ARAŞTIRMA MAKALESİ / *RESEARCH ARTICLE*

Emotional Burdens and Cognitive Decline: the Role of Anxiety in Mild Cognitive Impairment

Duygusal ve Bilişsel Gerileme Hafif Bilişsel Bozuklukta Kaygının Rolü

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ABSTRACT

Aim: *This study investigates the complex interactions between mild cognitive impairment (MCI), depression, and anxiety, focusing on how these factors affect cognitive function and progression risks. The goal is to inform early diagnostic strategies and targeted therapeutic interventions in individuals with MCI*

Matherial and Methods: *This prospective study included 45 patients diagnosed with MCI (mean age: 66.1±7.7 years; 23 males [51%], 22 females [49%]) at a neurology outpatient clinic. Sociodemographic data, including education level and medical history, were collected. Cognitive and psychiatric assessments were conducted using the Montreal Cognitive Assessment (MoCA), Standardized Mini-Mental State Examination (SMMT), Hamilton Depression Rating Scale (HDRS), and Hamilton Anxiety Scale (HAS). Stratification was done according to anxiety severity, and comparisons were made across these groups on the cognitive performances.*

Results: *Anxiety levels were significantly higher in females than males (p=0.001). While global MoCA and SMMT scores did not differ significantly by gender, males showed significantly better performance in verbal fluency (p=0.025) and a trend in abstract thinking (p=0.057). A significant decline in MoCA total scores was observed with increasing anxiety severity (p=0.024), with verbal fluency (p=0.011), abstract thinking (p=0.005), and attention (p=0.050) notably affected in the severe anxiety group.*

Conclusions: *This study highlights anxiety as a key modifiable risk factor for cognitive impairment in MCI, with domain-specific deficits in executive function. Unlike depression, anxiety showed a stronger correlation with cognitive decline. These findings suggest that early identification and targeted treatment of anxiety in MCI could help delay progression to dementia and improve clinical outcomes.*

Key words: *mild cognitive impairment; anxiety; depression; Montreal cognitive assessment; cognitive decline*

ÖZET

Amaç: *Bu çalışma, hafif bilişsel bozukluğu (HBB) olan bireylerde depresyon ve anksiyetenin bilişsel işlevler ile hastalığın ilerleme riski üzerindeki etkilerini incelemeyi amaçlamaktadır. Bu etkileşimleri anlamak, HBB'li bireylerde erken tanı stratejilerinin ve hedefe yönelik tedavi müdahalelerinin geliştirilmesini sağlayabilir. Hafif Bilişsel Bozukluk (HBB), normal yaşlanma ile demans arasında kilit bir köprü görevi görür ve çoğunlukla depresyon ile anksiyete gibi nöropsikiyatrik semptomlarla kendini gösterir. Bu semptomlar bilişsel gerilemeyi şiddetlendirebilir ve altta yatan nörodejeneratif sürecin en erken göstergeleri olabilir. Bu çalışma, HBB ile depresyon ve anksiyete arasındaki karmaşık ilişkileri araştırmayı, özellikle bu faktörlerin bilişsel sonuçlar ve hastalığın ilerleyişi üzerindeki ortak etkisine odaklanmayı amaçlamaktadır. Elde edilecek bulgular, HBB'li bireylere yönelik tarama yaklaşımlarının ve müdahale stratejilerinin iyileştirilmesine katkıda bulunacaktır.*

Yöntemler: *Hafif Bilişsel Bozukluk tanılı 45 hastadan oluşan (ortalama yaş: 66,1 yıl; %51 erkek) prospektif bir kohorta, şu test protokolleri uygulanmıştır: Montreal Bilişsel Değerlendirme (MoCA), Standartlaştırılmış Mini Mental Durum Testi (SMMT), Hamilton Depresyon Derecelendirme Ölçeği (HDRS) ve Hamilton Anksiyete Ölçeği (HAS). Hastalar anksiyete şiddetine göre sınıflandırılmış ve bu grupların bilişsel performansları karşılaştırılmıştır.*

Bulgular: *Montreal bilişsel değerlendirme ve SMMT puanlarında cinsiyetler arasında anlamlı bir farklılık görülmezken, sözel akıcılık ve soyut düşünme testlerinde erkekler kadınlardan daha yüksek puan almıştır. Anksiyete düzeyleri kadınlarda anlamlı derecede daha yüksek bulundu (p=0,001). Montreal bilişsel değerlendirme skorlarına göre, artan anksiyete şiddetiyle birlikte bilişsel işlevlerde belirgin bir düşüş gözlenmiştir.*

