female sex was independently associated with lower odds of psychiatric comorbidity, whereas fatigue, higher EDSS scores, and longer MS duration were associated with higher odds.

Conclusion: Psychiatric comorbidities are prevalent in MS, affecting more than one-third of patients. This study comprehensively evaluated the risk factors identified in the literature and found that, when assessed together, most did not remain independent predictors. Key independent predictors for psychiatric comorbidity include female sex, disability severity, disease duration, and fatigue.

Keywords: Expanded Disability Status Scale (EDSS), multiple sclerosis, psychiatric comorbidities

INTRODUCTION

Multiple sclerosis (MS) is a chronic autoimmune disease characterized by inflammation, demyelination, and neurodegeneration of the central nervous system. Clinically, the disease progresses in three main forms: relapsing-remitting (RR), primary progressive (PP), and secondary progressive (SP) (1).

Psychiatric comorbidities are common throughout the course of MS. Depression is the most

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prevalent psychiatric disorder (30–50%), occurring at rates two to three times higher than in the general population (2). Anxiety disorders are the second most common psychiatric condition, affecting 25–40% of patients with MS (3). Recent studies indicate that this population is also at increased risk for bipolar disorder, psychotic symptoms, obsessive-compulsive symptoms, substance use disorders, and suicide attempts (4). Additionally, many patients with MS experience several cognitive and affective symptoms, such as affective lability, apathy, irritability, fatigue, and impaired executive functioning, that significantly affect daily functioning, even when full diagnostic criteria for a psychiatric disorder are not met. Psychiatric symptoms in MS are thought to have a multifactorial pathophysiology. Direct damage related to demyelinating lesions and atrophy, as well as lesion localization, are among the proposed mechanisms (5). Additionally, sex (6, 7), smoking (8), and disease severity (6, 9, 10) have been reported to be associated with depressive symptoms, while the effects of certain disease-modifying therapies (e.g., interferon-beta [IFN-β]) remain controversial) (11). Furthermore, several studies have evaluated the associations between neurological manifestations of MS, such as seizures (12), neuropathic pain (6, 13), urinary incontinence (14), spasticity, and fatigue (6), and symptoms of anxiety and depression (15). Recent studies have shown that psychiatric comorbidities in patients with MS are often underrecognized in routine clinical practice. Untreated psychiatric conditions may lead to poor adherence to MS treatments, increased healthcare utilization, a higher risk of suicide, and reduced functional capacity (16). Given the high burden of psychiatric comorbidities in MS and their potential impact on clinical outcomes, comprehensive research on these comorbidities is increasingly important.

This study aimed to evaluate the prevalence of psychiatric comorbidities in patients with MS and their associations with demographic, clinical, and treatment-related variables. We hypothesized that psychiatric comorbidities in MS are associated with markers of disease severity and cumulative disease burden. Specifically, higher Expanded Disability Status Scale (EDSS) scores, longer disease duration, a progressive clinical course, and symptoms such as neuropathic pain, urinary incontinence, and fatigue were expected to increase the risk of psychiatric comorbidity.

METHODS

This medical record-based, descriptive, cross-sectional study was approved by the Ethics Committee of Baskent University (KA25/383, 21/10/2025). All study procedures adhered to the Declaration of Helsinki.

The study sample included all patients diagnosed with MS who were examined at the Neurology Department of Baskent University Ankara Hospital between January 1, 2022 and June 1, 2025. Neurology and, when available, psychiatry consultation notes were retrospectively reviewed to collect data on the following variables: age, sex, age at MS diagnosis, disease duration, disease severity (measured by the Expanded Disability Status Scale), type and duration of disease-modifying therapy (DMT), smoking and alcohol use, documented psychiatric diagnoses, psychotropic medication use, and MS-related clinical features, such as seizure history, neuropathic pain, spasticity, urinary or fecal incontinence, and fatigue. Clinical variables, including EDSS score, fatigue, urinary or fecal incontinence, neuropathic pain, and spasticity, were obtained from the most recent neurology visit. This visit corresponded to the time at which psychiatric status was documented.

Participants

Medical records of 494 patients were screened. After applying the exclusion criteria, 382 patients with complete and reliable longitudinal data were included in the final analysis. Patients were excluded if: (1) the initial MS diagnosis was subsequently revised to an alternative disorder, such as connective tissue disease or vasculitis (n=24); (2) they had an additional genetic or demyelinating neurological disorder (e.g., myelin oligodendrocyte glycoprotein antibody–associated disease [MOGAD], neuromyelitis optica spectrum disorder [NMOSD], hereditary spastic paraplegia) (n=3); (3) they had only one or two recorded visits for preoperative consultation, medical advice, or disability reports (n=50); (4) they had not attended follow-up appointments for more than two to three years (n=12); (5) they were undergoing treatment for an active malignancy (n=7); or (6) early disease-course records were missing or inaccessible (n=16).

The authors verified MS diagnoses by reviewing documented symptoms, examination findings, and radiological imaging data according to the Revised (2024) McDonald Criteria (17). No discrepancies were identified between prior and current assessments. The drugs used in MS treatment were categorized

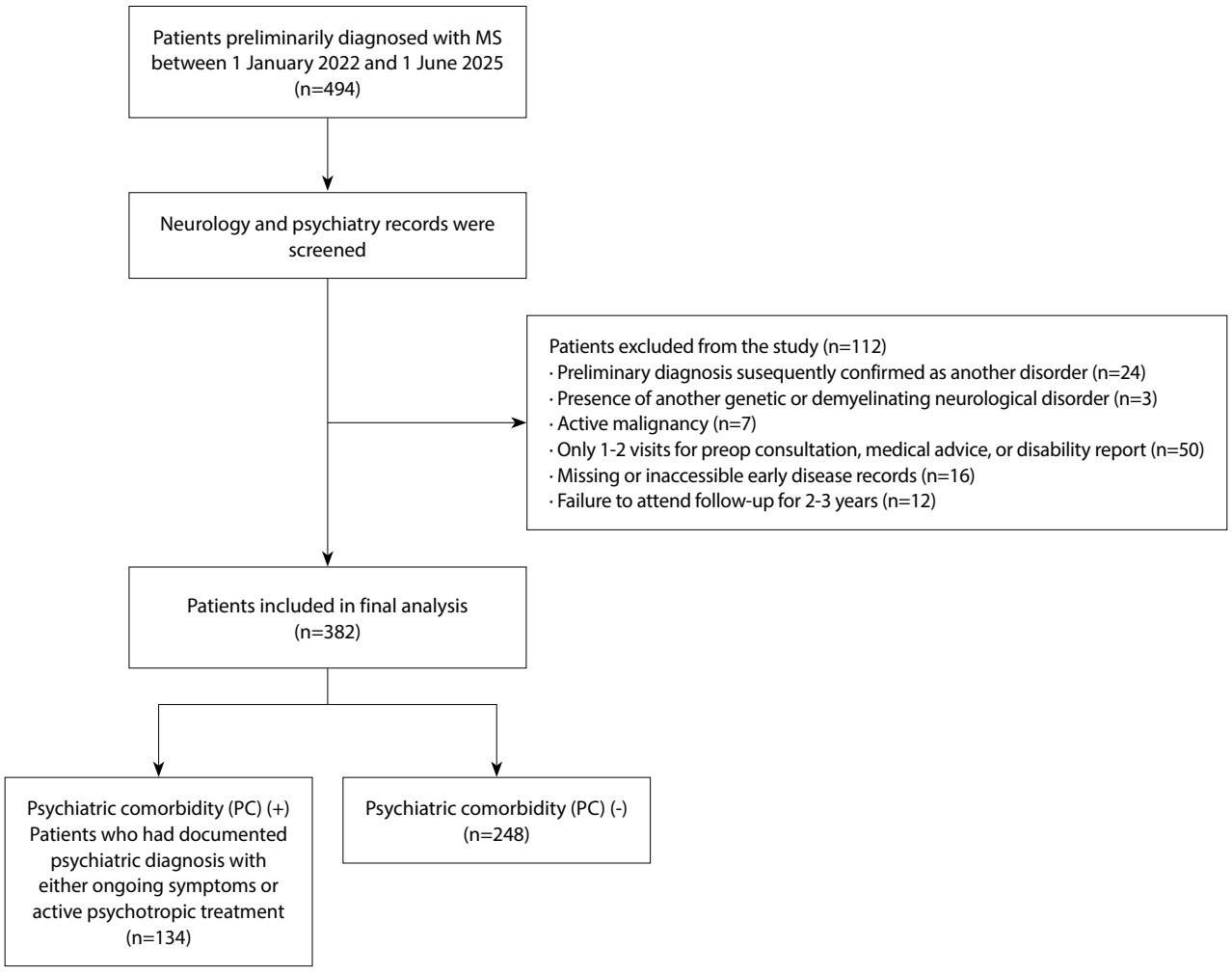

Figure 1. Flowchart illustrating participant selection and grouping.

according to the literature as low- to moderate-efficacy agents (dimethyl fumarate, IFN-β and peginterferon, glatiramer acetate, teriflunomide), high-efficacy drugs (fingolimod, natalizumab, alemtuzumab, ocrelizumab, cladribine), and other treatments (fenebrutinib, fentrepid, methotrexate) (18, 19).

Psychiatric comorbidity was determined retrospectively from electronic medical records. Patients with a documented psychiatric diagnosis and either ongoing symptoms or current psychiatric treatment were classified into the psychiatric comorbidity-positive (PC+) group. A psychiatric diagnosis was considered present if it had been established and documented by a psychiatrist or neurologist at the study center, or if neurology records included documentation from external psychiatric evaluations. All other patients were classified into the psychiatric comorbidity–negative (PC-) group.

Figure 1 presents the flowchart detailing the participant selection and data collection process.

Statistical Analysis

All statistical analyses were performed using SPSS 27.0 for Windows (SPSS, Chicago, IL, USA). A descriptive analysis of the sample, including key sociodemographic and clinical variables, was summarized in tables. Dichotomous variables were expressed as numbers and percentages, while continuous variables were presented as medians and interquartile ranges (IQR). The normality of continuous variables was assessed using the Kolmogorov-Smirnov test and visual tests. For univariate comparisons between the two groups (PC+ and PC-), the Mann–Whitney U test was used for non-normally distributed continuous variables (age, age at MS diagnosis, MS duration, and EDSS score), and chi-square tests were applied to categorical variables (e.g., sex, clinical course, DMT category). For multivariate analysis, variables identified as significant in the univariate analysis, along with previously reported risk factors for psychiatric comorbidity in MS,

were entered into a binary logistic regression model to determine independent predictors. Multicollinearity among independent variables was assessed using the variance inflation factor (VIF). Variables with high correlations (>0.40) in the regression correlation matrix were examined prior to regression model construction. The Hosmer-Lemeshow goodness-of-fit test was used to evaluate model fit. All tests were two-tailed, and a p-value <0.05 was considered statistically significant.

RESULTS

Of the 382 patients, 69.6% (n=266) were female. The mean age was 44.2±12.9 years (range: 18–85 years), the mean age at diagnosis was 31.6±10.6 years (range: 10–71 years), the mean disease duration was 12.5±7.8 years (range: 0–47 years), and the mean EDSS score was 3.0±1.7 (range: 0.5–7). Thirty-five percent of patients (n=134) had a history of at least one psychiatric diagnosis. Eleven patients (2.8%) had received a psychiatric diagnosis prior to their MS diagnosis, presenting with symptoms such as numbness, dizziness, and blurred vision. The distribution of sociodemographic characteristics, MS-related variables, and psychiatric diagnoses is presented in Table 1.

A comparison of the PC+ and PC- groups with respect to the study variables revealed significant differences in age (p<0.001), sex (p=0.003), MS duration (p<0.001), disease severity (p<0.001), presence of urinary incontinence (p=0.015), and fatigue (p<0.001). Detailed comparisons between the PC+ and PC- groups are presented in Table 1.

More than half of the patients (51.8%, n=198) were receiving at least one psychotropic medication. These medications were prescribed not only for psychiatric comorbidities but also for MS-related symptoms such as fatigue (n=62), neuropathic pain (n=65), and tremor (n=2). The distribution of psychotropic medications and their indications is presented in Supplementary Digital Appendix 1.

A logistic regression analysis was performed to evaluate the effects of variables identified in the univariate analysis (age, sex, MS duration, EDSS score, urinary incontinence, and fatigue), along with previously reported risk factors for psychiatric comorbidity in MS (smoking status, clinical course, treatment category, and neuropathic pain), on the likelihood of psychiatric comorbidity. Multicollinearity was assessed using the variance inflation factor, and all variables were within acceptable limits. The logistic regression model was statistically significant ($\chi 2(4)=43.256$, $p<0.001$). The model explained 15% of the variance in psychiatric comorbidity (Nagelkerke $R^2=0.153$) and correctly classified 67.6% of cases. In the final model (Hosmer-Lemeshow test, p=0.411), sex, MS duration, EDSS score, and fatigue were significant predictors. Longer MS duration, higher EDSS scores, and the presence of fatigue were associated with an increased risk of psychiatric comorbidity. Female sex was identified as a protective factor (Table 2).

DISCUSSION

This study aimed to investigate the prevalence of documented psychiatric comorbidities in patients with multiple sclerosis and their associations with demographic, clinical, and treatment-related variables. In our sample, more than one-third of patients with MS had a history of at least one psychiatric comorbidity. Approximately 20% were diagnosed with depression, and 10% had an anxiety disorder. Female sex was identified as a protective factor, whereas greater disease severity (as measured by EDSS), longer disease duration, and the presence of fatigue were independent risk factors for psychiatric comorbidity in patients with MS.

The prevalence rates of anxiety and depression diagnoses in patients with MS in this study are generally consistent with previous reports. However, several differences merit consideration. Previous studies have reported depression prevalence rates ranging from 27% to 33% and anxiety prevalence rates ranging from 10% to 35% (6, 20-22). These variations may be attributable to methodological differences across studies, including sample size and assessment methods. In particular, scale-based studies (21, 22) tend to report higher prevalence rates because they assess symptom severity rather than clinically documented diagnoses. Conversely, in the absence of standardized symptom screening instruments, our study may have underestimated subclinical psychiatric symptoms. In our cohort, the longer disease duration, lower representation of progressive MS forms, and reliance on clinically documented diagnoses rather than self-report scales may explain the lower prevalence of anxiety and depression compared to some previous studies (20). Consequently, these findings may not fully capture the overall burden of psychiatric symptoms in MS.

In our sample, approximately 2% of patients had a diagnosis of a sleep disorder, which is substantially lower than prevalence rates reported in the literature,

Table 1: Comparisons of variables by psychiatric comorbidity status (n=382)*

	Psychiatric comorbidity (+) (n=134)	Psychiatric comorbidity (-) (n=248)		ESM	p
Age (years), median (IQR)	46 (20)	41 (17)	Z: -3.956	r:-0.202[f]	**<0.001[b]**
Sex, n (%)			χ^2: 8.756	φ: -0.151	**0.003[a]**
Female	106 (27.7)	160 (41.9)			
Male	28 (7.3)	88 (23)			
Age at MS diagnosis (years), median (IQR)	33 (18)	29.5 (13)	Z: -1.86	r: -0.09[f]	0.063[b]
MS duration (years), median (IQR)	12 (12)	11 (9)	Z: -3.748	r: -0.191[f]	**<0.001[b]**
EDSS score, median (IQR)	3 (3)	2 (2)	Z: -4.178	r: -0.217[f]	**<0.001[b]**
Clinical course, n (%)			χ^2: 5.501	V: 0.12[e]	0.064[a]
PP	11 (2.9)	15 (3.9)			
SP	11 (2.9)	8 (2.1)			
RR	111 (29.2)	224 (58.9)			
Treatment history with IFN, n (%)				φ: -0.1	0.102[c]
No	134 (35.1)	241 (63.1)			
Yes	0	7 (1.8)			
Drug efficacy, n (%)			χ^2: 0.750	V: 0.045[e]	0.687[a]
No DMT	5 (1.3)	6 (1.6)			
Low/moderate efficacy DMTs (DMF, IFN, glatiramer acetate, teriflunomide)	45 (11.8)	90 (23.6)			
High-efficacy DMTs (fingolimod, natalizumab, alemtuzumab, ocrelizumab, cladribine)	82 (21.5)	147 (38.5)			
Other (fenebrutinib, fentrepid, MTX)	2 (0.5)	5 (1.3)			
Smoking status, n (%)			χ^2: 0.023	V: 0.008[e]	0.998[a]
No	122 (31.9)	226 (59.2)			
Yes	9 (2.4)	17 (4.5)			
Former	3 (0.8)	5 (1.3)			
Seizure, n (%)			χ^2: 0.291	φ: 0.028	0.59[a]
No	127 (32.2)	238 (62.3)			
Yes	7 (1.8)	10 (2.6)			
Fecal incontinence, n (%)			χ^2: 2.671	φ: 0.104	0.102[d]
No	129 (33.8)	246 (64.4)			
Yes	5 (1.3)	2 (0.5)			
Urinary incontinence, n (%)			χ^2: 5.885	φ: 0.124	**0.015[a]**
No	108 (28.3)	222 (58.1)			
Yes	26 (6.8)	26 (6.8)			
Spasticity, n (%)			χ^2: 0.529	φ: 0.037	0.467[a]
No	101 (26.4)	195 (51)			
Yes	33 (8.6)	53 (13.9)			
Neuropathic pain, n (%)			χ^2: 3.772	φ: 0.099	0.052[a]
No	104 (27.2)	212 (55.5)			
Yes	30 (7.9)	36 (9.4)			
Fatigue, n (%)			χ^2: 17.948	φ: 0.217	**<0.001[a]**
No	86 (22.6)	207 (54.5)			
Yes	47 (12.4)	40 (10.5)			
Psychiatric diagnosis, n (%)					
Depressive disorders	85 (22.3)				
Anxiety disorders	38 (9.9)				
Sleep disorders	6 (1.6)				
OCD	2 (0.5)				
SCH	2 (0.5)				
BAD	1 (0.26)				
Psychotropic medication use, n (%)			χ^2: 158.79	φ: 0.65	**<0.001[d]**
No	4 (1)	180 (47.1)			
Yes	130 (34)	68 (17.8)			

*Percentages are presented within each subgroup. †n: Number; %: Percentage; IQR: Interquartile range; ESM: Effect size measure; MS: Multiple sclerosis; EDSS: Expanded Disability Status Scale; PP: Primary progressive; SP: Secondary progressive; RR: Relapsing-remitting; DMT: Disease-modifying therapy; DMF: Dimethyl fumarate; MTX: Methotrexate; OCD: Obsessive-compulsive disorder; SCH: Schizophrenia; BAD: Bipolar affective disorder. a: Pearson's chi-square test; b: Mann–Whitney U test; c: Fisher's exact test; d: Corrected chi-square test; e: Cramer's V; f: Rank-biserial correlation.

Table 2: Final logistic regression model predicting psychiatric diagnoses in patients with multiple sclerosis (MS)

	Odds Ratio (95% CI)	p
Sex (female)	0.419 (0.245-0.715)	**0.001**
MS duration	1.037 (1.003-1.073)	**0.032**
EDSS score	1.194 (1.024-1.393)	**0.023**
Fatigue (yes)	2.447 (1.45-4.13)	**0.001**

CI: Confidence interval; MS: Multiple sclerosis; EDSS: Expanded Disability Status Scale. † Nagelkerke R^2=0.153.

where up to 55% of patients with MS are affected (23). Other studies have indicated that nearly one-fifth of MS patients experience sleep disturbances, with female sex, anxiety, and bladder dysfunction identified as independent predictors (24). The discrepancy between our findings and prior research may reflect methodological differences. Higher prevalence rates in some studies were frequently based on symptom rating scales rather than clinical diagnoses. Moreover, potential contributors to sleep disturbances, such as restless legs syndrome, neuropathic pain, bladder dysfunction, or comorbid depression, were not systematically evaluated in our study. Additionally, many patients in our cohort were using medications with sedative properties, including pregabalin, gabapentin, pramipexole, and benzodiazepines, which may have mitigated observable sleep-related complaints. These findings suggest that future research on sleep disorders in MS should incorporate comprehensive clinical assessments and account for both pharmacological and non-pharmacological factors. Studies should also systematically evaluate neurological and psychiatric factors to obtain more accurate prevalence estimates.