Sonuç: *Anksiyete ve depresyon, HBB hastalarında bilişsel işlevleri belirgin ölçüde etkilemekte ve MoCA alt testlerinde anlamlı etkilere yol açmaktadır. Bu bulgular, bilişsel gerilemeyi azaltmak ve yaşam kalitesini iyileştirmek için psikiyatrik komorbiditeleri ele alan erken tanı ve hedefe yönelik müdahalelerin önemini vurgulamaktadır.*

Anahtar kelimeler: *hafif bilişsel bozukluk; anksiyete; depresyon; Montreal bilişsel değerlendirmesi; bilişsel işlevler*

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Introduction

Mild cognitive impairment (MCI) is the transitional stage between normal cognitive aging and dementia, in which cognitive decline is more pronounced, yet not to a degree that markedly interferes with daily functioning[1,2]. There is growing recognition of the syndrome of MCI as being heterogeneous, including such subtypes as amnestic and non-amnestic forms, with different implications for progression to dementia[3]. The prevalence of MCI is increasing worldwide, underlining its public health importance and the urgent need for targeted interventions. Also MCI was common in older Turkish population especially in those with advanced age and low educational level[4].

Among the many neuropsychiatric symptoms associated with MCI, depression and anxiety are the most prevalent and debilitating conditions. The estimated incidence of depression is 16.9% to 55%, depending on the study design, while anxiety has variously been reported in 9.9% to 52%[5,6]. This not only exacerbates impairments in cognition and daily functioning but also apparently promotes the progression from MCI to dementia[7]. For instance, major depression has been linked with higher amyloid burden and hippocampal atrophy, hallmark pathologies of AD, whereas anxiety might interact with executive dysfunctions to further undermine cognitive resilience[8].

The bidirectional relationships between MCI, depression, and anxiety point to complex underlying mechanisms of neurodegeneration, vascular health, and stress-related pathways. White matter hyperintensities are often found accompanying late-life depression, thereby showing a vascular component in both cognitive and mood disorders[9]. Additionally, these neuropsychiatric conditions could be representing early manifestations of neurodegenerative processes rather than comorbid states per se, and therefore complicate the diagnosis and treatment process[10].

The interplay between MCI, depression, and anxiety is particularly important to understand for the purpose of early diagnosis and intervention, since these disorders together affect disease trajectory and quality of life[11]. The present study investigates cognitive correlates, and progression risks associated with depression and anxiety in MCI to add value to a nuanced understanding of these interactions and to inform evidence-based approaches to care.

Material and Methods

This prospective study included 45 patients (23 male [51%], and 22 female [49%] participants, with a mean age of 66.1±7.7 years [range: 55–86]). diagnosed with MCI in the neurology outpatient clinic between December 2023 and October 2024. The patients were followed up in the Neurology Department of Alanya Training and Research Hospital. Montreal Cognitive Assessment (MoCA) Test, Standardized Mini-Mental State Test (SMMT), Hamilton Depression Rating Scale (HDRS) and Hamilton Anxiety Scale (HAS) were used in this study. Patients who were examined by neurological physicians and diagnosed with MCI were included and also demographical data which contained age and educational status were recorded. A flowchart illustrating the patient selection process –including inclusion and exclusion criteria– is presented in Fig. 1.

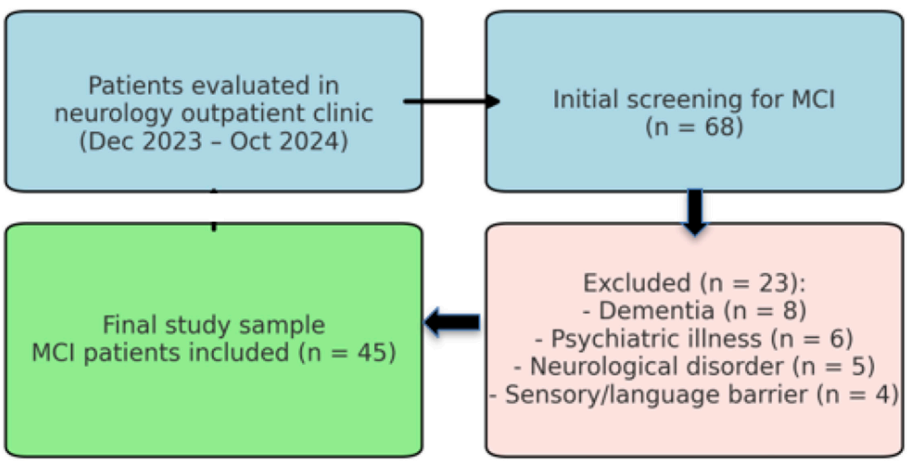

Figure 1. *Patient selection flowchart.*

Neurocognitive and Psychiatric Assessments

All patients were evaluated by trained neurologists and underwent a battery of standardized cognitive and psychiatric tests:

Standardized Mini-Mental State Test (SMMT)

Orientation, attention, memory, motor skills and language use were evaluated with the SMMT, which can be easily applied to evaluate the cognitive functions of the patients. A total of 30 points were scored, and it was concluded that the presence of a suspicious cognitive impairment was suspected in individuals with a score of 25 points and a significant cognitive impairment was suspected in individuals with a score of less than 20 points. Mini-mental status examination can be used in both differential diagnosis and treatment follow-up of various disorders. Its ease of application is another advantage. It has also been standardized in Turkish by the Cerrahpaşa Geriatric Psychiatry team and there is a modification for illiterates recommended by the same team[12]. The SMMT, which has a maximum score of 30, consists of items measuring 6-point memory, 5-point attention, 8-point language and 1-point visual-spatial functions, including 10-point time and space orientation, 3-point recording and 3-point recall. This test was administered separately to trained and untrained subjects.

Montreal Cognitive Assessment (MoCA)

Moca developed for evaluate MCI and cognitive functions. It is a quick and sensitive screening tool designed to detect mild cognitive impairment (MCI) and early dementia. Approximately conduction time is 10 minutes. Moca evaluates a broad range of cognitive domains: Visuospatial/Executive Functions, naming, memory, attention, language, abstraction, orientation. The total score ranges from 0 to 30, with 26 and below indicating anormal cognitive functioning. Its reliability and validity have been established for use by Ozdilek et al.[13].

Hamilton Depression Rating Scale (HDRS)

Hamilton depression rating scale (HDRS) is carried out using a semi-structured interview, usually 20–30 minutes long. The standardized scoring of its system facilitates consistent scoring of symptoms, which makes it an excellent tool for differential diagnosis and treatment monitoring in manypsychiatric disorders. Hamilton depression rating scale has been transcribed to Turkish and reliability and validity of HDRS have been investigated in Turkish groups[14]. The acceptability of the HDRS in psychiatric practice and the ease of administration hold it to be a dependable instrument for evaluation of depressive severity and treatment response. The total score ranges from 0 to 52, with severity levels typically interpreted as follows: 0–7:Normal (no depression), 8–13:Mild depression, 14–18:Moderate depression, 19–22:Severe depression, ≥23:Very severe depression.

Hamilton Anxiety Rating Scale (HAS)

This clinician-administered measure is designed to be applied easily in clinical settings and is especially helpful for tracking treatment course in anxiety disorders. Its structured format guarantees consistent evaluation, but the use of it depends on the interviewer's skill. The scale has been standardized inturkish, validated studies showing the reliability and usefulness of the Turkish-speaking population[15]. It has emerged as a practical measure for both clinic use and research, providing clues about the interaction between psychological manifestations and physical manifestations of anxiety. The HAS is generally administered by a semi-structured interview, which usually takes about 10–20 min. The maximum score of the scale is 56 points, with scores interpreted as follows: Mild anxiety (14–17), moderate anxiety (18–24) and severe anxiety (25 and over).

Ethical Approval

The study was approved by University of Aladdin Keykubat University, Date: 12.09.2023, decision number: 16072023/289. This article was done in accordance with the Declaration of Helsinki with the approval of the ethics committee

Statistical Analysis

The data were analyzed using Jamovi 2.3.28 software. P value <0.05 was considered statistically significant. Differences between parameter means according to gender and diagnosis were analyzed by independent samples t-test. Normality distribution was determined by normality tests. Moreover, the Kruskal-Wallis test was used to compare the continuous variables of more than two independent groups. Pairwise comparison was performed using the Mann-Whitney U test to determine which groups caused the difference between the variables found to be significant in the Kruskal-Wallis test. Power analysis was performed with G power 3.1 software. With a significance criterion of α=0.05 and power=0.798.