We found that most patients were female, consistent with the well-established higher prevalence of MS among women (25). When psychiatric comorbidities were analyzed according to disease course, no statistically significant differences were observed among relapsing-remitting, primary progressive, and secondary progressive forms, in line with previous reports (26). However, one study identified relapsing–remitting MS (RRMS) as a risk factor for anxiety (7).

Consistent with earlier findings, higher EDSS scores (6, 7, 9, 10), longer disease duration, and fatigue (6) were identified as significant risk factors for psychiatric comorbidity in our cohort. Several studies have demonstrated that greater neurological disability is associated with increased rates of depression and anxiety. This association may reflect the long-term psychological burden of functional impairment, loss of independence, and restriction of social roles (27). Similarly, longer disease duration may indicate prolonged exposure to disease-related uncertainty, treatment burden, and progressive limitations, each of which can increase vulnerability to psychiatric morbidity (4). However, some studies have reported higher rates of anxiety and depression at lower EDSS levels (21, 28), while others have found no association between psychopathology and EDSS (20) or disease duration (10, 20).

In contrast to previous studies identifying female sex as a risk factor (3, 7), our findings suggest that female sex is a protective factor. Additionally, some reports indicate that anxiety and depression are more prevalent among male patients with MS (29), whereas others have found no significant sex differences (20). These discrepancies may reflect differences in help-seeking behavior, healthcare utilization, clinician recognition, and symptom presentation between sexes, which may influence the documentation of psychiatric comorbidities in retrospective medical records. Furthermore, biological differences in disease expression, coping strategies, and social roles may contribute to distinct psychiatric profiles in male and female patients with MS. Longitudinal studies incorporating systematic symptom screening are needed to clarify sex-specific patterns of psychiatric morbidity in MS.

In this study, approximately one-third of patients reported fatigue, which is consistent with previous studies indicating that fatigue affects up to 80% of patients with MS (22). Although several pharmacological interventions, including selective serotonin reuptake inhibitors (SSRIs) (1), monoamine oxidase A (MAO-A) inhibitors (30), amantadine, and stimulants, have been evaluated for fatigue management, current evidence does not support the clear superiority of any specific agent (22, 31). In our cohort, modafinil, methylphenidate, and amantadine were the most commonly prescribed treatments, reflecting a pragmatic approach to symptom management rather than a strategy specifically targeting psychiatric comorbidity. Importantly, fatigue emerged as an independent risk factor for psychiatric comorbidity in this study. This finding underscores its impact not only on physical functioning and quality of life but also on psychological well-being. The relationship between fatigue and psychiatric symptoms appears to be bidirectional. Large cohort analyses have demonstrated that fatigue is independently associated with depression and

anxiety, even after adjusting for demographic factors and disease severity. Conversely, depression has been shown both to co-occur with fatigue and to increase the risk of persisting or worsening fatigue over time (32). Shared neurobiological mechanisms, including cytokine-mediated inflammation, monoaminergic dysregulation, and hypothalamic-pituitary-adrenal axis hyperactivity, may contribute to both fatigue and mood dysregulation in MS (33). Moreover, the subjective experience of profound fatigue may exacerbate psychological distress by reducing functional capacity, limiting social engagement, and diminishing perceived control, thereby increasing vulnerability to depression and anxiety. Regardless of the direction of causality, the co-occurrence of fatigue and psychiatric symptoms highlights the need for comprehensive clinical assessment in clinical practice.

Although urinary incontinence differed significantly between groups in the univariate analyses, it was not identified as an independent predictor in the regression model. Previous studies have reported associations between lower urinary tract symptoms, including storage and voiding disturbances, and elevated anxiety and depression scores in male patients with MS (14).

Similarly, neuropathic pain did not differ between groups in the univariate analyses and was not identified as a risk factor in the logistic regression model. This finding contrasts with a systematic review and meta-analysis reporting that neuropathic pain affects approximately one-quarter of patients with MS and is associated with higher levels of anxiety and depression (13). The discrepancy may be attributable to methodological differences, such as the evaluation of individual symptoms rather than a comprehensive assessment of psychiatric comorbidity, as well as potential correlations with other variables, including EDSS scores and fatigue. These findings suggest that although neuropathic pain contributes to overall symptom burden, it may not function as an independent predictor of psychiatric comorbidity when considered alongside other disease- and symptom-related factors.

In a large cohort study including 5,633 participants assessed using the Hospital Anxiety and Depression Scale (HADS), higher self-efficacy, greater confidence, and being married were identified as protective factors against anxiety and depression (34). Our regression model explained only 15% of the variance in psychiatric comorbidity, indicating that social and demographic factors may play a more significant role than isolated disease-related symptoms such as urinary incontinence or neuropathic pain. These findings underscore the importance of considering both social and clinical dimensions when evaluating psychiatric risk in MS populations and highlight the need for comprehensive, multidimensional assessments.

This study has several limitations. First, its cross-sectional and retrospective design precludes causal inferences regarding the relationship between MS-related variables and psychiatric comorbidity. Second, reliance on medical records and clinically documented diagnoses, without the use of standardized symptom screening instruments, may have led to an underestimation of subclinical psychiatric symptoms. This approach may have misclassified symptomatic but undiagnosed individuals as negative for psychiatric comorbidity. Such misclassification may have attenuated the observed effects in the regression analyses. Therefore, the results should be interpreted as reflecting correlations with clinically recognized psychiatric morbidity rather than the full spectrum of psychiatric symptom burden in MS. Additionally, patients with irregular follow-up, missing early-stage clinical records, or prolonged absence from care were excluded to ensure the reliability of longitudinal and diagnostic data. However, these exclusions may have introduced selection bias, as psychiatric comorbidity can influence healthcare utilization and clinic attendance. Consequently, individuals with a greater psychiatric burden may have been underrepresented in the study sample. Third, although the sample size was relatively large, the single-center design may limit the generalizability of the findings. Finally, several potential confounders, including social support, psychological resilience, and detailed cognitive functioning, were not assessed. These factors may influence the risk of psychiatric comorbidity, symptom reporting, healthcare utilization, and clinical outcomes. The omission of these variables may have contributed to residual confounding in the observed associations. Despite these limitations, this study provides a comprehensive evaluation of both neurological and psychiatric variables in a well-characterized MS cohort. It relies on clinically documented diagnoses rather than symptom-based scales and integrates both disease-related and symptom-specific risk factors into multivariate analyses. These strengths enhance the clinical relevance and interpretability of our findings.

CONCLUSION

In conclusion, more than one-third of patients with MS had a history of at least one psychiatric comorbidity. Higher EDSS scores, longer disease duration, and fatigue were identified as independent risk factors, whereas female sex emerged as a protective factor. These findings underscore the importance of systematic screening and management of psychiatric conditions in MS, particularly among patients with significant fatigue or disability. Future longitudinal and multicenter studies incorporating social, psychological, and cognitive variables are needed to better understand the determinants of psychiatric comorbidity in MS.

Online Supplementary Digital Appendix File:

https://dusunenadamdergisi.org/storage/upload/files/1774420246-appendix-en.pdf

Ethical Approval: The Baskent University Medical and Health Sciences Research Board granted approval for this study (No: KA25/383, Date: 21/10/2025).

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Category 1	Concept/Design	G.A., I.I.
	Data acquisition	G.A., I.I.
	Data analysis/Interpretation	G.A., I.I.
Category 2	Drafting manuscript	G.A.
	Critical revision of manuscript	I.I.
Category 3	Final approval and accountability	G.A., I.I.
Other	Technical or material support	G.A., I.I.
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RESEARCH ARTICLE

Predictors of parental stress in families of children with neurodevelopmental disabilities

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ABSTRACT

Objective: This cross-sectional study aimed to identify significant child-related, parent-related, and social predictors of parental stress among parents of children diagnosed with autism spectrum disorder (ASD) or intellectual disability (ID).

Method: A total of 100 parents were recruited from a child and adolescent psychiatry outpatient clinic (56 parents of children diagnosed with ASD and 44 parents of children with ID). Participants completed the Strengths and Difficulties Questionnaire (SDQ), the Multidimensional Scale of Perceived Social Support (MSPSS), the Parental Attitude Scale (PAS), the Impact on Family Scale (IFS), and the Parental Stress Scale (PSS). Descriptive statistics and multivariate regression analyses were conducted to determine which variables best predicted parental stress.

Results: Multivariate linear regression analysis indicated that the overall model significantly predicted parental stress, $F(9, 90)=6.877$, $p<0.001$, explaining 34.8% of the variance. Parental self-efficacy ($\beta=-0.285$, $p=0.003$) and perceived family support ($\beta=-0.213$, $p=0.024$) emerged as significant independent predictors of stress. In contrast, children's emotional and behavioral difficulties (SDQ scores) and family impact (IFS scores) were not significantly associated with parental stress in the final model.

Conclusion: The findings highlight parental self-efficacy and family support as key predictors of parental stress in families of children with neurodevelopmental disabilities (NDD). These results underscore the importance of strengthening parental competence and enhancing family-based support resources to alleviate parental stress.

Keywords: Family support, neurodevelopmental disabilities, parental stress, self-efficacy

INTRODUCTION

Children diagnosed with neurodevelopmental disabilities (NDD), such as autism spectrum disorder (ASD) and intellectual disability (ID), experience persistent challenges in communication, behavior, and adaptive functioning that begin in early childhood (1). Numerous studies have shown that parents of children with NDD report significantly higher levels of stress compared to parents of children without NDD (2). This parenting stress can permeate daily life, affecting overall family dynamics as well as parents' emotional well-being. It may also influence the quality of parent–child interactions and reduce the effectiveness of interventions that require active parental involvement (3).

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Parental stress in the context of NDD has been conceptualized as a multidimensional construct encompassing child-related, parent-related, and social domains. Recent theoretical models and reviews have expanded this perspective by emphasizing the transactional nature of stress processes. Specifically, Ilias et al. (2018) (4) and Enea and Rusu (2020) (5) synthesized evidence indicating that child characteristics (e.g., behavioral and sensory difficulties), parental factors (e.g., self-efficacy, coping strategies), and social influences (e.g., social support) jointly predict parental stress among parents of children with NDD. These frameworks, grounded in ecological and family adaptation theories such as the Double ABCX model (6), underscore that parental stress and resilience depend on both internal resources and external support.

Although research on parental stress in NDD has expanded substantially in recent years, the evidence base remains predominantly Western-centric. Systematic reviews have highlighted that most studies examining child-related, parent-related, and social predictors of stress have been conducted in North American and European samples, with limited representation from non-Western or culturally diverse populations (5) Moreover, recent comparative studies suggest that sociocultural norms influence how parental self-efficacy and caregiving burden are expressed (7, 8), underscoring the need for research conducted in diverse cultural contexts. The present study builds upon previous research by examining how child-related, parent-related, and social predictors—specifically emotional and behavioral difficulties, perceived social support, parental self-efficacy, and family impact—jointly contribute to parental stress among Turkish parents raising children with NDD (ASD or ID). Accordingly, we hypothesized that higher levels of parental stress would be associated with child-related difficulties (such as children's emotional and behavioral problems); parent-related characteristics, including greater personal strain related to the child and poorer coping abilities, and lower parental self-efficacy; and social-level factors, such as reduced social support and greater familial or social impact of the child's condition. By integrating these variables within a unified analytical framework, the study aims to identify predictors of parental stress in families of children with NDD. In doing so, it provides culturally grounded evidence that extends current understanding of parental stress mechanisms beyond Western context and highlights the importance of child- and family-level determinants, as well as sociocultural factors, in shaping caregiving experiences.

METHODS

Research Design

This cross-sectional study, conducted without a control group, took place between October 2024 and October 2025 at a child and adolescent psychiatry outpatient clinic. The absence of a control group was consistent with the study's objective of examining relationships within a clinical population. The study adhered to the STROBE guidelines (Strengthening the Reporting of Observational Studies in Epidemiology) for observational research, and ethical approval was obtained from the institutional ethics committee prior to data collection. All participants provided written informed consent. All study procedures adhered to the Declaration of Helsinki.

Participants and Data Collection

An a priori power analysis conducted using G*Power 3.1 indicated that a minimum of 93 participants was required to detect a medium effect size (Cohen's f^2=0.15) with 80% power at a 0.05 significance level, based on nine predictor variables and consistent with the multivariate regression model described by Strauss et al. (2024) (9). To account for potential data loss and to enhance the robustness of the analysis, the target sample size was set at 100 participants.

A total of 100 volunteer participants were recruited using purposive sampling from parents of children aged 6–12 years who had been diagnosed with ASD or ID. Participants were approached during routine visits to the child and adolescent psychiatry clinic and invited to participate in the study. Of the 105 parents who initially consented, five were excluded due to incomplete data, resulting in a final analytic sample of 100 participants. Table 1 summarizes the characteristics of the children.

Inclusion Criteria

The following inclusion criteria were applied:

- Children: Boys and girls aged 6–12 years diagnosed with ASD or ID.
- Parents: Literate parents without linguistic barriers that could interfere with comprehension of the questionnaires and without significant mental or physical disabilities that would impair participation (e.g., developmental delays).

Table 1: Clinical and demographic characteristics of the children (n=100)

	%	Mean±SD
Age		8.37±2.14
Sex		
Male	74	
Female	26	
Number of siblings		1.06±0.89
Diagnosis		
ASD	56	
ID	44	
Any comorbidity	35	
ADHD	27	
CD	4	
ODD	1	
Other	7	
Psychotropic medication use	57	
Duration of special education (months)		44.53±35.02
SDQ scores		
Total difficulties		19.91±4.90
Internalizing		9.77±3.27
Externalizing		10.14±2.73
Hyperactivity		6.09±1.97
Emotional difficulties		4.51±2.13
Conduct difficulties		4.05±2.40
Peer difficulties		5.26±2.13
Prosocial behavior		5.45±2.13
PSS		37.50±8.66
MDPSS		
Family		16.53±5.92
Friends		17.57±5.74
Significant other		16.51±6.12
PAS		
Self-efficacy		23.18±5.05
Parental involvement		6.32±2.09
Parental satisfaction		22.37±3.85
IFS		
Total		80.18±9.87
Financial burden		8.01±1.94
Familial/social impact		22.46±4.21
Personal strain		19.56±4.03
Coping		10.59±2.57

M: Mean; SD: Standard deviation; ADHD: Attention-deficit/hyperactivity disorder; CD: Conduct disorder; ODD: Oppositional defiant disorder; ASD: Autism spectrum disorder; ID: Intellectual disability; SDQ: Strengths and Difficulties Questionnaire; PSS: Parental Stress Scale; MDPSS: Multidimensional Scale of Perceived Social Support; PAS: Parental Attitude Scale; IFS: Impact on Family Scale.

Exclusion Criteria

Participants were excluded based on the following criteria:

- Incomplete or insufficient data for analysis
- Children requiring inpatient treatment, as determined by the treating healthcare provider.

Procedure

Children were diagnosed with ASD or ID according to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) criteria by a certified child and adolescent psychiatrist. The diagnostic process involved a comprehensive developmental and psychiatric evaluation, including an unstructured clinical interview with both the child and the parents. Standardized cognitive assessments were not systematically administered as part of the study protocol. The study was designed to reflect a naturalistic clinical sample of children with NDD (ASD and ID), and restricting participation to children capable of completing formal psychometric testing could have altered the representativeness of the cohort. Accordingly, cognitive level was not operationalized using standardized intelligence quotient (IQ) measures. Following confirmation of the ASD or ID diagnosis, appropriate treatment plans were either initiated or continued, as clinically indicated. As part of the clinical evaluation, the psychiatrist completed a Personal Information Form using data provided by the parents. After receiving a detailed explanation of the study's aims and procedures, all participating parents provided written informed consent. Only families whose children met all inclusion criteria and none of the exclusion criteria were enrolled in the study.

During the evaluation process, parents completed five standardized instruments: the Strengths and Difficulties Questionnaire (SDQ), the Multidimensional Scale of Perceived Social Support (MSPSS), the Parental Attitude Scale (PAS), the Impact on Family Scale (IFS), and the Parental Stress Scale (PSS).

Measurement

Personal Information Form

The Personal Information Form was developed by the researchers to collect comprehensive sociodemographic and clinical data from participants. Administered during parent interviews, the form gathered information on the child's gender, age, number of siblings, diagnosis, duration of special education (in months), psychiatric comorbidities, and current psychiatric treatments.

Parental Stress Scale (PSS)

The Parental Stress Scale is a 16-item, single-factor instrument developed to assess the level of stress parents experience in relation to childrearing within the Turkish context (10). Items are rated on a 4-point Likert scale ranging from 1 to 4, yielding total scores between 16 and 64. Higher scores indicate greater parental stress. In reliability analyses conducted with parents of children aged 5 to 12 years, the scale yielded a Cronbach's alpha coefficient of 0.85 and a Spearman-Brown split-half coefficient of 0.82 (10).

Strengths and Difficulties Questionnaire (SDQ)

The Strengths and Difficulties Questionnaire–Parent Form (SDQ-P), developed by Goodman, is a widely used 25-item behavioral screening tool designed to assess children's emotional and behavioral difficulties (11). The scale comprises five subscales: emotional symptoms, conduct problems, hyperactivity/inattention, peer problems, and prosocial behavior. Items are rated on a 3-point scale (0 to 2). The Total Difficulties Score is calculated by summing the first four subscales, with higher scores indicating greater levels of difficulty. The Turkish adaptation, validated by Guvenir et al. (2008) (12), demonstrated acceptable reliability, with Cronbach's alpha coefficients ranging from 0.37 (peer problems) to 0.84 (total difficulties).

Multidimensional Scale of Perceived Social Support (MSPSS)

Originally developed by Zimet et al. (1988), the Multidimensional Scale of Perceived Social Support assesses perceived social support from three primary sources: family, friends, and a significant other (13). The instrument consists of 12 items rated on a 7-point Likert scale, with higher scores indicating greater perceived support. The Turkish adaptation by Eker and Arkar (14) (2001) reported high internal consistency, with Cronbach's alpha coefficients ranging from 0.85 to 0.92 across subscales and 0.89 for the total score.

Impact on Family Scale (IFS)

The Impact on Family Scale (IFS), developed by Stein and Riessman (1980), is designed to assess the overall impact of raising a child with a chronic disability on the family unit (15). The Turkish version, adapted by Beydemir (2008) (16), consists of 27 items, 24 of which are included in the total score calculation. The score evaluates four domains: financial burden, social/familial impact, personal strain, and coping. Higher total scores indicate a greater perceived impact on the family. The Turkish version has demonstrated good reliability, with a Cronbach's alpha coefficient of 0.81.

Parental Attitude Scale (PAS)

The Parental Attitude Scale, originally developed by Gibaud-Wallston and Wandersman (1978) (17), was adapted into Turkish by Secer et al. (2008) (18). The instrument comprises 16 items distributed across three subscales: perceived parenting self-efficacy (7 items), involvement in the parenting role (2 items), and satisfaction with parenting (7 items). Items are rated on a 5-point Likert scale ranging from 1 (Strongly Disagree) to 5 (Strongly Agree), with higher scores reflecting more positive parental attitudes. In the present study, only the perceived parenting self-efficacy subscale was included in the multivariate regression analysis. This decision was based on prior research emphasizing the central role of parental self-efficacy in relation to stress, whereas empirical evidence linking the other dimensions to parental stress is scarce.