Results

A total of 45 participants were included with a mean age of 66.1 years (SD=7.70, range 55–86 years). Distribution of gender was similar as there were 51% males (n=23) and 49% females (n=22). The level of education of the participants, where most were primary school graduates (68%), followed by middle school (12%), high school (7%) and university graduates (13%), as shown in Table 1.

Table 1. *Demographical characteristics of patients*

Age		Percentage (%)
Mean ± SD	66.1±7.70	
Range	55–86 years	
Gender		
Male	23	0.51
Female	22	0.49
Education status		
Reader		
Primary school	31	68
Middle school	5	12
High school	3	7
University	6	13

1. Cognitive Performance by Gender

Cognitive test scores were compared between males and females using the SMMT and MoCA:

- **SMMT:** No significant difference was found between males (27.7±2.31) and females (27.1±2.01), p=0.429.
- **MoCA:** Both groups had identical mean scores (18.1), with males at 18.1±3.15 and females at 18.1±3.71, p=0.962.

Additional MoCA subdomain comparisons by gender are presented in Table 2.

- **Verbal Fluency:** Males scored significantly higher than females (0.652±0.487 vs. 0.318±0.477), p=0.025.
- **Abstract Thinking:** Males also performed better (1.13±0.757 vs. 0.682±0.780), with borderline significance, p=0.057.
- No significant gender differences were found in trail making, visuospatial ability, naming, attention, sentence repetition, memory, or orientation subdomains.

Table 2. *Cognitive parameters according to the gender*

Parameter	Male (mean ± SD)	Female (mean ± SD)	p value
SMMT	27.7±2.31	27.1±2.01	0.429
MoCA	18.1±3.15	18.1±3.71	0.962
Trail making test	0.391±0.499	0.455±0.510	0.676
Visuospatial	2.48±1.41	2.36 ±1.29	0.778
Naming	2.35±0.775	2.18±0.795	0.482
Attention	4.78±1.35	4.95±1.13	0.646
Sentence repetition	0.348±0.647	0.545±0.510	0.263
Verbal fluency	0.652±0.487	0.318±0.477	0.025*
Abstract thinking	1.13±0.757	0.682±0.780	0.057
Memory	0.522±1.24	0.591±1.10	0.844
Orientation	5.52±0.790	5.50 ±0.598	0.918
ANXIETY	9.09±6.69	18.50±8.91	0.001*
DEPRESSION	6.09±7.71	8.32±3.44	0.220

MoCA: Montreal cognitive assessment scale, SMMT: standartized minimental state examition,
* p value < 0.05 is significant.

2. Depression and Anxiety by Gender

- **HDRS Scores:** Mean depression scores were higher in females (8.32±3.44) than males (6.09±7.71), but the difference was not statistically significant (p=0.220).
- **HAS Scores:** Females exhibited significantly higher anxiety levels (18.50±8.91) compared to males (9.09±6.69), p=0.001.

3. Group Comparison Based on Anxiety Severity

Participants were categorized into four groups based on HAS scores: No anxiety (n=16), Mild anxiety (n=13), Moderate anxiety (n=7), Severe anxiety (n=9). Key findings across these groups are detailed in Table 3:

- **Age:** Significant differences were observed, with the highest mean age in the no-anxiety group (68.6±8.41 years) and lowest in the moderate group (63±3.87 years), p <0.001.
- **Gender:** No significant difference in distribution among anxiety groups, p=0.475.
- **SMMT:** No statistically significant differences among the four anxiety groups, p=0.259.
- **MoCA:** A significant decrease in MoCA scores was found in the severe anxiety group (15.2±3.03) compared to others, p=0.024.
- **HDRS:** Depression severity also increased with anxiety severity. Moderate (12±9.88) and severe (11.6±3.24) anxiety groups had the highest HDRS scores, p <0.001.

Table 3. *Demographic and cognitive characteristics of participants by anxiety groups*

	No (n=16)	Mild (n=13)	Moderate (n=7)	Severe (n=9)	Total (n=45)	P value
Age (mean ± SD)	68.6±8.41	66.2±9.54	63±3.87	64.2±4.63	66.1±7.70	<0.001*
	(65.5)	(65)	(62)	(64)	(64)	
SMMT (mean ± SD)	27.3±2.54	28±1.73	28.1±1.35	26.2±2.22	27.4±2.16	0.259**
(median)	(28)	(28)	(28)	(26)	(28)	
MoCA (mean ± SD)	19.1±3.58	18.2±2.80	19.3±2.75	15.2±3.03	18.1±3.39	0.024**
(median)	(20)	(20)	(20)	(14)	(19)	
Hdt (mean ± SD)	3.13±2.25	6.54±4.68	12±9.88	11.6±3.24	7.18±6.05	<0.001**
(median)	(3)	(5)	(10)	(11)	(6)	

* Wilcoxon test, ** Kruskal-Wallis, MoCA: Montreal cognitive assessment scale, SMMT: standartized minimental state examition, Hdt: Hamilton depression test, p value < 0.05 is significant.

Table 4. *Comparison of MoCA scores and cognitive subdomains across anxiety levels*

	No (n=16)	Mild (n=13)	Moderate (n=7)	Severe (n=9)	Total (n=45)	P value
MoCA (mean ± SD)	19.1±3.58	18.2±2.80	19.3±2.75	15.2±3.03	18.1±3.39	0.024*
(median)	(20)	(20)	(20)	(14)	(9)	
Trail making test (mean ± SD)	0.500±0.516	0.462±0.59	0.429±0.535	0.222±0.441	0.422±0.499	0.591
(median)	(0.500)	(0)	(0)	(0)	(0)	
Visuospatial (mean ± SD)	2.88±1.50	2.38±1.26	2.43±1.27	1.67±1.00	2.42±1.34	0.110
(median)	(3.50)	(2)	(3)	(2)	(3)	
Naming (mean ± SD)	2.50±0.516	2.15±0.801	2.71±0.488	1.67±1.00	2.27±0.78	0.053
(median)	(2.50)	(2)	(3)	(2)	(2)	
Attention (mean ± SD)	4.88±1.50	5.23±0.832	5.29±1.11	4.00±1.00	4.87±1.24	0.050
(median)	(5)	(5)	(6)	(4)	(5)	
Sentence repetition (mean ± SD)	0.50±0.632	0.308±0.40	0.714±0.756	0.333±0.500	0.444±0.586	0.556
(median)	(0)	(0)	(1)	(0)	(0)	
Verbal fluency (mean ± SD)	0.688±0.479	0.538±0.59	0.571±0.535	0±0	0.489±0.506	0.011*
(median)	(1)	(1)	(1)	(0)	(0)	
Abstract thinking (mean ± SD)	1.19±0.75	1.23±0.599	0.571±0.787	0.222±0.667	0.911±0.793	0.005*
(median)	(1)	(1)	(0)	(0)	(1)	
Memory (mean ± SD)	0.875±1.45	0.538±1.33	0.429±0.535	0.111±0.333	0.556±1.16	0.353
(median)	(0)	(0)	(0)	(0)	(0)	
Orientation (mean ± SD)	5.75±0.447	5.38±0.870	5.29±0.756	5.44±0.726	5.51±0.695	0.386
(median)	(6)	(6)	(5)	(6)	(6)	

MoCA: Montreal Cognitive Assessment Scale, * p value < 0.05 is significant.

4. MoCA Subdomain Performance Across Anxiety Groups

As presented in Table 4, MoCA subdomains showed significant variation by anxiety severity:

- **Verbal Fluency:** Performance was significantly lower in the severe anxiety group (0±0) compared to all other groups, p=0.011.
- **Abstract Thinking:** Severe anxiety group performed worse (0.222±0.667) than no and mild anxiety groups, p=0.005.
- **Attention:** Lower scores were found in the severe group (4.00±1.00), with marginal significance, p=0.050.
- **Other Domains (Visuospatial, Naming, Sentence Repetition, Memory, Orientation):** No statistically significant differences were observed across anxiety levels.

Discussion

This study has highlighted the complex inter-relationships between MCI, depression, and anxiety and their interactional effects on cognitive functions. Our findings are in agreement with previous studies that anxiety and depression significantly affect cognitive performance[8].