Statistical Analysis

All statistical analyses were conducted using SPSS version 25.0 (Statistical Package for the Social Sciences; IBM Corp., 2019, New York, USA). Descriptive statistics were used to summarize the study variables. Internal consistency of the scales was assessed using Cronbach's alpha coefficients. Pearson correlation analyses were conducted to examine bivariate associations between the dependent variable (parental stress) and candidate predictors, as well as to assess intercorrelations among independent variables. Following the correlation analyses, multicollinearity was further evaluated prior to the regression analysis using variance inflation factor (VIF) values. Variables with VIF values greater than 3 were excluded from the regression model (19). To identify predictors of parental stress among parents of children with NDD, multiple linear regression analysis was performed using the enter method, with nine independent variables entered simultaneously into the final model. Statistical significance was set at $p<0.05$.

RESULTS

As presented in Table 1, the mean age of the children was 8.37 years (standard deviation [SD]=2.14), and 74% were male. Clinical diagnoses were distributed as follows: 56% ASD and 44% ID. Descriptive statistics for all study variables, including SDQ subscales, PSS, PAS, MSPSS, and IFS scores, are also provided in Table 1.

Prior to conducting the multivariate linear regression analyses, the suitability of candidate predictors was evaluated using a structured preliminary screening procedure. In the first step, the internal consistency of all scales and subscales was assessed. Measures with Cronbach's alpha coefficients below 0.60 were excluded from further analyses, consistent with commonly accepted guidelines for minimum internal consistency (Supplementary Digital Appendix 1) (20). In the second step, bivariate associations between the dependent variable (parental stress, measured by the PSS) and the remaining candidate predictors were examined to inform variable selection. Only variables demonstrating at least a small-to-moderate correlation with parental stress ($r \geq 0.20$) were retained as independent variables (Supplementary Digital Appendix 2) (21). Subsequently, intercorrelations among the retained predictors were examined to minimize redundancy. Variables with intercorrelation coefficients exceeding 0.70 were considered to reflect substantial overlap and were excluded accordingly (Table 2) (22). Finally, multicollinearity among the remaining predictors was formally assessed using variance inflation factor values. Predictors exceeding the conservative cut-off value of 3 were excluded from the final regression model (Supplementary Digital Appendix 3) (19). Child age and sex were included as covariates in the final multivariate regression model, which comprised a total of nine independent variables. Detailed information regarding these preliminary analyses is provided in the Appendices File.

Bivariate Pearson correlations among the study variables are presented in Table 2. Parental stress (PSS) showed significant positive correlations with SDQ total difficulties ($r=0.458$, $p<0.001$), internalizing symptoms ($r=0.395$, $p<0.001$), externalizing symptoms ($r=0.349$, $p<0.001$), hyperactivity ($r=0.336$, $p<0.001$), emotional difficulties ($r=0.456$, $p<0.001$), conduct difficulties ($r=0.268$, $p<0.05$), and peer difficulties ($r=0.263$, $p<0.05$). In contrast, parental stress was negatively correlated with perceived family support ($r=-0.437$, $p<0.001$) and parental self-efficacy ($r=-0.460$, $p<0.001$). The association with coping ($r=0.206$, $p<0.05$) was weaker but statistically significant, whereas correlations with prosocial behavior and several family impact subscales were not statistically significant. These findings informed the subsequent multivariate modeling.

Results of the multivariate linear regression analysis (Table 3) indicated that the overall model significantly predicted parental stress, $F(9, 90)=6.877$,

Table 2: Bivariate correlations among variables demonstrating acceptable internal consistency (Cronbach's α≥0.60)

	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
1. PSS	0.458**	0.395**	0.349**	-0.71	0.336**	0.456**	0.268*	-0.137	-0.437**	-0.460**	0.117	0.263*	-0.094	0.021	0.206*
2. SDQ Total Difficulties	1	0.850**	0.776**	0.247*	0.668**	0.680**	0.633**	-0.150	-0.340**	-0.397**	0.041	0.273**	-0.096	0.040	0.019
3. SDQ Internalizing		1	0.327**	-0.064	0.766**	0.425**	0.765**	-0.174	-0.258**	-0.326**	-0.020	0.224	-0.111	-0.004	-0.053
4. SDQ Externalizing			1	0.520**	0.281**	0.711**	0.219*	-0.061	-0.301**	-0.303**	0.097	0.222*	-0.039	0.076	0.030
5. SDQ Hyperactivity				1	-0.064	-0.231*	-0.034	0.079	0.021	0.289**	0.072	0.129	0.046	0.042	-0.028
6. SDQ Emotional Difficulties					1	0.373**	0.172	-0.093	-0.159	-0.244*	0.021	0.280**	-0.045	-0.008	-0.031
7. SDQ Conduct Difficulties						1	0.277**	-0.134	-0.360**	-0.583**	0.052	0.147	-0.082	0.052	0.057
8. SDQ Peer Difficulties							1	-0.174	-0.236*	-0.255*	-0.053	0.063	-0.125	0.002	-0.050
9. SDQ Prosocial Behavior								1	0.207*	0.120	-0.034	0.047	0.027	-0.086	0.058
10. MDPSS Family									1	0.410**	0.041	-0.172	0.239*	-0.005	-0.091
11. PAS Self-efficacy										1	-0.012	-0.005	-0.204*	-0.083	-0.115
12. IFS Total											1	0.033	0.535**	0.865**	0.226*
13. IFS Financial Burden												1	-0.210*	-0.073	-0.058
14. IFS Familial/Social Impact													1	0.174	0.030
15. IFS Personal Strain														1	-0.044
16. IFS Coping															1

SDQ: Strengths and Difficulties Questionnaire; MDPSS: Multidimensional Scale of Perceived Social Support; PAS: Parental Attitude Scale; IFS: Impact on Family Scale. * p<0.05; ** p<0.001.

Table 3: Final multivariate linear regression model predicting parental stress (n=100)

	Standardized β	Unstandardized coefficients (B)	95% CI for B	t	p
Constant		35.735	21.174, 50.275	4.878	**<0.001**
Age (covariate)	-0.002	-0.007	-0.708, 0.694	-0.020	0.984
Sex (covariate)	0.013	-0.261	-3.656, 3.134	0.153	0.879
Diagnosis (ASD vs. ID) (covariate)	0.110	0.671	-0.415, 1.757	1.227	0.223
SDQ					
Emotional difficulties	0.172	0.696	-0.038, 1.430	1.883	0.063
Peer difficulties	0.126	0.509	-0.190, 1.209	1.446	0.152
MDPSS					
Family support	-0.213	-0.312	-0.582, -0.042	-2.296	**0.024**
PAS					
Self-efficacy	-0.285	-0.489	-0.808, -0.169	-3.036	**0.003**
IFS					
Financial burden	0.164	0.731	-0.048, 1.511	1.865	0.065
Coping	0.160	0.541	-0.021, 1.102	1.912	0.059

ASD: Autism spectrum disorder; ID: Intellectual disability; SDQ: Strengths and Difficulties Questionnaire; MDPSS: Multidimensional Scale of Perceived Social Support; PAS: Parental Attitude Scale; IFS: Impact on Family Scale. Bolded predictors indicate statistically significant results ($p<0.05$). Model statistics: $F(9, 90)=6.877$, $p<0.001$, Adjusted $R^2=0.348$.

$p<0.001$, explaining approximately 34.8% of the variance (Adjusted $R^2=0.348$). Significant predictors included lower family support ($\beta=-0.213$, $p=0.024$) and lower parental self-efficacy ($\beta=-0.285$, $p=0.003$). Other variables, including children's emotional and behavioral problems (SDQ scores) and family impact (IFS scores), were not significantly associated with parental stress in the final model.

DISCUSSION

The present study examined the relative contribution of contextual factors to parental stress among parents of children with NDD. The findings indicate that parental self-efficacy emerged as the strongest predictor of stress, with perceived family support representing the second most influential factor in the model. Consistent with social cognitive perspectives that conceptualize parental self-efficacy as a central regulator of stress appraisal (23), as well as prior empirical research linking parental self-efficacy to stress processes (9), these results underscore the pivotal role of perceived competence in shaping parental stress responses. Family support also accounted for a meaningful proportion of variance, aligning with stress-buffering theories embedded within broader family stress frameworks (6, 24). These models suggest that support from close family members functions as a protective factor, mitigating parental stress. Collectively, the findings situate parental stress within a relational–cognitive framework in which parental self-efficacy and proximal family support serve as central organizing influences.

Parental self-efficacy emerged as the most powerful predictor of parental stress in the multivariate model, retaining its explanatory relevance even after accounting for child-related difficulties and other contextual variables. Within the Double ABCX framework (6), self-efficacy can be conceptualized as a key internal resource shaping cognitive appraisal processes, consistent with Bandura's formulation of mastery beliefs as regulators of stress responses (23). This positioning is empirically supported by findings from Almendingen and Pilkington (25), who demonstrated that mastery beliefs predicted parental stress through parental self-efficacy among parents of children with ASD. Empirical evidence similarly identifies parental self-efficacy as a mediating mechanism linking child impairment and stress (9), caregiving demands and stress (26), and family functioning and stress (27) in parents of children with ASD or other NDD. Extending this body of literature, the present findings suggest an important conceptual refinement in understanding the role of parental self-efficacy within the stress process. In contrast to mediation-focused frameworks, our findings support a more proximal positioning of parental self-efficacy within the Double ABCX structure (6), where it operates

not only as a resource but also as a central organizing mechanism of stress appraisal. In this sense, parental stress in the context of NDD appears to be anchored less in the mere presence of child-related difficulties and more in parents' perceived capacity to respond effectively to those demands.

Family support emerged as the second strongest predictor of parental stress in the model, underscoring the regulatory role of close familial resources in the stress process. Consistent with the stress-buffering model, social support is theorized to mitigate the psychological impact of caregiving demands (24). Empirical findings support this theoretical proposition, demonstrating a significant negative association between social support and parental stress in families of children with NDD (28). Moving beyond correlational findings, regression-based studies have shown that social support independently predicts parental stress among parents of children with ASD (29). In the present study, however, this effect was observed specifically for perceived family support, as other support subdimensions were excluded from the regression model due to insufficient internal consistency. This distinction is theoretically meaningful, given evidence that emotionally proximal and practically engaged forms of support—particularly from spouses and relatives—may exert stronger stress-buffering effects than more generalized sources of support (30). Taken together, these findings suggest that parental stress in families of children with NDD is shaped not only by parent-level characteristics, such as self-efficacy, but also by the availability of functionally relevant, family-based support. In line with recommendations to strengthen family-centered support services (29), interventions that simultaneously enhance parental self-efficacy and promote sustained couple- and family-level collaboration may represent a coherent direction for practice.

Contrary to expectations, SDQ subscale scores did not emerge as significant predictors of parental stress, suggesting that the association between child behavioral difficulties and parental stress may vary across developmental stages (31). The present sample was restricted to children aged 6–12 years, thereby excluding earlier developmental periods and later transitional phases. Studies including broader developmental ranges have reported stronger associations between behavioral difficulties and parental stress (32). Within a developmentally circumscribed age range, these associations may be less clearly differentiated from other clinical characteristics, particularly when parental stress reflects broader interactions between child-related demands and parental coping resources rather than discrete behavioral dimensions. Greater cognitive impairment (32) and higher levels of autistic symptom severity (27) have been associated with increased parental stress, indicating that stress in the context of NDD often reflects overall clinical complexity rather than isolated behavioral domains. In the present NDD sample (ASD+ID), cognitive functioning was not operationalized through formal IQ testing to avoid excluding children with more severe impairments. Consequently, variability in cognitive and adaptive functioning may have influenced the extent to which behavioral symptoms were associated with parental stress outcomes. Attention-deficit/hyperactivity disorder (ADHD) was present in 27% of children, and conduct disorder (CD) in 4%, underscoring the presence of clinically meaningful comorbidity with disruptive behavior disorders. At the same time, the reliance on parent-report measures for both child behavioral difficulties and parental stress may have introduced shared method variance, as elevated parental stress has been shown to influence perceptions of child behavior severity. In heterogeneous populations of children with developmental disabilities, parental stress is more consistently associated with the cumulative burden of cognitive, functional, and behavioral demands than with isolated symptom subdomains (27, 32). Within this context, the non-significant SDQ findings are best interpreted as reflecting the multidimensional and developmentally embedded nature of stress in NDD, rather than as evidence for the absence of behavioral contributions.

Several limitations should be considered when interpreting these findings. First, the cross-sectional design precludes conclusions regarding directionality or causality of the observed associations. Second, reliance on parent-report measures may have influenced the reporting of child-related difficulties, potentially introducing shared method variance. Third, cognitive functioning was not systematically assessed using standardized IQ measures. Although this approach reflected the naturalistic design of the study and enabled the inclusion of children with varying levels of impairment, the absence of formal cognitive stratification limited the ability to examine whether differences in cognitive functioning influenced the observed associations. Fourth, psychiatric comorbidities were described

categorically rather than assessed in terms of severity or dimensional variation, which may have affected the strength of the associations between SDQ subscales and parental stress. Finally, the restricted age range (6–12 years) and the recruitment of families already engaged in clinical services limit the generalizability of the findings to broader community populations.

CONCLUSION

By examining child-related, parent-related, and social predictors within a single model, this study clarifies which domains carry the greatest weight in explaining parental stress among parents of children with NDD. Parental self-efficacy and perceived family support emerged as the most robust predictors, distinguishing them from the child-related and other parent-related characteristics assessed. This pattern underscores the relative prominence of parental self-efficacy and proximal familial support in shaping parental stress experiences. Longitudinal and multi-method research is warranted to further elucidate how these factors evolve over time and influence trajectories of parental stress.

Online Supplementary Digital Appendix File:

https://dusunenadamdergisi.org/storage/upload/thumbnails/1774334687.jpeg

Ethical Approval: The Izmir City Hospital Non-Interventional Clinical Research Ethics Committee granted approval for this study (Date: 25.09.2024, number: 2024/133).

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RESEARCH ARTICLE

Comparison of cognitive function, depression, fall-related behaviors, and quality of life in elderly individuals according to age

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ABSTRACT

Objective: As the aging process progresses, individuals experience various changes in physical, cognitive, and psychological domains that can directly affect their quality of life. This study aimed to compare cognitive function, depressive symptoms, fall-related behaviors, and quality of life across different age groups and to examine their associations with quality of life in older adults.

Method: A total of 98 community-dwelling older adults aged 65 years and older, living independently in two districts of Istanbul, were included in the study. Participants were classified into three age groups: young-old (65–74 years), middle-old (75–84 years), and old-old (85 years and older). Assessments included the Standardized Mini-Mental State Examination (SMMSE), the Geriatric Depression Scale, the Falls Behavioral Scale for Older People, and the World Health Organization Quality of Life–Older Adults Module (WHOQOL-OLD).

Results: The findings revealed that the young-old group had significantly better cognitive function, lower levels of depression, and higher quality of life scores compared to the other groups. Moreover, significant positive correlations were found between quality of life and cognitive function, while significant negative correlations were observed between quality of life and depression level across all age groups ($p<0.05$). Individuals who exhibited safer fall-related behaviors also demonstrated higher levels of quality of life ($p<0.05$).

Conclusion: These results suggest that quality of life in older adults is closely associated with cognitive, emotional, and behavioral factors, highlighting the importance of age-specific, multidisciplinary assessment approaches.

Keywords: Aging, cognitive function, depression, fall-related behaviors, quality of life

INTRODUCTION

Aging is a natural process that begins at birth and continues throughout life, leading to changes in physiological functions, cognitive abilities, and psychological states (1). Since the 20th century, advances in healthcare and technology, the prevention of infectious diseases, and the expansion of public health services have significantly increased life expectancy (1). Accordingly, the number of

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individuals aged 65 years and older has been steadily rising both globally and in Turkiye. According to the World Population Prospects 2022 report, the global population of individuals aged 65 years and over has reached 771 million (2). In Turkiye, the number of people in this age group was approximately 8 million in 2021 (2). Population projections indicate that the proportion of older adults will continue to increase in the coming years. Therefore, aging has become one of the foremost public health priorities today.

The World Health Organization (WHO) and the United Nations define the lower chronological threshold of old age as 65 years. Older adults are classified into subgroups as follows: "young-old" (65–74 years), "middle-old" (75–84 years), and "old-old" (85 years and older) (3). According to data from the Turkish Statistical Institute, 64.7% of the older adult population falls within the 65–74 age group, 27.3% within the 75–84 group, and 8% are 85 years or older (2). This classification allows for a more detailed understanding of the heterogeneous characteristics associated with the aging process.

Aging is accompanied by various functional changes in physical, cognitive, and psychological domains (4, 5). Age-related decline in cognitive functions such as attention, learning, memory, and language may lead to cognitive impairments in older individuals (6). Moreover, age-related multisystem deterioration, an increased burden of chronic diseases, dependency resulting from care needs, and the loss of a spouse or partner may lead to feelings of loneliness. When combined with social status or financial losses, these factors significantly increase the risk of depression (7). Additionally, degenerative changes in the musculoskeletal system may result in impaired postural control and balance problems, leading to a higher risk of falls—one of the most common and serious health concerns among older adults. Falls not only cause injury and disability but also lead to a fear of falling, which may reduce self-confidence, decrease physical activity levels, and promote social withdrawal. Avoidance of activity and increased social isolation—common coping behaviors among older adults attempting to prevent falls—further reduce physical capacity and exacerbate cognitive and psychological decline, thereby negatively impacting quality of life on multiple levels (8).

According to the WHO, quality of life in older adults is defined as an individual's subjective perception of their position in life within the context of their culture and value systems, and in relation to their goals, expectations, standards, and concerns (9). Quality of life is a multidimensional concept reflecting the integrated interaction of various factors, including physical health, psychological well-being, level of independence, social relationships, and personal beliefs (9). In older individuals, age-related decline in cognitive and physical functions, fear of falling, and depressive symptoms have been associated with reduced quality of life. Numerous studies have examined the impact of physical, cognitive, and psychological functions on quality of life (10-14).

However, studies in the literature that classify individuals aged 65 and older into age subgroups and simultaneously evaluate the interrelationships among cognitive functions, depression level, fall-related behaviors, and quality of life remain limited. Therefore, the primary aim of this study was to investigate the relationships among cognitive function, depressive symptoms, fall-related behaviors, and quality of life in older adults, and to compare these variables across different age groups. We hypothesized that (i) cognitive function, depressive symptoms, fall-related behaviors, and quality of life would differ across age groups; and (ii) cognitive status, depressive symptoms, and fall-related behaviors would be associated with quality of life in older adults.

METHODS

Study Design and Participants

This cross-sectional study was conducted between June 25 and September 1, 2025, in accordance with the Declaration of Helsinki. Ethical approval was obtained from the Non-Interventional Clinical Research Ethics Committee of Istanbul Medipol University (Approval No: E-10840098-202.3.02-3769; 19 June 2025). The sample consisted of 98 community-dwelling older adults aged 65 years and older residing in the Cekmekoy and Umraniye districts of Istanbul, Turkiye. Participants were recruited through local senior centers and neighborhood associations using convenience sampling. The sample size was determined using an a priori power analysis conducted with G*Power version 3.1. As the primary objective was to examine the associations among cognitive function, depressive symptoms, fall-related behaviors, and quality of life, the sample size estimation was based on a two-tailed bivariate correlation analysis. Assuming a medium effect size (ρ=0.30), a 95% confidence level (α=0.05), and 80% statistical power (1-β), the minimum required sample size was calculated as 84. The final sample (N=98) exceeded this requirement.