Cognitive Impairment and Utility of MoCA

The MoCA scores were significantly lower among subjects with severe anxiety and depression, an indication that psychiatric conditions aggravated cognitive decline. This is supported by various reports on the acceleration of cognitive decline and reduction in resilience due to emotional distress. MoCA therefore provides a

better neuropsychological tool because it assesses other domains that include verbal fluency and abstraction compared to the MMT. For example, verbal fluency and abstract thinking were most significantly affected in those subjects who showed severe psychiatric symptoms. This is in line with earlier reports of anxiety and executive dysfunction sharing a common neural basis involving frontal and temporal regions[16,17].

Anxiety and Cognitive Function

Anxiety likely influences cognitive functioning via more than one pathway. Neurobiological mechanisms that have been implicated in anxiety-related deficits in cognition include the hyperactivation of the hypothalamic-pituitary-adrenal axis and disturbances in fronto-limbic connectivity[18]. Chronic anxiety also has been associated with heightened amygdala activity and decreased prefrontal cortex regulation, which may exacerbate deficits in cognition[19,20]. The strong relationship of anxiety severity with cognitive impairment in the present study was further supported by previous reports that anxiety may be not only a causal factor but also an early indicator of neurodegenerative processes[21]. Besides, the participants with severe anxiety had substantial deficits in MoCA scores, mainly in the subdomains of verbal fluency, abstraction, and attention. These findings indicate that increased anxiety has a negative effect on executive functions and general cognitive ability.

Depression and Cognitive Outcomes

In addition, there was a significant difference in gender, where females had a significantly higher anxiety level than males. This concurs with previous literature depicting higher prevalence and severity of anxiety disorders in females, perhaps due to hormonal factors, life stress, or different coping strategies[22,23]. Curiously, though females manifested higher anxiety, males outperformed their female counterparts in cognitive functions like verbal fluency and abstract attitude[24]. These differences must be further elucidated for their underlying mechanisms.

Clinical and Research Implications

These findings underpin the value of MoCA in capturing a broad cognitive consequence of psychiatric disorders and, hence, their suitability as supporting diagnostic tools in identifying MCI. The significant variations found in several subdomains of MoCA, such as verbal fluency and abstract thinking, are an accent on the use of comprehensive neuropsychological diagnostics which capture detailed effects of anxiety. Addressing anxiety early may improve not only cognitive performance but also the quality of life. Pharmacological interventions such as selective serotonin reuptake inhibitors (SSRIs), in combination with the cognitive-behavioral therapy (CBT) have shown some promise in decreasing anxiety symptoms and enhancing cognitive outcomes in older adults with cognitive impairment[25,26]. Personalized care plans that consider the subject's unique interaction between anxiety and cognitive function will optimize the therapeutic outcomes.

The bidirectional relationship between anxiety and cognitive impairment poses a special challenge in managing MCI. Anxiety may act additively to cognitive deterioration by impairing executive functioning, attention, and memory consolidation. On the other hand, cognitive impairment can increase anxiety because the patient has a better awareness of cognitive deficits. This negative cycle may accelerate the transition from MCI to dementia. This reaffirms the need for early intervention.

Limitations and Future Directions

Because this study has a cross-sectional design, it is limited in that no causal inferences can be made, and by a relatively small sample size. These findings have to be extended by future longitudinal studies that explain exactly how anxiety influences the course of MCI and its conversion to dementia. In addition, advanced structural and functional neuroimaging-including functional MRI-could provide further insight into neurobiological pathways underlying this association. Furthermore, the identification of treatments aimed at selective cognitive domains impaired due to psychiatric symptoms may yield specific therapeutic approaches.

Conclusion

This research addresses a significant gap in the existing literature by demonstrating that anxiety, but not depression, is independently linked to certain cognitive deficits in individuals who experience MCI, specifically in executive functions including verbal fluency, abstract reasoning, and attentional skills. Although earlier research has demonstrated extensive correlations between neuropsychiatric symptoms and cognitive deterioration, our results take the field further by specifying certain impairments within domains and enhancing the diagnostic utility of MoCA subcomponents in early executive dysfunction detection.

Importantly, the findings characterize anxiety not merely as a comorbid symptom but also as a possible early clinical indicator and a modifiable risk factor for cognitive impairment. These findings are particularly applicable to neurologists, geriatricians, and mental health practitioners engaged in the management of elderly individuals. Given the prospect of early diagnosis and intervention, clinicians can look forward to an even better outcome for MCI patients against possibly developing dementia.

In summary, this study adds fresh evidence to the growing body of literature in favor of including psychiatric evaluation in MCI management and underscores the need for personalized interventions toward cognitive and emotional health.

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