The inclusion criteria were: (a) being aged 65 years or older and (b) willingness to participate in the study. The exclusion criteria were: (a) having a clinically diagnosed severe orthopedic, neurological, psychiatric, or rheumatologic disorder that could substantially limit mobility or prevent participation in the assessments; (b) having an acute or unstable medical illness; and (c) having a diagnosed major neurocognitive disorder or cognitive impairment severe enough to hinder communication. Participants with diagnosed psychiatric disorders were excluded; however, individuals with subthreshold or undiagnosed depressive symptoms were not excluded and were assessed using the Geriatric Depression Scale. Participants with stable chronic systemic diseases and common age-related musculoskeletal conditions were not excluded. Eligibility screening was performed through structured interviews and a review of participants' medical history records. Eligibility regarding cognitive status was determined based on participants' ability to communicate effectively during the interview and consent process. All assessments were conducted through face-to-face interviews by a single physiotherapist. No medical diagnoses were made by the physiotherapist; when necessary, participants were asked to verify existing medical conditions with physician documentation.

Measurements

Sociodemographic Data Form

This form included information on age, gender (female/male), education level, and marital status. In addition to basic sociodemographic variables, data regarding living arrangement (living alone or with family), history of falls within the past 12 months, and the presence of at least one chronic disease were collected for descriptive purposes.

Standardized Mini-Mental State Examination (SMMSE)

This test is used to evaluate cognitive function and consists of five subdomains: orientation, short-term memory, attention, calculation, recall, and language skills. It is scored on a scale ranging from 0 to 30 points. The Turkish validity and reliability study was conducted by Gungen et al. (15).

Geriatric Depression Scale (GDS)

This 30-item scale, developed to assess depressive symptoms in older adults, consists of "Yes/No" responses. Each depressive response is scored as one point, and the total score reflects the severity of depression. The scale was developed by Yesavage et al. (16), and its Turkish validity and reliability study was conducted by Ertan and Eker (17). Scores of 14 and above indicate the presence of depression.

Falls Behavioral Scale for Older People (FaB)

This scale is used to assess attitudes and behaviors related to falling. It consists of 10 subcategories, including cognitive adaptation, safe movement, avoidance, awareness, and attentiveness. The scale includes 30 items, each rated from 1 to 4. The total score is divided by the number of items to obtain an average score. Higher scores indicate safer or more protective behaviors against falls, whereas lower scores reflect riskier or unsafe behaviors. The scale was developed by Clemson et al. (18), and its Turkish validity and reliability study was conducted by Uymaz et al. (19).

World Health Organization Quality of Life Instrument-Older Adults Module (WHOQOL-OLD)

Developed by the WHOQOL Group, this instrument consists of six subdomains: sensory abilities, autonomy, past, present and future activities, social participation, death and dying, and intimacy. It includes 24 items rated on a 1–5 scale, with higher scores indicating better quality of life. The Turkish validity and reliability study of the instrument was conducted by Eser et al. (20).

Statistical Analysis

Statistical analyses were performed using Jamovi (version 2.6.2) and SPSS version 22.0 (Statistical Package for the Social Sciences). Descriptive statistics were presented as mean ± standard deviation (mean±SD). Prior to inferential analyses, the assumptions underlying the statistical tests were evaluated. The normality of variables was assessed using the Shapiro–Wilk test. As the variables were not normally distributed, non-parametric methods were applied. Group differences were examined using the Kruskal–Wallis test, and post hoc pairwise comparisons were conducted using the Dwass–Steel–Critchlow–Fligner (DSCF) procedure. Spearman's rank correlation analysis was applied to examine the relationships among cognitive function (SMMSE), depression level (GDS), fall-related behaviors (FaB), and quality of life (WHOQOL-OLD). The independence of observations and appropriate measurement levels were verified prior to conducting the analyses. Correlation coefficients between 0.00 and 0.30 were considered weak, 0.30–0.50 low, 0.50–0.70 moderate, and 0.70–0.90 strong. Values above 0.90 were considered indicative of a very strong correlation (21). Statistical significance was set at $p<0.05$.

Table 1: Demographic and clinical characteristics of participants

	Young-old group (n=46)	Middle-old group (n=33)	Old-old group (n=19)	p
Age, mean±SD (years)	68.90±2.33	80.50±3.16	89.20±2.94	**<0.001**[a]
Gender, n (female/male)	18/28	13/20	10/9	0.569[b]
Educational status, n (illiterate/primary school/high school/university)	11/20/14/1	18/11/3/1	11/7/1/0	**0.028**[b]
Marital status, n (single/married)	13/33	7/26	8/11	0.275[b]
Living arrangement, n (%)				
Alone	10 (21.7)	11 (33.3)	9 (47.4)	
With family	36 (78.3)	22 (66.7)	10 (52.6)	
Fall history within the past 12 months, n (%)				
Yes	13 (28.3)	14 (42.4)	11 (57.9)	
No	33 (71.7)	19 (57.6)	8 (42.1)	
Presence of a chronic disease (≥1), n (%)				
Yes	24 (52.2)	22 (66.7)	15 (78.9)	
No	22 (47.8)	11 (33.3)	4 (21.1)	

SD: Standard deviation; a: Kruskal-Wallis test; b: Chi-square test; p<0.05. Continuous variables are presented as mean±standard deviation; categorical variables as n (%).

Table 2: Cognitive status, depression, fall-related behaviors, and quality of life by age group

	Young-old group (n=46) Mean±SD	Middle-old group (n=33) Mean±SD	Old-old group (n=19) Mean±SD	p
SMMSE	22.26±0.48	19.00±0.43	18.68±0.50	**<0.001**[a]
GDS	12.33±0.40	14.09±0.36	14.89±0.54	**0.001**[a]
FaB	2.97±0.09	2.25±0.09	2.19±0.12	**<0.001**[a]
WHOQOL-OLD	71.61±3.71	45.21±3.43	43.05±3.94	**<0.001**[a]

SMMSE: Standardized Mini-Mental State Examination; GDS: Geriatric Depression Scale; FaB: Falls Behavioral Scale for Older People; WHOQOL-OLD: World Health Organization Quality of Life Instrument–Older Adults Module; Mean: Mean; SD: Standard deviation; a: Kruskal-Wallis test; p<0.05.

RESULTS

Participants' demographic characteristics, cognitive status, depression levels, fall-related behaviors, and quality of life were compared across age groups. Additionally, the relationships between quality of life and other clinical variables were examined using correlation analysis.

The mean age differed significantly among the age groups ($\chi^2(2)=83.0$, $p<0.001$). The mean age was 68.90±2.33 years in the young-old group, 80.50±3.16 years in the middle-old group, and 89.20±2.94 years in the old-old group. No statistically significant differences were found among the groups in terms of gender distribution or marital status ($p>0.05$). However, a statistically significant difference was observed in educational status ($p=0.028$); the proportion of participants with a high school or university education was higher in the young-old group compared to the other age groups (Table 1). Living arrangement, fall history within the past 12 months, and the presence of at least one chronic disease are also summarized in Table 1 for descriptive purposes.

Cognitive status was assessed using the Standardized Mini-Mental State Examination, depression symptoms were evaluated with the Geriatric Depression Scale, fall-related behaviors were measured using the Falls Behavioral Scale for Older People, and quality of life was assessed with the WHOQOL-OLD. SMMSE scores differed significantly among the groups ($\chi^2(2)=24.7$, $p<0.001$, $\varepsilon^2=0.255$). Post hoc comparisons indicated that the young-old group had significantly higher SMMSE scores than both the middle-old ($p<0.001$) and old-old groups ($p<0.001$), indicating an age-related decline in cognitive function. GDS scores also differed significantly among the groups ($\chi^2(2)=14.0$, $p<0.001$, $\varepsilon^2=0.145$). Post hoc analyses demonstrated that the young-old group had significantly lower GDS scores than both the middle-old ($p=0.016$) and old-old groups ($p=0.004$),

Table 3: Correlation between WHOQOL-OLD scores and clinical variables by age group

	Young-old group (n=46) p (r)	Middle-old group (n=33) p (r)	Old-old group (n=19) p (r)
SMMSE – WHOQOL-OLD	**p<0.001 (r=0.770)**	**p<0.001 (r=0.599)**	**p=0.009 (r=0.581)**
GDS – WHOQOL-OLD	**p<0.001 (r=-0.681)**	**p=0.002 (r=-0.519)**	**p=0.005 (r=-0.619)**
FaB – WHOQOL-OLD	**p<0.001 (r=0.563)**	p=0.069 (r=0.321)	**p=0.002 (r=0.671)**

SMMSE: Standardized Mini-Mental State Examination; GDS: Geriatric Depression Scale; FaB: Falls Behavioral Scale for Older People; WHOQOL-OLD: World Health Organization Quality of Life Instrument–Older Adults Module; p: statistical significance value; r: Spearman's correlation coefficient; p<0.05.

suggesting an increase in depressive symptoms with advancing age. FaB scores, reflecting fall-related behaviors, showed significant differences among groups ($\chi^2(2)=25.5$, $p<0.001$, $\varepsilon^2=0.263$). Post hoc comparisons revealed that the young-old group had significantly higher FaB scores than both the middle-old ($p<0.001$) and old-old groups ($p<0.001$), indicating safer fall-related behaviors in the young-old age group. Similarly, WHOQOL-OLD scores differed significantly across groups ($\chi^2(2)=24.3$, $p<0.001$, $\varepsilon^2=0.251$). Post hoc analyses demonstrated that the young-old group had significantly higher WHOQOL-OLD scores than both the middle-old ($p<0.001$) and old-old groups ($p<0.001$), reflecting a decline in quality of life with increasing age (Table 2).

The relationships between quality of life and cognitive status, depression level, and fall-related behaviors were examined using Spearman's correlation coefficients. In the young-old group, WHOQOL-OLD scores showed a strong positive correlation with cognitive function as measured by the SMMSE ($r=0.770$, $p<0.001$). Additionally, WHOQOL-OLD scores were moderately positively correlated with fall-related behaviors (FaB) ($r=0.563$, $p<0.001$) and moderately negatively correlated with depressive symptoms assessed by the GDS ($r=-0.681$, $p<0.001$). In the middle-old group, WHOQOL-OLD scores were moderately positively correlated with SMMSE scores ($r=0.599$, $p<0.001$) and moderately negatively correlated with GDS scores ($r=-0.519$, $p=0.002$). The correlation between WHOQOL-OLD and FaB scores approached statistical significance in this group ($r=0.321$, $p=0.069$). In the old-old group, WHOQOL-OLD scores were moderately positively correlated with SMMSE scores ($r=0.581$, $p=0.009$) and strongly positively correlated with FaB scores ($r=0.671$, $p=0.002$). A moderate negative correlation was also observed between WHOQOL-OLD and GDS scores ($r=-0.619$, $p=0.005$) (Table 3).

Although education level differed among age groups, additional analyses indicated that the observed associations between quality of life and SMMSE, FaB, and GDS scores were consistent across education levels (Supplementary Digital Appendix 1).

DISCUSSION

This study examined demographic characteristics, cognitive function, depressive symptoms, fall-related behaviors, and quality of life among 98 community-dwelling adults aged 65 years and older, comparing outcomes across age groups. Additionally, the relationships between quality of life and these clinical variables were assessed using correlation analyses. The findings indicated that older age groups were characterized by lower cognitive function, higher levels of depressive symptoms, fewer protective fall-related behaviors, and lower quality of life. Furthermore, quality of life was positively associated with cognitive function and protective fall-related behaviors, and negatively associated with depressive symptoms. Across age groups, cognitive status and depressive symptoms were consistently associated with quality of life. These results suggest that not only chronological age but also physical, cognitive, and psychosocial conditions are closely linked to quality of life in older adults. Rather than operating independently, these domains may interact in shaping perceived well-being; thus, quality of life in older adulthood may reflect the cumulative interplay of cognitive vulnerability, emotional distress, and behavioral adaptation processes rather than isolated impairments. Sex was reported as a biological variable in accordance with the SAGER (Sex and Gender Equity in Research) guidelines and is presented among the descriptive characteristics of the sample (Table 1). Because sex distribution did not differ significantly between age groups, the observed differences in cognitive function, depression, fall-related behaviors, and quality of life are unlikely to be confounded by sex. Future studies with larger samples may further investigate sex-specific differences in cognitive and psychosocial outcomes.

Numerous studies have reported age-related declines in quality of life; however, this relationship is often moderated by cognitive status, emotional well-being, and environmental factors (4). Ilhan et al. (22) found that quality of life scores were lower among older individuals in more advanced age groups. Similarly, a study by Besikci et al. (1), which examined factors affecting quality of life in individuals aged 65 years and older, reported an age-related decline in quality of life. Our findings are consistent with these results, demonstrating a decrease in quality of life with increasing age. However, this pattern is not universally applicable to all individuals, as quality of life is influenced by numerous personal, social, and environmental factors beyond chronological age. Although physiological and functional decline may negatively affect perceived quality of life, positive experiences, such as accumulated knowledge and life experience, sustained social relationships, and increased free time following retirement, may help preserve or even enhance quality of life in some individuals. Therefore, a comprehensive understanding of the multidimensional factors affecting quality of life is warranted.

Significant differences in cognitive status were observed among the age groups, with the young-old group demonstrating higher SMMSE scores. This finding suggests an age-related decline in cognitive function. Moreover, positive correlations were identified between cognitive status and quality of life across all age groups, with a particularly strong association observed in the young-old group ($r=0.770$, $p<0.001$). This magnitude indicates a clinically meaningful relationship between cognitive function and quality of life. These findings support the notion that better cognitive functioning is positively associated with perceived quality of life. Similar results have been reported in the literature (10, 23). For example, Missotten et al. (24) reported that older individuals with cognitive dysfunction experience significant declines in quality of life domains such as social participation, autonomy, and emotional well-being. Cognitive decline may negatively affect quality of life through reduced engagement in daily activities and diminished capacity for environmental adaptation. Impaired executive functioning, in particular, may limit adaptive coping strategies and adjustment to environmental demands, thereby increasing the perceived impact of age-related functional limitations on overall well-being. Our findings underscore the importance of maintaining cognitive health in older adults, not only for preserving mental function but also for sustaining overall quality of life. It should be noted that the Standardized Mini-Mental State Examination is a screening instrument designed to estimate global cognitive status rather than to establish a definitive clinical diagnosis of cognitive impairment. Therefore, the cognitive scores obtained in this study should be interpreted cautiously as indicators of probable cognitive functioning. Although participants with diagnosed psychiatric or neurological disorders were excluded, lower SMMSE scores may still be observed in community-dwelling older adults due to factors such as advanced age, lower educational attainment, and sociocultural characteristics. In the present study, the SMMSE was used solely as a screening tool rather than a diagnostic criterion, and no cut-off score was applied for exclusion. In addition, educational level differed significantly among age groups and may have influenced cognitive performance, as SMMSE scores are known to be education-dependent. Educational attainment may also affect perceived quality of life and therefore represents a potential confounding factor in interpreting these findings. To further explore this issue, additional education-stratified analyses were conducted (Supplementary Digital Appendix 1). Spearman correlation analyses between WHOQOL-OLD and SMMSE, GDS, and FaB scores were repeated within low- and high-education strata. The direction and magnitude of these associations were comparable across education levels, suggesting that the observed relationships are unlikely to be explained solely by differences in educational attainment. Nevertheless, residual confounding cannot be entirely excluded.

In our study, depression levels differed significantly among age groups, with higher GDS scores observed in older participants. Additionally, significant negative correlations were found between GDS and WHOQOL-OLD scores across all age groups, indicating that higher levels of depressive symptoms were associated with lower quality of life. Consistent with these findings, several previous studies have reported strong associations between depression and reduced quality of life (25, 26). In a cross-sectional study conducted by Altun et al. (27) among Turkish older adults, depressive symptoms were found to significantly decrease life satisfaction. Similarly, Sivertsen et al. (28) reported that older adults with depressive symptoms had lower quality of life scores compared to those without depression, and that lower quality of life was associated with greater depression severity. Overall, our findings align with the existing literature, indicating that lower levels of depressive symptoms are associated with better

quality of life in older adults. These results emphasize the clinical importance of supporting mental health in older adults—not only to promote psychological well-being but also to preserve overall quality of life. Depressive symptoms may contribute to activity restriction, reduced social participation, and diminished self-efficacy, thereby reinforcing a reciprocal cycle between emotional distress and functional decline.

Age-related declines in mobility, postural control, and balance are associated with an increased risk of falls in older adults, while fear of falling may further negatively affect quality of life (12). In our study, higher FaB scores reflected safer and more protective behaviors related to fall awareness and fear, whereas lower scores indicated riskier and unsafe behaviors (18). Our findings revealed significant differences in fall-related behaviors among the age groups, with the young-old group exhibiting higher FaB scores, indicating safer behavioral patterns. Additionally, positive correlations between FaB scores and quality of life were found in the young-old and old-old groups. In contrast, the association between fall-related behaviors and quality of life did not reach statistical significance in the middle-old group, although the direction of the relationship was positive. This finding may be partially explained by the relatively small sample size of this subgroup and the transitional characteristics of this age period, during which adaptive behavioral strategies may partially attenuate the perceived impact of fall-related behaviors on quality of life. Consistent with the literature, our findings indicate that individuals who exhibited safer fall-related behaviors reported higher quality of life, whereas those demonstrating unsafe behaviors and lower awareness had lower quality of life scores. Cinarli et al. (12) reported that fear of falling is associated with impaired balance, reduced participation in daily activities, and social isolation. Other studies have shown that fear of falling increases fall risk, reduces quality of life, and contributes to greater dependency and higher healthcare costs (29, 30). In this context, our findings indicate that greater fall awareness and more protective behaviors are associated with better quality of life and lower healthcare burden among older adults. Recent evidence examining cognitive status, depressive symptoms, fall-related behaviors, and quality of life within an integrated analytical framework has similarly demonstrated strong interrelationships among these domains in community-dwelling older adults (31). Taken together, these findings support an integrated conceptualization of quality of life in older adulthood, shaped by interacting cognitive, emotional, and behavioral processes. Although the present study primarily focused on depressive symptoms, fall-related behaviors may also be influenced by other psychopathological factors, such as anxiety and fear-avoidance beliefs. Previous research suggests that the severity of anxiety and depressive symptoms may exacerbate fear of falling and activity restriction in older adults. Therefore, the interaction between fall-related behaviors and broader psychological profiles should be considered in future multidisciplinary research. The associations among fall-related behaviors, cognitive function, and depressive symptoms are further supported by the age-stratified correlation analyses presented in Supplementary Digital Appendix 2.

With advancing age, the prevalence of cognitive decline, reduced physical performance, and mental health issues increases. These three domains are known to interact and collectively influence quality of life (32). The literature indicates that cognitive dysfunction and depressive symptoms are closely associated with lower quality of life. For example, Kitis et al. (11) reported that cognitive dysfunction and depression negatively affected quality of life in older individuals. Similarly, Sertel et al. (14) found that among individuals aged 65 years and older, cognitive decline and depression were accompanied by physical impairments, increased fall risk, and ultimately reduced quality of life. In line with these findings, our study demonstrated that lower cognitive status, higher depression scores, and reduced fall awareness were associated with poorer quality of life. These findings suggest that cognitive, emotional, and physical parameters are closely related to overall well-being in older adults, both directly and indirectly, through their interactions with one another. This multidimensional interplay highlights the need for integrated assessment and intervention strategies in geriatric care. Cognitive vulnerability may increase emotional distress; depressive symptoms may reduce adaptive engagement; and avoidance-oriented behaviors related to fall risk may further restrict participation. Such mutually reinforcing pathways underscore the importance of early, coordinated, and multidisciplinary approaches in geriatric care.

Overall, our findings emphasize the importance of comprehensive assessment strategies in older adults that encompass not only physical but also cognitive and psychosocial dimensions. Quality of life in older adulthood is influenced by multiple factors and is

closely associated with factors such as cognitive decline, depressive symptoms, and fear of falling. Therefore, healthcare planning for older adults should incorporate multidimensional evaluation processes that include functional, environmental, and emotional components. In particular, physiotherapy practices that integrate these dimensions may enhance individual quality of life while also reducing healthcare costs. Early identification, preventive interventions, and multidisciplinary approaches can significantly support life satisfaction, independence, and social participation in older adults. In this regard, the findings of our study provide an evidence-based foundation for individual-, community-, and institution-level strategies aimed at improving quality of life in older populations.

The findings of this study should be interpreted in light of several methodological and conceptual limitations. First, the cross-sectional design does not permit conclusions regarding causality or temporal direction among cognitive status, depressive symptoms, fall-related behaviors, and quality of life. The observed associations may reflect complex and potentially reciprocal processes rather than direct causal mechanisms. Longitudinal and prospective studies are required to clarify the direction, stability, and dynamic interplay of these relationships over time.

Second, several variables were assessed using screening instruments and self-report measures. The SMMSE provides an estimate of global cognitive functioning rather than a comprehensive neuropsychological evaluation, and both the WHOQOL-OLD and the GDS rely on subjective perceptions. Consequently, shared method-related influences may have affected the strength of the observed associations. Future studies incorporating objective functional assessments and more detailed cognitive measures may provide a more comprehensive understanding of these interrelationships.

Third, although additional analyses stratified by educational level were conducted, residual confounding cannot be fully excluded. Cognitive screening performance is influenced by educational and sociocultural background, factors that may also shape individuals' perceptions of quality of life. Accordingly, the findings should be interpreted within the sociodemographic context of the sample.

Fourth, the use of bivariate correlation analyses provides an overview of relationships among variables but does not allow examination of potential mediating or moderating mechanisms. Quality of life in older adulthood is likely influenced by multifactorial and interacting pathways. Future research employing multivariate statistical models or structural approaches may better capture these complexities.

Fifth, the sample consisted of community-dwelling, independently living older adults recruited through convenience sampling from two districts of Istanbul. Therefore, the generalizability of the findings to institutionalized older adults, individuals with advanced neurocognitive disorders, or populations from different sociocultural contexts may be limited.

Finally, the conceptual framework of the present study focused primarily on cognitive status, depressive symptoms, and fall-related behaviors as correlates of quality of life. Other potentially relevant determinants—such as anxiety, social support, comorbidity burden, and environmental accessibility—were not examined. Therefore, the proposed framework represents a partial rather than comprehensive explanation of quality of life in older adulthood.

CONCLUSION

This study provides important insights into the relationships among cognitive function, depressive symptoms, fall-related behaviors, and quality of life in community-dwelling older adults across different age groups. By categorizing participants into young-old, middle-old, and old-old subgroups, age-related differences were examined in detail. The findings revealed that the older age groups were characterized by lower cognitive performance, higher levels of depressive symptoms, fewer protective fall-related behaviors, and lower quality of life. Furthermore, these factors were found to be interrelated and jointly associated with overall well-being.

The comprehensive assessment of multiple health dimensions underscores the importance of adopting a person-centered, multidisciplinary approach in geriatric healthcare and expanding preventive strategies to support healthy and independent aging. These findings provide an evidence-based foundation for the development of geriatric rehabilitation strategies that concurrently address physical, cognitive, and psychosocial domains.

Future studies with larger, multicenter samples conducted in diverse sociocultural settings are warranted to further validate and extend these findings and to inform targeted strategies aimed at improving quality of life among older adults.

Online Supplementary Digital Appendix File:

https://dusunenadamdergisi.org/storage/upload/thumbnails/1774335122.jpeg

Ethical Approval: The Istanbul Medipol University Non-Interventional Clinical Research Ethics Committee granted approval for this study (Date: 19.06.2025, number: E-10840098-202.3.02-3769).

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RESEARCH ARTICLE

Evaluation of brexpiprazole as adjunctive therapy in treatment-resistant depression: Real-world data

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ABSTRACT

Objective: Brexpiprazole (BRX) is an antipsychotic used as an adjunctive agent in the treatment of major depressive disorder. We aimed to evaluate the effectiveness of BRX in treatment-resistant depression (TRD).

Method: This study was conducted between May 1, 2024 and January 1, 2025. Medical records of patients who were started on BRX as adjunctive treatment for TRD were retrospectively reviewed. Patient files containing sociodemographic data and scores from the Beck Depression Inventory (BDI), Beck Anxiety Inventory (BAI), and Global Assessment Scale (GAS) were included in the analysis.

Results: A total of 30 patients were included in the study. The mean age was 32.50±11.38 years (range: 18–63), and 63.3% (n=19) were female. The median BRX dose was 2 mg/day. Of the 30 patients, 20 (66.7%) continued treatment regularly. Among those who discontinued treatment, three patients stopped due to akathisia, two due to sedation, and two due to an urgent need for electroconvulsive therapy. For the 20 patients who continued treatment, scale scores were reassessed during follow-up visits between weeks 4 and 8. A significant improvement was observed in both BDI scores (32.05±8.96 vs. 12.45±9.74; p<0.001) and BAI scores (28.00±10.07 vs. 12.75±10.83; p=0.001) after treatment. Meanwhile, no significant change was observed in body weight (73.05±20.93 kg vs. 75.30±20.32 kg; p=0.123). Among patients whose GAS scores indicated moderate functioning before BRX treatment, 80% (n=16) achieved good functioning after treatment.

Conclusion: BRX may be an effective adjunctive treatment option for patients with TRD, with potential benefits for anxiety symptoms and overall functioning. Although some patients experienced weight gain, this effect did not appear to be clinically significant in our sample.

Keywords: Brexpiprazole, depression, treatment-resistant depression, anxiety, functioning

INTRODUCTION

Brexpiprazole (BRX) is a newer-generation psychotropic medication approved by the United States Food and Drug Administration (FDA) in 2015. In addition to its efficacy in treating the negative symptoms of schizophrenia, it is also used as an adjunctive agent in the treatment of major depressive disorder (MDD). In 2023, the FDA also approved its use for the treatment of agitation associated with dementia due to Alzheimer's disease (1, 2). BRX acts as a partial agonist at dopamine D2 and serotonin

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5-HT1A receptors. It also demonstrates strong antagonistic activity at serotonin 5-HT2A and α1B/2C adrenergic receptors. Compared with aripiprazole, it has a higher binding affinity for these receptors, particularly 5-HT2A, 5-HT1A, and α1B receptors (3).

Experimental studies have shown that brexpiprazole prevents dextran sulphate sodium-induced depressive-like behaviors and demyelination in the prefrontal cortex of mice (4). Following adjunctive therapy with BRX, patients treated for MDD have been reported to feel calmer and less anxious or irritable. Adjunctive BRX therapy has also been associated with improvements in overall mood and increased participation in daily activities (5). Moreover, case reports suggest a potential role for BRX in reducing suicidality, aggression, and substance misuse in some patients (6).

A study conducted in Japan suggested that 1 mg/day BRX is an appropriate initial dose, with both 1 mg/day and 2 mg/day doses being effective and well tolerated in patients with an inadequate response to antidepressant therapy (7). In another randomized double-blind study, BRX doses of 1 mg/day and 3 mg/day were well tolerated, with the 3 mg/day dose demonstrating effectiveness in treatment-resistant MDD compared to placebo (8). BRX has been shown to improve symptom clusters including anhedonia, dysphoria, psychomotor retardation, vegetative symptoms, loss of interest, and lassitude beginning as early as the first week of treatment (9). Adjunctive BRX therapy has also been shown to improve overall functioning and reduce anxiety symptoms (10). In addition to alleviating depressive and anxiety symptoms in patients with MDD, adjunctive BRX therapy has demonstrated favorable effects on sleep disturbances, impulsivity, and sexual dysfunction. Furthermore, it has been reported to improve academic and occupational functioning and enhance quality of life in young adult patients (11-15).

Despite being approved by the FDA in 2015, BRX was introduced into clinical practice in Turkiye in May 2024. Accordingly, data regarding its effectiveness and tolerability in the Turkish population remain limited. Furthermore, real-world studies reflecting routine clinical practice are still scarce. Therefore, this study aimed to evaluate the real-world effectiveness of BRX as an adjunctive treatment in patients with treatment-resistant depression (TRD). We hypothesized that adjunctive BRX treatment would be associated with significant improvements in depressive symptoms, anxiety symptoms, and overall functioning.

METHODS

Sample and Procedure

This retrospective study was conducted in the Psychiatry Polyclinic of Akdeniz University and the Psychiatry Polyclinic of Specialized Dr. Huseyin Kara between May 1, 2024 and January 1, 2025. Medical records of patients diagnosed with treatment-resistant depression who were started on BRX as adjunctive therapy were retrospectively reviewed. TRD is defined as the failure to respond to at least two antidepressants administered at adequate doses and durations (16). In our study, TRD was determined through clinical evaluation. Patients who had not responded to at least two antidepressants during their treatment history were included. Specifically, patients who failed to respond to adequate doses of antidepressants (fluoxetine 20 mg/day, venlafaxine 150 mg/day, duloxetine 60 mg/day, sertraline 50 mg/day, escitalopram 10 mg/day, or paroxetine 20 mg/day) within an average treatment duration of four weeks were eligible for inclusion. Patients' sociodemographic and clinical characteristics were obtained from their medical records. BRX dosing followed routine clinical practice. Consistent with standard augmentation strategies, all patients were initially started on BRX 1 mg/day, with planned titration to 2 mg/day after one week, which represents the commonly recommended target dose. Dose adjustments were individualized based on clinical response, tolerability, and adverse effects. Patients demonstrating adequate clinical improvement or sensitivity to side effects were maintained at 1 mg/day, whereas others were titrated to 2 mg/day to optimize therapeutic benefit. This approach reflects naturalistic prescribing patterns in real-world clinical settings. Beck Depression Inventory (BDI), Beck Anxiety Inventory (BAI), and Global Assessment Scale (GAS) scores obtained before treatment and at the first follow-up visit were evaluated. Follow-up assessments were conducted between weeks 4 and 8 after treatment initiation. Thus, evaluations were performed at the time of BRX initiation and at the subsequent follow-up visit (4-8 weeks). The median evaluation period was four weeks. During the study period, all patients diagnosed with TRD and prescribed BRX as augmentation therapy were screened.

Inclusion Criteria

- Patients aged between 18 and 65 years
- Diagnosis of TRD according to the Diagnostic and

Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) and initiation of BRX as adjunctive therapy
- Availability of scale scores in the patient file.

Exclusion Criteria
- Diagnosis of a neurological disorder
- Presence of an additional psychiatric disorder (e.g., obsessive-compulsive disorder, bipolar disorder, substance use disorder, etc.) other than anxiety disorders
- Use of adjunctive therapies other than BRX
- Use of additional antipsychotic or mood-stabilizing medications besides antidepressants
- Intellectual disability
- Electroconvulsive therapy within the preceding year.

Global Assessment Scale (GAS)
The Global Assessment Scale was developed by Endicott et al. (17) in 1976. The scale can be administered to both patient and healthy populations and ranges from 0 to 100 points, with higher scores indicating better functioning. Scores between 61-100 indicate good functioning, scores between 31-60 indicate moderate functioning, and scores below 30 indicate poor functioning.

Beck Depression Inventory (BDI)
The Beck Depression Inventory was developed by Beck et al. in 1961 to assess the severity of depressive symptoms. A validity and reliability study of the Turkish version has been conducted. The BDI consists of 21 items, each scored from 0 to 3, resulting in a total score range of 0-63. The inventory has been shown to have a sensitivity above 90% for detecting depression requiring treatment when a cutoff score of 17 or higher is used. However, some studies consider remission to be defined as a score below 10 (18, 19).

Beck Anxiety Inventory (BAI)
The Beck Anxiety Inventory was developed by Aaron T. Beck et al. in 1988 and was adapted into Turkish by Ulusoy et al. in 1998 with demonstrated validity and reliability. The inventory consists of 21 items, including 13 items assessing subjective anxiety and 8 items assessing somatic symptoms. Each item is scored from 0 to 3, yielding a maximum possible score of 63. The severity ranges are defined as follows:
- 0-7 points: No anxiety symptoms,
- 8-15 points: Mild anxiety,
- 16-25 points: Moderate anxiety,
- 26-63 points: Severe anxiety (20, 21).

The present study received ethical approval from the Akdeniz University Medical Scientific Research Ethics Committee on January 2, 2025 (decision number TBAEK-43). All stages of this study were conducted in accordance with the principles of the Declaration of Helsinki. This study was a retrospective file review, and all analyzed data were obtained from assessment scale results collected during routine clinical practice. The data used in the study were derived exclusively from standard clinical evaluations performed as part of patients' diagnosis, follow-up, and treatment monitoring. No additional contact was established with the patients, no new assessments were conducted, and no interventions outside routine clinical practice were undertaken for research purposes. Therefore, in accordance with the evaluation of the local ethics committee and considering the retrospective design of the study, obtaining informed consent from the patients was not deemed necessary.

Statistical Analysis
Data analysis was performed using IBM SPSS version 23.0. Continuous variables were presented as mean±standard deviation, median, minimum, and maximum values. Categorical variables were presented as frequencies and percentages. The normality of continuous variables was assessed using the Shapiro–Wilk test and visual inspection of histograms and Q–Q plots. Post-treatment Beck Depression Inventory scores, post-treatment Beck Anxiety Inventory scores, and both pre- and post-treatment Global Assessment Scale scores did not meet normality assumptions. Therefore, comparisons involving these variables were performed using the Wilcoxon signed-rank test. Pre-treatment BDI and BAI scores and body weight measurements met normality assumptions. Although nonparametric tests were used for variables that did not meet normality assumptions, these variables are presented as mean±standard deviation for ease of clinical interpretation. Effect sizes for Wilcoxon signed-rank test comparisons were calculated using the r statistic ($r=|Z|/\sqrt{N}$). Statistical significance was set at $p<0.05$.

RESULTS

This study included a total of 30 participants, of whom 20 (66.7%) continued treatment regularly. The antidepressants used prior to BRX augmentation, along with their dose ranges and durations of use, were as follows: escitalopram (10 mg for 4 weeks),

sertraline (50 mg for 4 weeks), paroxetine (20-30 mg for 4-6 weeks), fluoxetine (20 mg for 4 weeks), and venlafaxine (150-300 mg for 4-8 weeks). The recommended target dose of BRX in TRD is 2 mg/day (7). Accordingly, all patients were initially started on 1 mg/day and were instructed to increase the dose to 2 mg/day after one week. However, five patients reported that they continued treatment at the same dose (1 mg/day). Upon comorbid physical conditions were evaluated, four patients were found to have essential hypertension and one patient had diabetes mellitus. No other medical conditions were identified. Sociodemographic and clinical characteristics of the participants are summarized in Table 1.

In our study, five participants discontinued medication due to side effects. Three individuals discontinued treatment due to akathisia and two due to sedation. Two additional patients required urgent electroconvulsive therapy and discontinued medication for this reason. Three patients did not attend follow-up after the initial visit and were considered to have discontinued treatment. Overall, 20 of the 30 patients (66.7%) continued treatment regularly. For these 20 patients, comparisons of scale scores before and after BRX treatment are summarized in Table 2.

A comparative analysis was conducted to determine whether patients who continued treatment (n=20) differed from those who discontinued treatment (n=10) in terms of sociodemographic variables. The analyses revealed no statistically significant differences between the groups in terms of age, sex, weight, marital status, education level, or employment status (all p>0.05).

Treatment response and remission were evaluated separately for depressive and anxiety symptoms among the 20 patients who continued treatment. According to the BDI, treatment response, defined as a ≥50% reduction from baseline scores, was observed in 70% of patients (14/20), while complete remission (BDI<10) was achieved in 50% (10/20).

Anxiety outcomes were assessed using the BAI. A treatment response, defined as a ≥50% reduction in BAI scores, was observed in 50% of patients (10/20), and complete remission of anxiety symptoms (BAI≤7) was achieved in 45% of patients (9/20).

Of the 20 patients who continued treatment, 14 were receiving selective serotonin reuptake inhibitors (SSRIs) and six were receiving serotonin–norepinephrine reuptake inhibitors (SNRIs). Separate analyses were conducted for these subgroups. BDI and BAI scores decreased significantly in the SSRI group (p=0.001 and p=0.009, respectively) and in the SNRI group (p=0.027 and p=0.028, respectively), as assessed using the Wilcoxon signed-rank test.

Table 1: Sociodemographic and clinical characteristics of participants (n=30)

	n	%
Gender		
Female	19	63.3
Male	11	36.7
Marital status		
Single	15	50.0
Married	13	43.3
Divorced/other	2	6.77
Education level		
Elementary school	3	10.0
High school	7	23.3
University	20	66.7
Employment status		
Employed	14	46.7
Unemployed	16	53.3
Current antidepressant treatment		
Escitalopram	5	16.7
Sertraline	2	6.7
Paroxetine	5	16.7
Fluoxetine	7	23.3
Venlafaxine	11	36.7
Age (years) (mean±SD) (min-max)	32.50±11.38 (18-63)	
Brexpiprazole dose (mg/day) (n=20), mean±SD	1.75±0.44	
Median (min-max)	2.00 (1.00-2.00)	

SD: Standard deviation; Min: Minimum; Max: Maximum.

Functioning was evaluated based on GAS scores. According to GAS scores, all patients demonstrated moderate functioning before BRX treatment. After receiving BRX, 80% (n=16) of the patients were classified as having good functioning, whereas 20% (n=4) continued to demonstrate moderate functioning.

DISCUSSION

This study represents one of the first investigations evaluating the effectiveness of BRX as adjunctive therapy in patients with TRD in our country. Our results demonstrate that the use of BRX as an adjunct to antidepressants in the treatment of depression

Table 2: Comparison of scale scores before and after brexpiprazole treatment

	Before brexpiprazole (n=20)	After brexpiprazole (n=20)	p
Beck Depression Inventory (mean±SD)	32.05±8.96	12.45±9.74	**<0.001** (effect size r=0.877)
Beck Anxiety Inventory (mean±SD)	28.00±10.07	12.75±10.83	**0.001** (effect size r=0.768)
Weight (kg) (mean±SD)	73.05±20.93	75.30±20.32	0.141
Global Assessment Scale (mean±SD)	48.00±6.95	78.50±10.89	**<0.001** (effect size r=0.885)

Body weight before and after treatment was compared using the paired-samples t-test. Beck Depression Inventory, Beck Anxiety Inventory, and Global Assessment Scale scores were compared using the Wilcoxon signed-rank test. Effect size was calculated as $r=Z/\sqrt{n}$. SD: Standard deviation.

leads to significant clinical improvement. Both BDI and BAI scores showed significant reductions following treatment, and overall patient functioning improved. Although patients experienced an average weight gain of 2.25 kg, this increase was not statistically significant.

Our findings regarding the effectiveness of BRX as adjunctive therapy in patients with TRD are consistent with previous literature. Our findings suggest that BRX is effective in patients with TRD. As an adjunctive treatment, BRX has been reported to alleviate core depressive symptoms, improve sleep and appetite disturbances, and enhance functioning (22). A study conducted in elderly patients aged 65 years and older reported improvements in depressive symptoms, social functioning, and quality of life (23). Doses of 1-2 mg/day have generally been found to be effective for adjunctive BRX therapy (24). In a randomized controlled study conducted in Japan, BRX at a dose of 3 mg/day demonstrated significant improvement compared to placebo (8). Adjunctive BRX therapy at doses between 0.5 and 3 mg/day has also been shown to be generally safe and well tolerated for up to 52 weeks (25). Consistent with these findings, our study showed that a median dose of 2 mg/day of BRX was associated with reductions in depressive symptoms and improvements in patient functioning. Therefore, a dose of 2 mg/day may be considered an effective target dose for reducing depressive symptoms. More than 50% of patients receiving adjunctive BRX therapy demonstrated improved participation in daily life, with significant positive changes reported as early as one month after treatment initiation. Among indicators of life participation, the most prominent improvements were observed in the emotional and social domains (26). In the present study, inventory scores improved significantly within 4-8 weeks after adjunctive BRX treatment. These findings support previous evidence suggesting that the therapeutic effects of BRX in treatment-resistant depression may emerge within a relatively short period.

In addition to improving depressive symptoms and functioning, BRX may also help patients achieve significant improvements in emotional, physical, social, and cognitive domains (22, 27). A 52-week open-label, multicenter study reported that, following adjunctive BRX therapy at a dose of 2 mg/day in patients with depression, clinicians tended to focus more on depressive symptom severity, whereas patients prioritized improvements in functioning and daily life activities (28). In the present study, functioning improved from moderate to good in 80% of patients according to GAS scores, suggesting that the functional benefits of BRX may represent a significant clinical advantage.

Furthermore, adjunctive BRX is not only effective for depressive symptoms but also for anxiety symptoms. This finding was demonstrated in our study by improvements in BAI scores and is consistent with previous reports. Earlier studies have shown BRX to have anxiolytic effects (1, 10, 24). These results highlight the multifaceted effect profile of the drug and its potential to improve overall patient quality of life. In addition, our study found BRX to be well-tolerated, with no serious adverse effects observed in the majority of patients. Treatment with BRX was tolerated for up to three months with a low rate of discontinuation due to side effects, consistent with previous studies (10).

The present study did not observe a statistically significant change in body weight among participants; however, a mean increase of approximately 2 kg was noted. The rate of weight gain associated with adjunctive BRX was reported as 8.3% in a study by Lepola et al. (23) and 33.2% in a study by Kato et al. (7) A study involving 2,944 patients reported the rate of weight gain associated with BRX therapy to be 17.7%, with a mean increase of 2.7 kg by week 26 and 3.2 kg by week 52 (25). In the present study, a mean weight gain of 2.25 kg was observed during the 4-8-week follow-up period. Although this increase was not statistically

significant, a weight gain of 2.25 kg within such a short period may still be clinically relevant. The relatively rapid weight gain observed raised concerns regarding potential long-term effects. Therefore, even though the difference was not statistically significant in our study, we recommend that patients receiving BRX be carefully monitored for weight changes. Longer-term follow-up studies (e.g., 1–2 years) are clearly needed to evaluate the long-term impact of BRX on body weight.

This study has certain limitations. These include the difficulty of establishing cause-effect relationships due to its retrospective nature, the absence of a control group, the selection of the study sample from only two centers, and the limited sample size. The relatively small sample size should be considered when interpreting the findings, as it may limit the generalizability of the results. The absence of a control or comparison group makes causal inference difficult. The small sample size may also have limited our ability to detect domain-specific functional changes. In addition, relying solely on the GAS may not fully capture detailed aspects of functioning. The fact that GAS assessments were not blinded may have introduced potential observer bias. Another important limitation is that standard diagnostic tools, such as the Structured Clinical Interview for DSM-5 (SCID-5), were not used for diagnosis. Other limitations of the study include the short follow-up period, which did not allow for the assessment of long-term effects, selective attrition, and potential reporting bias in self-report measures. Because outcome scales could not be administered to patients who discontinued treatment, an intention-to-treat analysis could not be performed. This represents another limitation of the study and should be addressed in future research. Because our sample consisted predominantly of young female patients (mean age: 32.5 years), the generalizability of our study to broader populations (e.g., elderly patients or those with severe TRD) is limited.

The strengths of our study include that it is the first study conducted in our country examining BRX in patients with TRD and that it is based on real-world clinical data. We believe that real-world evidence regarding new pharmacological treatments is an important complement to findings from randomized controlled trials. Future studies with larger sample sizes and longer follow-up periods are needed to further evaluate the effectiveness of BRX in patients with TRD.

CONCLUSION

In this retrospective real-world study, adjunctive BRX treatment was associated with significant improvements in depressive symptoms, anxiety symptoms, and overall functioning in patients with TRD. BRX augmentation was generally well tolerated, and no statistically significant weight change was observed during the short-term follow-up period. These findings suggest that BRX may be an effective and feasible augmentation option in routine clinical practice for patients with TRD. Nevertheless, prospective studies with larger sample sizes and longer follow-up periods are needed to confirm these findings and to better evaluate long-term outcomes.

Ethical Approval: The Akdeniz University Medical Scientific Research Ethics Committee granted approval for this study (date: 02.01.2025, number: TBAEK-43).

Informed Consent: Informed consent was not required due to the retrospective nature of this study.

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	Critical revision of manuscript	H.K., A.E.
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LETTER TO THE EDITOR

From early psychiatric symptoms to an adolescent diagnosis: Clues from childhood in spinocerebellar ataxia Type-42

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Dear Editor,

Spinocerebellar ataxias (SCAs) comprise a group of genetically inherited, heterogeneous neurodegenerative disorders that primarily affect the cerebellum, brainstem, spinal cord, and cranial nerve nuclei. These disorders are characterized by progressive gait and limb ataxia and may be accompanied by varying degrees of nystagmus, dysarthria, intention tremor, and ophthalmoparesis (1).

Spinocerebellar ataxia type 42 (SCA42) is a rare subtype that typically presents with slowly progressive cerebellar ataxia. It has been associated with a c.5144G>A (p.Arg1715His) mutation in the CACNA1G gene (2, 3). In cases reported by Coutelier, the age of onset ranged from 9 to 78 years, whereas in the series reported by Morino et al. (4), the age of onset ranged from 20 to 70 years (5). A recent study demonstrated that de novo mutations in the CACNA1G gene can result in a clinical picture characterized by prominent neurodevelopmental impairment and cerebellar ataxia beginning in early childhood (6). Increasing reports from different countries, along with the identification of novel mutations, have highlighted the clinical and genetic heterogeneity of SCA42 (7).

Here, we present the case of a 15-year-old male who exhibited developmental and psychiatric symptoms nearly a decade before the onset of motor manifestations. The patient has been followed in a child and adolescent psychiatry outpatient clinic for speech fluency disorder, social anxiety disorder, specific phobias, and mild intellectual disability.

No significant complications were reported during the prenatal period, and both second- and third-trimester screening tests were within normal limits.

Following birth, the patient required 11 days of incubator care due to infection, although respiratory support was not needed. During infancy, he was monitored by pediatric neurology for macrocephaly.

He began walking independently at approximately 24 months, and his first meaningful words emerged between 2.5 and 3 years of age. Toilet training was delayed, and nocturnal enuresis persisted until 9–10 years of age.

At age 4, due to global developmental delay, the patient began receiving special education. Speech difficulties also became apparent around this time and have shown only minimal improvement despite numerous speech and language therapy interventions.

At age 6, he began to exhibit symptoms of social anxiety and specific phobias, which were later diagnosed as social anxiety disorder and specific phobia according to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) criteria (8).

At age 8, a Wechsler Intelligence Scale for Children–Fourth Edition (WISC-IV) assessment yielded a full-

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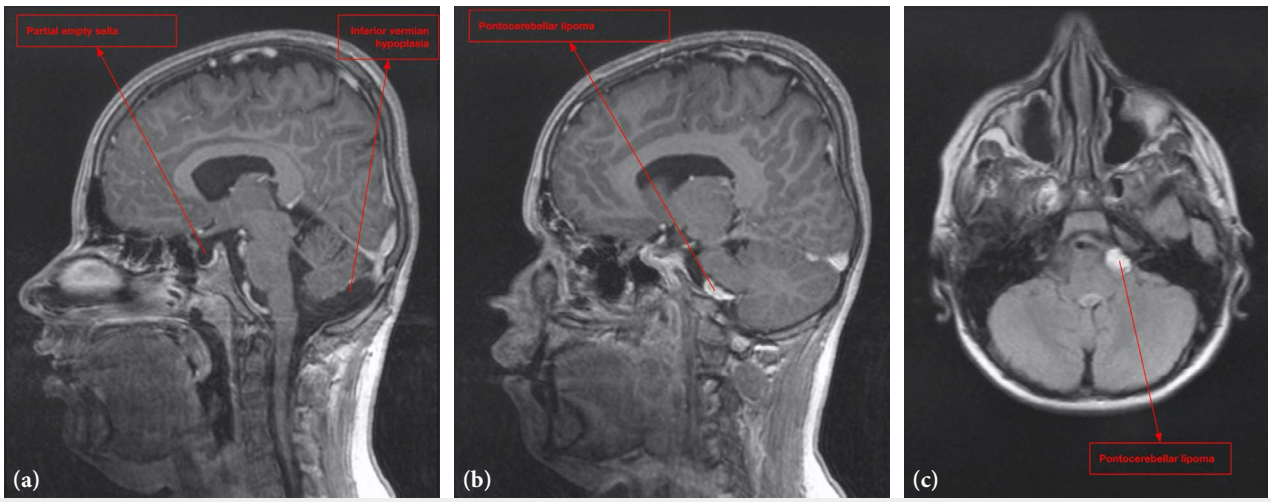

Figure 1. (a) Sagittal MRI scan revealing additional radiological findings: Partial empty sella (left arrow) and inferior vermian hypoplasia (right arrow). **(b)** Sagittal T1-weighted MRI scan demonstrating the localization of the pontocerebellar lipoma (indicated by the red arrow). **(c)** Axial T1-weighted MRI scan showing a pontocerebellar lipoma (indicated by the red arrow) in the posterior fossa.

scale IQ score of 50, consistent with a diagnosis of mild intellectual developmental disorder according to DSM-5 criteria (8).

Metabolic evaluations performed as part of the differential diagnosis (including lysosphingolipid panel, oligosaccharide analysis, and mucopolysaccharide screening) were within normal limits and did not support a diagnosis of mucopolysaccharidosis. The patient had no history of epileptic seizures. He was also followed by ophthalmology for strabismus.

At age 14, the patient was referred to neurology because of frequent falls. Neurological examination revealed a broad-based gait, dysmetria, and slowed fine motor performance. Brain magnetic resonance imaging (MRI) demonstrated inferior vermian hypoplasia (Fig. 1a), partial empty sella (Fig. 1a), right pontine atrophy, and a 17×13×11 mm left ponto-cerebellar lipoma (Fig. 1b, c).

Due to anxiety symptoms, the patient has been receiving fluoxetine at a dose of 30 mg/day for the past year and continues to benefit from the treatment.

Genetic analysis identified a pathogenic CACNA1G variant (p.Arg1715His) as well as a heterozygous variant in the SACS gene. These findings confirmed the diagnosis of SCA42. Both parents tested negative for the CACNA1G mutation; the patient's mother was identified as a heterozygous carrier of the SACS variant. Genetic counseling was provided to the family.

Neuropsychiatric symptoms are frequently observed in hereditary ataxias, although they are often underrecognized or misdiagnosed. Depression is the most commonly reported psychiatric comorbidity, while anxiety, apathy, agitation, and psychotic symptoms have also been reported to varying degrees (9). In SCA, anxiety is more prevalent than in the general population and often co-occurs with depression (10, 11). Additionally, impulsive and compulsive behaviors, as well as sleep disturbances, have been described (12).

Beyond its role in motor control, the cerebellum also plays a key role in cognitive and emotional regulation. Cerebellar Cognitive Affective Syndrome (CCAS), as defined by Schmahmann and Sherman, is characterized by impairments in executive functioning, social cognition, affect regulation, and language (e.g., verbal fluency and prosody). This syndrome can be observed in both children and adults with cerebellar dysfunction and underscores the importance of recognizing non-motor features in cerebellar disorders (13–15). In the present case, the presence of speech difficulties, social anxiety, and intellectual disability may be considered within the spectrum of CCAS.

Cases in which psychiatric symptoms begin in childhood and a diagnosis of spinocerebellar ataxia type 42 (SCA42) is established during adolescence are extremely rare in the literature (16). Although psychiatric and cognitive manifestations have been reported in SCAs, these features are most commonly described in adult-onset cases, and reports of childhood-onset presentations remain very rare (14, 15).

Given the broad clinical spectrum of SCA42, a comprehensive assessment integrating neurological, developmental, and psychiatric evaluations is essential for timely and accurate diagnosis. Recognition of early neuropsychiatric and developmental symptoms may facilitate earlier suspicion of SCA42, thereby enabling genetic counseling and anticipatory guidance for families. In the absence of disease-modifying treatments, multidisciplinary management focused on rehabilitation, educational support, and psychiatric care remains crucial.

Future studies should aim to clarify genotype–phenotype correlations and explore potential targeted therapies (17).

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LETTER TO THE EDITOR

A growing concern: Carbamazepine abuse in Turkish correctional settings and its clinical and ethical implications

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Dear Editor,

Carbamazepine (CBZ) is a widely used antiepileptic drug with established efficacy in epilepsy, bipolar disorder, trigeminal neuralgia, and selected impulse-control disorders (1). It is also prescribed for alcohol withdrawal syndromes in selected cases, although benzodiazepines remain the standard first-line treatment (2). However, recent clinical observations from correctional psychiatry units in Turkiye point to an unsettling trend: the increasing misuse and non-indicated demand for CBZ among incarcerated individuals, particularly those with histories of substance use and antisocial personality traits.

Across multiple prison settings, clinicians working in high-security forensic psychiatry hospitals, forensic units of major general hospitals, and correctional institutions throughout Turkiye have observed that CBZ is being explicitly requested—often by brand name or formulation—despite the absence of appropriate psychiatric or neurological indications. This behavior is especially pronounced among inmates who show little interest in standard pharmacological treatments such as selective serotonin reuptake inhibitors (SSRIs), mood stabilizers, or atypical antipsychotics. A disproportionate preference for the immediate-release (IR) formulation over the controlled-release (CR) form has been noted, likely due to its more rapid central nervous system effects. In some cases, patients reportedly feign epileptic symptoms or present falsified prescriptions to obtain CBZ, occasionally seeking access through neurology departments when denied by psychiatric services.

Clinical staff in correctional settings have also reported that some inmates stockpile CBZ—acquired through legitimate or illicit means—and consume it in large quantities. Although this phenomenon has not yet been systematically documented in the Turkish literature, anecdotal observations suggest that these individuals describe subjective effects such as "feeling good," "getting high," or "calming down"—descriptions that parallel the "quiet euphoria," "light-headedness," "getting a buzz," and mild sedative effects previously reported in the literature (3, 4). The paradox in this context is notable: although CBZ lacks a clearly defined addictive pathway, it appears to be used for self-soothing or euphoric purposes (3, 5). Reports from correctional officers and healthcare professionals suggest that, for some individuals, CBZ may reduce impulsivity, aggression, or affective instability—raising the complex question of whether its misuse may, in some cases, represent a form of self-medication in emotionally dysregulated, trauma-exposed, or high-impulsivity populations. Incarcerated individuals frequently experience limited and inconsistent access to psychiatric care, including

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shortages of qualified clinicians and restricted availability of psychotherapeutic interventions, which may contribute to self-medication as a coping strategy for psychological distress. Such barriers represent modifiable deficiencies within correctional mental healthcare and underscore the need for improved and more continuous access to structured treatment.

The existing case literature, although limited, supports the dual nature of CBZ. For example, Stuppaeck et al. (3) reported a patient who described experiencing a "quiet euphoria" when using CBZ at therapeutic doses and clearly distinguished this effect from placebo. Crawford et al. (4) described a series of polysubstance users who misused CBZ recreationally, emphasizing that in the absence of readily available benzodiazepines, individuals may experiment with whatever agents are accessible, leading to emergent patterns of misuse, findings that closely parallel our clinical observations. Other reports have noted subjective experiences of sedation, mild euphoria, or behavioral disinhibition at supratherapeutic doses, even among patients without histories of polysubstance abuse (5–7).

The mechanism underlying the psychoactive misuse of carbamazepine remains speculative. CBZ acts through sodium channel blockade and modulation of glutamatergic activity but may also indirectly influence serotonergic, dopaminergic, or peripheral benzodiazepine systems (8, 9). Some studies have postulated potential interactions with glucocorticoid and neurosteroid pathways (10). Notably, Zullino et al. (11) suggested that CBZ may reduce cravings in individuals undergoing withdrawal from alcohol, benzodiazepines, or cocaine.

Based on our clinical experience in Turkiye, CBZ misuse appears to be neither isolated nor benign. Some inmates openly admit to "borrowing" CBZ from other prisoners. In rare but illustrative cases, such as that reported by Hanada et al. (12), discontinuation of CBZ in a youth with hippocampal agenesis was followed by an immediate resurgence of criminal behavior, which again subsided upon resumption of treatment—highlighting CBZ's potential regulatory role in affect and behavior.

Nevertheless, the associated risks are substantial. CBZ overdose can result in ataxia, diplopia, confusion, seizures, and severe toxicity, posing a safety concern in poorly monitored environments such as correctional facilities. Moreover, CBZ is a potent inducer of cytochrome P450 enzymes, which can alter the plasma concentrations of numerous concomitantly administered medications (13). In incarcerated individuals receiving multiple psychotropic agents, these interactions complicate both therapeutic efficacy and safety.

Inmates frequently request progressively higher doses over time in the absence of documented clinical deterioration. Others insist on CBZ use for off-label indications, such as restless leg syndrome, despite current guidelines not recommending it as a first-line treatment (14). This pattern of behavior—characterized by persistent medication-seeking, diagnostic manipulation, and resistance to alternative treatments—resembles classic drug-seeking behavior and must be approached with vigilance.

Nonetheless, not all CBZ use within correctional settings is problematic. Based on our experience in prison psychiatric wards, inmates with well-established diagnoses of bipolar disorder or impulse-control syndromes who are prescribed either IR or CR CBZ under structured monitoring sometimes demonstrate notable improvements in emotional regulation, sleep quality, and interpersonal functioning. These subjective improvements are often corroborated by correctional staff observing fewer disciplinary incidents. In contrast, individuals engaging in manipulative medication-seeking behaviors rarely exhibit behavioral improvement.

This duality illustrates the therapeutic ambiguity surrounding CBZ use in carceral environments. Its potential utility in managing impulsivity must be carefully balanced against the emerging risk of misuse. Clinical decision-making therefore requires both ethical clarity and strong institutional support.

We propose the following measures:

- Prescriptions should be strictly limited to documented psychiatric indications, such as bipolar disorder or impulse-control pathology.
- Immediate-release formulations should be prescribed with particular caution, especially in individuals with a history of substance use.
- Clinicians should verify prior treatment records across departments and institutions to confirm the appropriateness of indications.
- Multidisciplinary collaboration—including psychiatrists, correctional officers, and nursing staff—along with structured contextual risk assessments, is essential (15).
- Blood level monitoring, although challenging in correctional settings, should not be neglected when behavioral warning signs or unexplained dose escalation are observed.

- The implementation of institutional prescribing protocols for high-risk medications such as CBZ may help protect both patients and clinicians from ethical dilemmas.

To our knowledge, the misuse of CBZ in correctional psychiatry has not yet been systematically studied in Turkiye. We therefore call for urgent national surveillance efforts, multicenter collaboration, and the development of evidence-based clinical guidelines to better understand and address this evolving phenomenon. In particular, partnerships among major psychiatric hospitals, high-security forensic psychiatry centers, and correctional institutions will be critical for designing translational research that bridges theory and clinical practice. Only through such coordinated efforts can we balance ethical patient care with the systemic need to prevent misuse and ensure safe prescribing.

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LETTER TO THE EDITOR

Next-morning vomiting as a withdrawal symptom of immediate-release methylphenidate

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Dear Editor,

Methylphenidate (MPH) has been a first-line and effective treatment option for attention-deficit/hyperactivity disorder (ADHD) for many years (1). Various formulations are available, including immediate-release (IR) and long-acting (OROS) preparations, which differ in duration of action, efficacy, and side-effect profiles (2). Although MPH is generally well tolerated, the most commonly reported adverse effects include nausea, abdominal pain, headache, and decreased appetite, particularly during the initial phase of treatment (3–5). Here, we report an unusual adverse event: morning vomiting as a possible withdrawal symptom occurring during treatment with IR-MPH in a young adult male.

A 19-year-old male presented with his parents, reporting attention difficulties, forgetfulness, poor academic performance, and inability to complete examinations on time. Following a detailed psychiatric evaluation, he was diagnosed with attention-deficit/hyperactivity disorder, inattentive presentation, and specific learning disorder, according to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5). His developmental history was unremarkable. He had graduated from high school with moderate academic success and had no prior history of pharmacological treatment for attention-related problems. Treatment was initiated with immediate-release methylphenidate (IR-MPH) at a dose of 10 mg administered at 9:00 a.m. while he was attending a university entrance examination preparation course. He reported no significant side effects during the day following administration of IR-MPH 10 mg. However, approximately 30 minutes after awakening the next morning, around 8:30 a.m., he experienced multiple episodes of vomiting. These episodes occurred regardless of food intake, were not self-induced, and were typically not accompanied by nausea or abdominal pain. The vomiting lasted approximately 10–15 minutes and consisted of 5–6 episodes with gradually decreasing intensity. When he omitted his morning dose on a day when vomiting had occurred, he did not experience vomiting the following morning. Conversely, upon resuming IR-MPH, next-morning vomiting reappeared. Despite recognizing a probable association between his symptoms and IR-MPH, he continued treatment because of the marked improvement in his inattention and learning difficulties. Over a period of approximately four weeks, he took IR-MPH 10 mg at around 9:00–9:30 a.m. on 12 separate occasions, each followed by next-morning vomiting. Vomiting occurred consistently after all 12 doses and was absent on days without medication. The intensity and duration of symptoms remained similar across episodes, indicating no evidence of tolerance development over this short exposure period. During this time, the patient was evaluated by an internal medicine specialist to exclude

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alternative causes of vomiting. Physical examination revealed no gastrointestinal or systemic abnormalities. Laboratory investigations, including complete blood count and infection screening, were within normal limits. His past medical history was unremarkable, and he was not taking any concurrent medications. Although the patient was experiencing stress related to preparation for the university entrance examination, there were no anticipatory symptoms or situational triggers suggestive of psychogenic vomiting.

Subsequently, his treatment was switched to OROS MPH 36 mg, administered in the morning. During one month of treatment with OROS MPH, he reported no significant side effects or episodes of next-morning vomiting. For further evaluation, he was asked to substitute IR-MPH 10 mg for Concerta for one day. When IR-MPH was administered at 11:30 a.m., he experienced vomiting the following day at approximately 5:00 p.m., with slightly reduced intensity. He did not take any medication on the day the vomiting occurred. He was then advised to continue treatment with OROS MPH 36 mg. These findings were interpreted as indicating that the vomiting episodes were most likely a withdrawal symptom associated with IR MPH. Assessment using the Naranjo Causality Assessment Scale yielded a score of 7, indicating probable causality (6). However, it should be noted that the Naranjo algorithm is not specifically designed to assess withdrawal-related or delayed adverse effects, which represents a methodological limitation.

Methylphenidate remains the primary pharmacological treatment for ADHD, with an estimated therapeutic response rate of 70–80% (1). Its mechanism of action primarily involves inhibition of dopamine and norepinephrine transporters in presynaptic neurons, resulting in increased extracellular concentrations of these neurotransmitters, particularly within the prefrontal cortex (7). While these dopaminergic and noradrenergic effects underlie MPH's therapeutic efficacy, they are also associated with a range of adverse effects (8–11). The onset and severity of such effects depend on the concentration of MPH in the bloodstream, which varies significantly between immediate-release and extended-release formulations because of their different pharmacokinetic profiles (2, 12–15).

Immediate-release methylphenidate reaches peak plasma concentrations within 1–2 hours of administration and is commonly associated with peak-related adverse effects, including insomnia, appetite suppression, and nausea (3). As drug levels decline, some patients experience rebound symptoms—transient worsening of ADHD symptoms—or withdrawal-like effects, which may include both physical and behavioral manifestations attributable to abrupt reductions in dopaminergic activity (16). These rebound and withdrawal phenomena are well documented and typically occur within predictable time frames that correspond to MPH pharmacokinetics. In the present case, however, the onset of vomiting nearly 24 hours after dosing suggests an atypical withdrawal mechanism extending beyond the expected pharmacodynamic window of IR-MPH. Notably, the literature also describes atypical presentations that fall outside these conventional temporal boundaries. For example, acute dystonia has been described in an adolescent following a missed dose of MPH and was interpreted as an atypical withdrawal phenomenon (17). Additionally, next-day neuromuscular pain—manifesting as painful morning leg cramps—has been reported after discontinuation of IR-MPH, further supporting the notion that withdrawal-like effects may extend temporally beyond the dosing day (18). Notably, those reports involved longer prior exposure, whereas in the present case the delayed adverse effect occurred consistently from the initial doses during ongoing treatment, highlighting a distinct temporal pattern.

Vomiting is a well-documented adverse effect of MPH, although its precise pathophysiology remains incompletely understood (3). Accumulating evidence suggests that abrupt fluctuations in dopaminergic transmission may precipitate gastrointestinal dysregulation, either through direct dopaminergic pathways or via secondary neurotransmitter alterations (19). While dopaminergic overstimulation, rather than a decrease, is more commonly associated with emesis, the occurrence of vomiting in this patient during a phase of declining dopamine levels raises the possibility of a compensatory withdrawal-related mechanism triggering the emetic response. The complete resolution of symptoms following a switching to an extended-release formulation further supports this hypothesis. Extended-release formulations, such as OROS MPH, provide more gradual drug delivery, resulting in steadier plasma concentrations throughout the day (2). This pharmacokinetic profile minimizes abrupt neurotransmitter fluctuations associated with IR-MPH. Previous studies have demonstrated improved tolerability and reduced rebound effects with extended-release MPH compared to IR formulations (20).

This case also highlights that adverse effects may vary substantially across individuals. Interindividual differences in drug metabolism, receptor sensitivity,

and downstream neurotransmitter responses can influence both the phenotype and timing of adverse events (3). From a pharmacokinetic perspective, genetic polymorphisms in enzymes such as carboxylesterase 1 (CES1) (and, to a lesser extent, cytochrome P450 2D6 [CYP2D6]) can alter methylphenidate metabolism. Variability in the formation and clearance of ritalinic acid—the major but pharmacologically inactive metabolite—may indirectly contribute to delayed adverse responses by reflecting individual differences in elimination pathways (2). Beyond peripheral metabolism, central pharmacodynamic factors are also relevant: although MPH is rapidly cleared from plasma, synaptic and receptor-level adaptations may persist longer than systemic drug levels (21). Taken together, these sources of variability provide a plausible explanation for why some patients experience adverse effects outside the expected pharmacokinetic window, even early in treatment.

Although a single case cannot definitively establish causality, the Naranjo score of 7 in this case indicates a probable association between IR-MPH use and next-morning vomiting (6). Clinicians should therefore remain vigilant not only for commonly expected adverse reactions (e.g., decreased appetite, insomnia) but also for atypical presentations, particularly when prescribing short-acting stimulant formulations. In cases of delayed-onset or persistent adverse events, switching to an extended-release formulation or adjusting the dosage regimen may alleviate symptoms without compromising therapeutic benefit (22). Recognition of such rare presentations in clinical practice is important, as it may inform individualized treatment strategies and ultimately improve the safety and effectiveness of ADHD pharmacotherapy.

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LETTER TO THE EDITOR

Paroxysmal body pain without headache

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Dear Editor,

Recurrent pain in the body and extremities that improves with migraine-specific treatment in patients with migraine headaches may be associated with migraine (1-4). The prevalence of recurrent limb pain in children has been reported to be 2.6%, suggesting a close clinical and epidemiological relationship, as well as a shared pathogenesis, between recurrent extremity pain and childhood migraine (3). The literature also describes cases of extracranial (i.e., outside the head) pain occurring in association with migraine headaches (1, 5-7). The temporal relationship between headache and limb pain is defined as episodes of pain in one or more limbs occurring immediately before or after headache onset, during the headache, or shortly thereafter (5-7). We present the case of a woman with paroxysmal (sudden and transient) body pain without accompanying headache that responded positively to flunarizine treatment. The clinical features resemble migraine-associated extracranial pain described in the literature, suggesting that this presentation may represent a case of migrainous corpalgia.

A 41-year-old woman presented to the neurology outpatient clinic with complaints of body pain that had begun five years earlier and had increased in both intensity and frequency over the past three years. Prior to the onset of pain, she experienced symptoms including weakness, speech difficulty, numbness on the right posterior side of the head, and tingling in the right leg. These symptoms were followed by pain throughout the body, sparing the head. She described the pain as a pressure-like sensation enveloping her body, with greater intensity in the right arm and leg. Initially, the attacks occurred once every three to four months and lasted two to three days. By the time of presentation, however, they were occurring weekly and lasting up to five days. Pain intensity was rated as 8 on the Visual Analog Scale (VAS). The pain did not have throbbing, stabbing, burning, or dull characteristics, although it was occasionally accompanied by tingling sensations. After two to three days of continuous pain, severe exacerbations may recur several times during subsequent periods of weakness. During these episodes, the patient reports marked fatigue and an increased need for sleep. Although pain intensity gradually decreases over the course of each attack, she experiences significant difficulty with movement due to severe pain and requires bed rest. Following the attacks, she describes a generalized numbness sensation affecting the entire body, particularly the right arm and back, while sparing the head. The attacks are not accompanied by dizziness, headache, nausea, vomiting, or hypersensitivity to light, sound, or odors. There is no association with menstruation cycles, nor are there symptoms of morning weakness or stiffness. The attacks are stereotypical in nature, differing only in intensity. They may occur at various times throughout the day, but not during sleep. There is no evidence of allodynia (pain elicited by normally non-painful stimuli), and no triggering factors have been reported. The patient has no known chronic medical conditions and was not receiving any regular treatment.

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The patient's neurological examination was normal, as were her laboratory tests and cranial magnetic resonance imaging (MRI) results. Cervical MRI showed minimal bulging at the C3-4 and C4-5 levels but was otherwise normal. Electroencephalography (EEG) and electromyography (EMG) results were normal, and bilateral median and tibial nerve SEP (somatosensory evoked potentials) studies were also considered normal. The patient was evaluated by the departments of rheumatology, physical therapy and rehabilitation (PTR), and psychiatry. The rheumatology department recommended steroid therapy for three months. Psychiatry prescribed duloxetine 60 mg, which resulted in approximately a 60% reduction in the frequency, duration, and intensity of the pain for eight months. However, the patient experienced no further benefit after this period. Subsequently, psychotherapy was recommended, but the patient did not find monthly or bimonthly sessions beneficial. A return to duloxetine treatment did not yield improvement. Therefore, flunarizine 5 mg daily was initiated, leading to an 80% reduction in pain intensity and a 50% reduction in duration. When the dose was increased to 10 mg daily, evaluation after seven months showed that the duration of attacks had decreased to 1-2 days, indicating a good response to treatment. The patient has been using flunarizine for five years. The dose of flunarizine was increased or decreased according to the frequency of attacks.

Migraine can be associated with limb pain in both adults and children. Extremity pain should be considered one of the periodic syndromes associated with migraine in childhood and part of the migraine spectrum in adulthood (8). The estimated prevalence of extremity pain among adults with migraine ranges between 2% and 4.4% (5, 6, 8). The literature has documented cases of body pain associated with migraine (1, 5-7). Cuadrado et al. (1) described three female patients aged 30 to 41 years with migraine with or without aura. In these cases, body pain occurred in various regions, including the face, back, and upper and lower extremities, and its onset could precede, accompany, or follow the migraine headache. The pain was described as heavy, pressing, burning, constricting, or throbbing in nature, and allodynia could accompany the pain in the affected area. The duration of body pain was irregular, often beginning in one area and spreading. Pain intensity was generally mild to moderate (rated 2–4 out of 10), although in one patient it reached 7 (1). Guiloff and Fruns reported 22 patients aged 19 to 79 years with diagnoses of migraine and/or cluster headache. In these patients, body pain occurred in the face, neck, shoulders, chest, abdomen, and upper or lower extremities. The pain could occur concurrently with the headache, follow it, or occasionally arise in isolation. The nature of the pain varied and was described as throbbing, dull, shooting, constricting, burning, tender, or prickling. The frequency and duration of attacks also varied (5).

Raudino identified two male and eight female patients aged 11 to 57 years with migraine with or without aura. In these cases, body pains occurred in the upper and lower extremities and could precede, accompany, or follow the headache (6). Prakash et al. (7) reported six cases of extremity pain associated with migraine headache. Attacks could occur before, during, after, or independently of the migraine headache. The duration of pain ranged from 1 to 72 hours, and limb pain was described as tearing, burning, or pressing in nature. Triggering factors included exposure to sunlight, weather changes, stress, fatigue, hunger, and sleep disturbances (7). A case of familial migraine with limb pain affecting eight family members, consistent with a dominant inheritance pattern, has also been reported in the literature (8). The characteristics of body pain in our case align with previously reported features of extracranial pain associated with migraine. The patient described the pain as a pressure-like sensation, sometimes accompanied by tingling. Interestingly, she did not report migraine headaches or other recurrent headache types commonly described in the literature.

In another study, levels of substance P (SP) and calcitonin gene-related peptide (CGRP) were measured in three children with extremity pain, both during the attacks and three days after resolution. SP levels increased during pain episodes, whereas CGRP levels were elevated both during and after the attacks. Thermographic assessments demonstrated a decrease in temperature in the affected area at pain onset, followed by an increase after pain resolution (4). The rise in plasma CGRP levels during extremity pain attacks suggests a pathophysiological process similar to that observed in migraine. These findings support the hypothesis that, analogous to the trigeminovascular theory of migraine, abnormal release of CGRP and SP within the vascular walls of the limbs could play a significant role in the pathophysiology of limb pain (4, 9, 10). The presence of cephalic and extracephalic allodynia, indicative of increased sensory sensitivity during migraine attacks, and reports of allodynia in areas of body pain support a potential relationship between spontaneous body pain and migraine. This suggests that spontaneous body pain associated with migraine may result from central sensitization. Migraine has been proposed to represent not merely a headache disorder

but a broader disorder of nociceptive processing (1). However, reports of extremity pain without accompanying allodynia indicate that central sensitization may not be the sole mechanism of underlying limb pain in individuals with migraine. The notion that extremity pain cannot be explained solely by activation of the trigeminovascular system suggests clinical heterogeneity. This observation raises the possibility that additional mechanisms, such as vasospasm, central sensitization, complex regional pain syndrome-like mechanisms, and ion channel dysfunction, may play a role in the etiology of extremity pain (7).

In the management of extracranial pain associated with migraine attacks, analgesics and acute migraine-specific treatments can be effective in reducing extremity pain, suggesting that migraine preventive therapies may also be recommended (1, 5, 7, 8).

The present case is noteworthy for demonstrating a significant reduction in the duration, frequency, and intensity of paroxysmal body pain following treatment with flunarizine, a medication used for migraine prophylaxis. This response supports the hypothesis that body pain may represent a component of the migraine spectrum. The literature indicates that paroxysmal body pain may occur before, during, after, or independently of migraine headache; in some isolated cases, patients have ultimately been diagnosed with migraine. However, no headache complaints were reported in the present case, reinforcing the possibility that extremity pain may occur without headache.

These findings support the view that migraine is not limited to headache but encompasses a wide spectrum of symptoms, including atypical presentations in certain patients. Therefore, individualized diagnostic and therapeutic approaches are essential, with treatment strategies tailored to the patient's clinical profile. Recognizing extracranial pain manifestations in migraine management underscores the importance of a holistic approach that may improve patients' quality of life.

Informed Consent: Written informed consent was obtained from the patient.

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LETTER TO THE EDITOR

Skin picking disorder among adult psychiatric inpatients

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Dear Editor,

Skin-picking disorder (SPD) (excoriation disorder/dermatillomania) is a body-focused repetitive behavior characterized by recurrent skin picking resulting in excoriations, erosions, and sometimes ulcerations with secondary scarring, accompanied by distress and functional impairment. SPD is classified within the obsessive–compulsive and related disorders chapter in the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, Text Revision (DSM-5-TR) (1). Population-based studies have reported SPD prevalence estimates ranging from approximately 1.4% to 3.4% (2–4). However, data on SPD specifically within psychiatric inpatient settings remain limited. In these settings, symptoms that are not the primary reason for admission may be overlooked unless specifically assessed. Given potential underrecognition, impaired insight, and overlapping psychopathology in severe mental illness, investigating SPD in inpatient settings is clinically relevant. Accordingly, we aimed to describe the frequency and clinical characteristics of SPD detected through a joint dermatologist–psychiatrist evaluation among adult psychiatric inpatients.

Between February and August 2025, adult inpatients (≥18 years) hospitalized at Bakirkoy Prof. Mazhar Osman Training and Research Hospital were evaluated. All adult patients admitted to two different general psychiatry wards during the study period were approached consecutively. The study was approved by Bakırkoy Dr.Sadi Konuk Training and Research Hospital Clinical Research Ethics Committee (decision number: 2024-08-04; date: 19.08.2024). Written informed consent was obtained from all participants. Each patient underwent a joint clinical assessment by a dermatologist and a psychiatrist. Psychiatric diagnoses were established according to DSM-5-TR criteria, and the diagnosis of SPD was determined by a psychiatrist based on DSM-5-TR diagnostic criteria. A total of 186 patients were assessed, including 73 women; the mean age was 38.6±12.9 years. SPD was identified in 13 of 186 inpatients (7.0%); only two of these patients had a documented SPD diagnosis prior to the study. The demographic and clinical characteristics of the cases, including psychiatric diagnoses, active psychoactive substance use status, duration of SPD, history of suicide attempt, prior dermatology visit, and main sites of involvement, are summarized in Table 1.

Our inpatient prevalence (7.0%) is higher than estimates from community studies (current ~2.1%; lifetime ~3.1%) and pooled prevalence across epidemiologic studies (~3.45%), yet comparable to rates reported in acute psychiatric samples (e.g., 9% in a partial hospital sample) (5) and consistent with reports that skin picking may be enriched in psychiatric inpatient settings (11.8% among adolescent inpatients) (5, 6).

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Table 1: Case series summary of skin-picking disorder in adult psychiatric inpatients

No	Age/ Sex	Primary psychiatric diagnosis (admission)	Substance use	History of suicide attempt	Duration of SPD (years)	Prior dermatology visit	Main sites involved
1	43/M	Schizophrenia	No	No	4	No	Arms
2	33/F	Schizophrenia	No	Yes	3	Yes	Face, arms, legs
3	26/M	Schizophrenia	No	Yes	8	No	Arms, nails
4	34/F	Major depressive disorder	No	Yes	<1	Yes	Face
5	27/M	Substance use disorder	Yes (synthetic cannabinoid)	No	6	No	Nails, trunk
6	34/M	Alcohol use disorder	No	Yes	5	Yes	Scalp, arms
7	45/M	Bipolar disorder	No	Yes	5	No	Arms, legs
8	27/F	Bipolar disorder	No	Yes	<1	No	Face, scalp
9	51/M	Schizoaffective disorder	No	Yes	3	No	Trunk, legs
10	41/M	Substance use disorder	Yes (methamphetamine)	No	1.5	No	Arms, legs, trunk
11	41/F	Bipolar disorder	No	Yes	6	No	Face, arms, trunk
12	34/M	Substance use disorder	Yes (multiple)	No	2	Yes	Arms, nails
13	43/M	Schizophrenia	Yes (cannabinoid)	No	4	No	Arms, trunk

M: Male; F: Female; SPD: Skin-picking disorder; Substance use: Active psychoactive substance use during the index admission.

Anatomical involvement in our cases predominantly affected the extremities and trunk, with less frequent head (face/scalp) involvement. This pattern is broadly consistent with clinical cohorts in which the upper limbs are the most common sites, followed by the trunk and lower limbs, with head involvement reported less frequently (7).

Active psychoactive substance use was present in 4 of 13 SPD cases. Although prior epidemiologic research has reported associations between SPD and substance-related conditions, we did not observe a significant difference in active substance use between inpatients with and without SPD in our sample (30.8% vs. 29.6%, p=0.922). This null finding may partly reflect our diagnostic approach: skin picking judged to occur primarily in the context of acute substance effects or withdrawal was not classified as SPD according to DSM-5-TR criteria. The relatively high rate of active substance use among SPD cases in our series likely reflects the characteristics of an inpatient psychiatric population rather than a specific association within our cohort (8).

In our sample, a history of suicide attempt was identified in 8 of 13 patients with SPD (61.5%) and was significantly more frequent than in patients without SPD (32.2%, p=0.031). While the overall rate of suicide attempts in our cohort likely reflects the severity and complexity of psychiatric morbidity in an inpatient setting, the significantly higher proportion among SPD cases underscores the importance of systematically assessing suicidality in SPD. The literature on the association between SPD and suicidal behavior remains mixed: one acute psychiatric sample study found no significant association after controlling for age and sex (5), whereas a study from Turkiye reported a higher rate of suicide attempts in individuals with SPD compared with healthy controls (15.0% vs. 1.9%) (9). Taken together, our findings highlight the need for further research to clarify whether the observed association reflects shared vulnerability factors (e.g., elevated impulsivity) or serves as a marker of greater severity of the primary psychiatric disorder.

The fact that only two of the thirteen SPD cases had been previously diagnosed suggests potential underrecognition of SPD in inpatient settings, as symptoms may be overlooked unless specifically assessed and patients may not spontaneously report them. This underscores the need to improve clinician awareness and to incorporate brief, structured screening questions into routine assessments. Only 4 of 13 patients reported a prior self-referred dermatology visit, which may reflect limited help-seeking, barriers to accessing dermatologic care, or low awareness that the condition is treatable. Limitations include the single-center design, the modest number of cases, and the lack of longitudinal follow-up, which may limit generalizability.

These findings highlight that SPD may be missed in psychiatric inpatient settings unless systematically assessed. Brief, structured inquiry about repetitive picking behaviors during admission, coupled with basic dermatologic examination, may facilitate earlier recognition and timely intervention, consistent with the broader psychodermatology framework that underscores the close skin–brain relationship, including their shared embryologic origin from the ectoderm. Increasing psychiatrists' awareness of dermatologic conditions such as SPD may improve detection and enable appropriate, timely management, and specialized collaborative models (e.g., psychodermatology clinics) may be particularly valuable for the integrated care of these patients.

Ethical Approval: The study was approved by Bakırköy Dr.Sadi Konuk Training and Research Hospital Clinical Research Ethics Committee (decision number: 2024-08-04; date: 19.08.2024).

Informed Consent: Written informed consent was obtained from all the patients.

Conflict of Interest: The authors declare that there is no conflict of interest.

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Manuscripts should be prepared in accordance with the ICMJE Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals. Authors are also expected to follow the appropriate international reporting guidelines, including CONSORT for randomized controlled trials, STROBE for observational studies, STARD for diagnostic accuracy studies, PRISMA for systematic reviews and meta-analyses, ARRIVE for animal experiments, and CARE for clinical case presentations submitted as letters to the editor. Authors are also encouraged to consult the EQUATOR Network for comprehensive guidance on reporting standards.

Manuscripts should be written in clear, concise, and grammatically correct English. Authors whose first language is not English are strongly encouraged to seek professional editing services.

All measurements must be presented using the International System of Units (SI) to ensure consistency and comparability across studies. Authors should use metric units throughout the text, tables, and figures, and adhere to standard scientific conventions for symbols and abbreviations. The spelled-out term should be followed by the abbreviation in parentheses upon first mention, unless the abbreviation represents a standard unit of measurement.

The use of brand names or commercial product names for drugs, devices, or materials is not permitted; only generic names should be used.

4.2. Manuscript Organization and Format

Manuscripts should be prepared as a single Microsoft Word document. The anonymized main document must be arranged in the following order, with each section starting on a new page:

(i) Title, abstract, and keywords,
(ii) Body text,
(iii) References, and
(iv) Tables, graphics, and/or figures.

All manuscript types except Letters to the Editor and Guest Editorials must include an abstract and keywords. Research Articles and Brief Reports should be structured under the following main headings: Introduction, Methods, Results, Discussion, and Conclusion. Systematic Reviews and Meta-Analyses should include the headings Introduction, Methods, Discussion, and Conclusion, with additional subheadings adapted to the content as appropriate.

Manuscripts must be prepared in 12-point Times New Roman, double-spaced, and left-justified throughout the entire text, including references, tables, and figure captions. All pages must be numbered consecutively in the lower right corner.

4.3. Manuscript Submission

Manuscripts must be submitted through the online submission and evaluation system available at eJManager. Submissions made via other means will not be considered for evaluation. Pre-submission inquiries are generally not required but may be accepted in specific cases at the discretion of the Editorial Office.

All submissions are initially checked by the Editorial Office for compliance with journal formatting and ethical standards. Manuscripts not meeting these requirements may be returned to the authors for technical revision before peer review, which may result in delays in the evaluation process.

During submission, authors must complete all mandatory fields in the eJManager system. Incomplete submissions will not proceed to the peer review process. The required information includes article type, full title, abstract, keywords, information for all authors (including ORCID ID and affiliation), patient consent and ethics committee approval details (if applicable), conflict of interest statement, funding information, and corresponding author details. The corresponding author is responsible for ensuring that all required information is entered accurately in the online submission system and that all necessary forms are completed and uploaded on behalf of all contributors.

Any supporting data or other required files, such as reporting checklists or additional tables and figures exceeding the stated limits, may be submitted as supplementary files.

The authors are required to suggest four potential peer reviewers during submission. The suggested reviewers must not be affiliated with the same institution as any of the authors and must have no conflict of interest.

The following documents must be prepared and uploaded at the time of submission:

- Cover letter
- Title page
- Main document (no author names or affiliations)
- Author Contribution Form
- Copyright Transfer Form
- Declaration of Interest Form

4.3.1. Cover Letter

A cover letter is required for all submissions. It should introduce the manuscript to the editorial team in a concise and professional manner, emphasizing its relevance, originality, and contribution to the journal readership. The letter should briefly explain why the study fits within the journal scope and how it advances knowledge in the field. Authors may also use this opportunity to confirm that the manuscript has not been published or submitted elsewhere and that all authors have approved the submission. The cover letter must be limited to one page and signed by the corresponding author.

4.3.2. Title Page

Essential title page information includes the full title, a short running head (maximum 50 characters), full names of all authors, their affiliations, ORCID identifiers, and complete contact details for the corresponding author (including postal address, phone number, and e-mail). It must also include declarations of interest, funding information, ethical committee approval details (if applicable), and acknowledgments.
Authors must state whether any AI–assisted technologies were used in preparing the manuscript. If applicable, the use of such tools should be described in detail in the Methods section.

The title should be non-declaratory, concise, and informative. Since titles are indexed in information retrieval systems, abbreviations and formulae should be avoided.

Please note that the title page is not shared with reviewers and must therefore be uploaded as a separate file through the online submission system.

4.3.3. Main Document

The main document must not contain any author names, institutional affiliations, or identifying information to maintain the integrity of the double-blind peer review process. It should begin with the first page containing the title, abstract, and keywords.

4.3.3.1. Abstract and Keywords

The abstract must not exceed 250 words and should be structured under the subheadings Objective, Method, Results, and Conclusion (excluding letters to the editor and guest editorials).

- Objective: State the main aim or purpose of the study.
- Method: Describe the study design, data sources, sample or subjects, assessments, and primary measures.
- Results: Summarize the key findings, emphasizing their relevance to clinical or scientific practice.
- Conclusion: Present the main outcomes and implications derived from the study. Three to five keywords should be listed directly below the abstract.

Keywords are recommended to align with the National Library of Medicine's Medical Subject Headings (MeSH) terminology. Since abstracts are indexed and searchable in electronic databases, authors must ensure that their abstract accurately reflects the content and significance of the article.

4.3.3.2. Body Text

The Introduction should briefly outline the study background and rationale, highlight the research question, and clearly state the objectives and hypotheses. It should be focused and purpose-driven rather than a broad literature review. The Method section should detail the study design, data sources, participants or subjects, instruments or scales, assessments, and primary measures. The research process and statistical methods should be described in sufficient detail to allow replication. The Results section should present the findings of the study clearly and objectively. Primary outcomes should be summarized in the text and supported by appropriately designed tables, figures, or graphs where applicable. The Discussion section should interpret and contextualize the findings in relation to previous studies, highlighting both supporting and conflicting evidence. Authors should discuss the implications of the findings, possible explanations for discrepancies, and the strengths and limitations of the study. The Conclusion section should provide a concise summary of the main results, their clinical or scientific relevance, and potential directions for future research. It should clearly state the key takeaway message derived from the study.

4.3.3.3. References

References should be numbered in parentheses and listed in the order in which they appear in the text, under the heading "References" at the end of the manuscript. The reference style must follow the Vancouver format.

There should be no inconsistency between the numbering and the reference order. Authors are solely responsible for ensuring the accuracy and completeness of all references. When there are seven or more authors, list the first six followed by "et al."

Abbreviations of journal names must comply with Medline/PubMed standards. Journals that are not indexed in Medline/PubMed should be written in full. Authors are encouraged to review previously published articles in the journal to ensure proper formatting and consistency when preparing the reference list.

4.3.3.4. Tables, Graphics, and Figures

Tables, graphics, and figures should be numbered consecutively in Arabic numerals (e.g., Table 1, Figure 1) according to the order in which they are cited in the text. Their approximate placement should be clearly indicated within the manuscript.

Tables should present information concisely and effectively, allowing data to be displayed with clarity and precision. Presenting data in tables rather than in the text often reduces the overall manuscript length. Each table must appear on a separate page with a descriptive title. Column or row headings should be short and specific, and any explanatory notes should be placed as footnotes—not within the heading. All nonstandard abbreviations and statistical measures of variation (e.g., standard deviation, standard error) should be defined in footnotes. Line spacing for tables should be double-spaced, and the maximum allowable size is 120 characters in width and 70 lines in length.

When materials such as tables, figures, or images are reproduced from another source, written permission from the copyright holder must be obtained, and the source must be appropriately cited in the text. Legends must be provided for all figures. Figure legends should be concise yet specific and must be listed together on a separate page at the end of the main manuscript text.

All figures should be submitted as separate high-quality digital files in JPEG format through the online submission system, in addition to being included at the end of the main document with their corresponding legends. Electronic images (e.g., photographs, radiographs, CT scans) must have a minimum resolution of 300 dpi to ensure print quality.

4.3.4. Author Contribution Form

This form must clearly specify the individual contributions of each author according to the ICMJE criteria. Each author should have participated in the conception, design, data acquisition, analysis, and/or interpretation, as well as in drafting or revising the manuscript and approving its final version. Authors who do not meet all authorship criteria should be listed in the acknowledgments section.

4.3.5. Copyright Transfer Form

This form confirms that the submitted manuscript is original, unpublished, and not under consideration elsewhere. It also verifies that all authors approve the submission and agree to transfer the copyright to Dusunen Adam Journal of Psychiatry and Neurological Sciences under the CC BY-NC 4.0 license. The form must be signed by all authors before publication.

4.3.6. Declaration of Interest Form

All authors must disclose any financial, institutional, or personal relationships that could be perceived as influencing the research. If no conflicts exist, this must be explicitly stated. The form also includes a section for declaring financial support or grants related to the study.

4.4. Manuscript Types

Dusunen Adam Journal of Psychiatry and Neurological Sciences accepts various types of submissions, including research articles, brief reports, systematic reviews and meta-analyses, and letters to the editor. Guest editorials are accepted by invitation only. Authors are encouraged to select the manuscript type that best represents the scope, design, and contribution of their study. The specific structure, length, and formatting requirements for each manuscript type are detailed below.

4.4.1. Research Articles

Research articles present substantial and original scientific findings within the scope of the journal. Each research article should contain an abstract, keywords, introduction, methods, results, discussion, conclusion, references, and tables or figures. The abstract and main text must follow the structured format described above. Ethics committee approval and informed consent information must be obtained and clearly stated in the manuscript.

4.4.2. Brief Reports

Brief reports follow the same general format and guidelines as research articles but focus on small-scale studies or research in early stages of development. They may include preliminary investigations with simple research designs or small sample sizes that provide initial findings and pilot data suggesting the need for further research. Ethics committee approval and informed consent information should also be obtained and clearly stated in the manuscript.

4.4.3. Systematic Reviews and Meta-Analyses

Systematic reviews and meta-analyses should address a clearly defined, relevant, and up-to-date research question within the scope of the journal. Only manuscripts that adhere to recognized methodological standards (such as PRISMA) or registered protocols (e.g., PROSPERO) and demonstrate a systematic approach will be considered for review. Narrative, scoping, or other non-systematic reviews are not accepted. Systematic reviews and meta-analyses should include an abstract, keywords, introduction, methods, discussion, and conclusion, with additional subheadings adapted to the content as appropriate, as well as references and tables or figures.

4.4.4. Letters to the Editor

Letters to the Editor are considered only if they do not exceed 750 words, include no subheadings, and contain a maximum of one table or figure (or up to two figures). All letters must begin with "Dear Editor" and, if commenting on previously published articles, be submitted within one month of publication. Letters may also present small-scale research or concise discussions of timely clinical topics.
Case reports are accepted only in the form of a Letter to the Editor and should present unique, informative, and clinically relevant original cases. They must describe novel clinical approaches or techniques, highlight rare comorbidities or uncommon adverse drug reactions, and provide concise, educational insights of clinical value. Written informed consent from the patient must be obtained and clearly stated in the manuscript.

4.4.5. Guest Editorials

Guest Editorials are invited opinion articles written by experts or researchers who have made significant contributions to a specific field. These articles aim to evaluate and discuss the current state of knowledge, recent developments, and emerging perspectives on topics relevant to clinical practice. Guest Editorials are accepted by invitation only and are not open to regular submission. Manuscripts should include an introduction and a conclusion, along with any additional subheadings considered appropriate by the author. Guest Editorials are not sent for external peer review; they are evaluated by the Editorial Board before publication.

Table: Manuscript types and corresponding word, abstract, reference, and table/figure

Type of manuscript	Word limit	Abstract word limit	Reference limit	Table/ figure limit (total)
Research article	3500	250 (*structured*)	50	6
Systematic reviews and meta-analyses	4000	250	No limit	10
Brief report	1500	250 (*structured*)	15	2
Letter to the editor	750	No abstract	10	1
Guest editorial	1200	No abstract	20	2

Information For Reviewers

1. GENERAL INFORMATION

Dusunen Adam Journal of Psychiatry and Neurological Sciences publishes high-quality research and scholarly work in psychiatry, neurology, clinical psychology, and neuroscience. The journal promotes interdisciplinary perspectives on mental health and brain sciences and prioritizes studies offering novel insights with clear relevance to clinical practice.

The journal accepts submissions in the following categories:

- Research articles
- Brief reports
- Systematic reviews and meta-analyses
- Letters to the editor
- Guest editorials (invited, not peer-reviewed)

The journal employs a double-blind peer review process in accordance with the Committee on Publication Ethics (COPE) and the European Association of Science Editors (EASE) guidelines.

All submissions are evaluated for originality, methodological rigor, and ethical standards before being sent for external review. Each submission is assessed according to its type, scope, and adherence to the journal's scientific and ethical principles.

2. PEER REVIEW SYSTEM

The journal follows a double-blind peer review process in which both authors and reviewers remain anonymous. All submissions are initially assessed by the Editor-in-Chief or Deputy Editors for scope, originality, methodological rigor, scientific quality, and ethical compliance before being sent for external review.

Authors must confirm that the manuscript has not been published or submitted elsewhere and that all listed authors have approved the submission. Manuscripts should be submitted exclusively through the journal online submission system (eJManager), while reviewers access assignments via the Reviewer Login section on the journal's website.

Each manuscript is evaluated by at least two independent experts under the supervision of a handling editor. Reviewers provide objective and constructive feedback to support editorial decisions and help authors improve their work. The handling editor reviews the reports and recommends acceptance, revision, or rejection. When revisions are requested, authors receive reviewer and editorial comments with a deadline for resubmission. Revised manuscripts are re-evaluated, and additional review rounds may be conducted if needed. The Editor-in-Chief or Deputy Editors make the final decision—acceptance, rejection, or further revision.

Reviewers are expected to provide detailed, objective, and constructive feedback that assists both the editor in making informed decisions and the authors in improving their work.

Reviewers are also responsible for identifying and reporting any potential research or publication misconduct, including plagiarism, data fabrication, falsification, duplication, or unethical study design. Any conflict of interest must be declared before agreeing to review a manuscript. When reviewers seek input from a trainee or colleague, these contributions must be acknowledged in the confidential comments to the editor.

Confidentiality must be strictly maintained throughout the review process. Reviewers must not upload any part of the manuscript or their review reports to software platforms or AI-assisted technologies where confidentiality cannot be ensured. Permission from the Editorial Office is required before using any AI-based tools for language editing or assistance in preparing review reports.

3. CONDUCTING A REVIEW FOR THE JOURNAL

Reviewers play a critical role in maintaining the scientific quality and integrity of publications. When accepting or performing a review, the following principles should be observed:

- Respond to the review invitation promptly and confirm availability before the deadline.
- Accept the review only if the manuscript is within your area of expertise.
- Disclose any potential conflict of interest (e.g., recent collaboration, institutional affiliation, or personal relationship with the authors).
- Report any ethical concerns such as plagiarism, data manipulation, or unethical research design to the editor.
- Maintain strict confidentiality throughout the review process; the manuscript and related materials must not be shared or discussed with anyone without prior editor approval.
- Provide objective, evidence-based, and constructive feedback, avoiding personal or emotional language.
- Please conduct your reviews in English and present your comments in a clear, structured, and itemized manner.
- Avoid making annotations or comments directly on the manuscript file.
- If you choose to upload an additional document, ensure that it does not contain any reviewer-identifying information.
- Begin your review with a brief summary of the manuscript, showing you understood its aims and contribution.
- Clearly identify major and minor issues, suggesting ways to strengthen the study.
- Conclude with a clear recommendation: accept, revise, or reject.
- When revisions are requested, be specific and transparent in outlining what needs to be improved.
- Use the confidential comments to the editor section for sensitive or ethical concerns that should not be shared with the authors.

4. REVIEWER CHECKLIST

Before submitting your review, ensure that you have considered:

- Conflicts of interest that could affect your objectivity.
- Research or publication misconduct, including plagiarism or data manipulation.
- Relevance and alignment of the manuscript with the journal's scope and standards.
- Scientific structure and clarity: clearly stated problem, methodology, results, and conclusions.
- Originality and novelty of the research question and findings.
- Quality of references: adequacy, accuracy, and use of primary sources.
- Language and readability: clarity, coherence, and appropriate terminology.
- Figures and tables: accuracy, sufficiency, and consistency with the text.
- Contribution and impact: importance and potential influence on the field.
- Timeliness and completeness: ensure your review is submitted within the requested deadline.

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Journal of Psychiatry and Neurological Sciences

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DUSUNEN ADAM

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GUEST EDITORIAL

RESEARCH ARTICLES

LETTERS TO THE EDITORS