

## Comparison of Cognitive Reserve, Depression and Anxiety in Diabetes Mellitus Patients

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### ABSTRACT

**Aim:** Few studies have comprehensively examined the cognitive reserve in patients with Diabetes Mellitus (DM). The purpose of this study was to compare cognitive reserve, depression, and anxiety in patients with DM.

**Material and Methods:** A prospective cross-sectional study was conducted with a total of 80 participants (40 with DM and 40 with healthy controls). Patients with DM diagnosed at a hospital's internal medicine outpatient clinic were included. Patients' cognitive reserve was evaluated with Cognitive Reserve Index Questionnaire (CRI). Depression and anxiety of the individuals were assessed with Beck Depression Inventory (BDI) and Beck Anxiety Inventory (BAI), respectively. The difference between the groups was analyzed by independent sample t-test. In addition, Pearson's correlation coefficient was used to assess the relationship between the parameters.

**Results:** Individuals with DM had significantly lower CRI-total ( $p=0.009$ ) and CRI-education ( $p=0.011$ ) scores. In addition, BDI ( $p=0.001$ ) and BAI ( $p=0.019$ ) scores were higher in individuals with DM. Correlational analyses showed a statistically significant weak negative correlation between BDI and CRI-total ( $r=-0.373$ ,  $p=0.001$ ), CRI-education ( $r=-0.294$ ,  $p=0.008$ ) and CRI-work ( $r=-0.386$ ,  $p=0.001$ ) scores in individuals with DM.

**Conclusion:** The results of the present study revealed a lower cognitive reserve (particularly education-related component) in patients with DM. Besides, depression and anxiety were higher in individuals with DM than in healthy controls. In participants with DM, depression was associated with cognitive reserve (except leisure time).

**Keywords:** Anxiety and depression, Cognition, Psychological status, Type 2 diabetes

## Diabetes Mellitus Hastalarında Bilişsel Rezerv, Depresyon ve Anksiyetenin Karşılaştırılması

### ÖZ

**Amaç:** Diabetes Mellitus (DM) hastalarında bilişsel rezervi kapsamlı bir şekilde araştıran bir çalışma bulunmamaktadır. Bu çalışmanın amacı DM'li hastalarda bilişsel rezerv, depresyon ve anksiyetenin karşılaştırılmasıdır.

**Gereç ve Yöntemler:** Toplam 80 katılımcı (40 DM'li ve 40 sağlıklı kontrol) ile prospektif kesitsel bir çalışma yürütülmüştür. Çalışmaya bir eğitim ve araştırma hastanesinin dahiliye polikliniğine DM tanısıyla başvuran hastalar dahil edilmiştir. Hastaların bilişsel rezervi Bilişsel Rezerv İndeksi Anketi (KRİ) ile değerlendirilmiştir. Bireylerin depresyon ve anksiyeteleri sırasıyla Beck Depresyon Envanteri (BDE) ve Beck Anksiyete Envanteri (BAE) ile değerlendirilmiştir. Gruplar arasındaki fark bağımsız örneklem t-testi ile analiz edilmiştir. Ayrıca, parametreler arasındaki ilişki için Pearson korelasyon katsayısı kullanılmıştır.

**Bulgular:** DM'li bireylerin KRİ-toplam ( $p=0,009$ ) ve KRİ-eğitim ( $p=0,011$ ) skorları anlamlı derecede düşüktü. Ayrıca, BDE ( $p=0,001$ ) ve BAE ( $p=0,019$ ) puanları DM'li bireylerde daha yüksekti. Korelasyon analizleri DM'li bireylerde BDI ile KRİ-toplam ( $r=-0,373$ ,  $p=0,001$ ),

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KRİ-eğitim ( $r=-0,294$ ,  $p=0,008$ ) ve KRİ-iş ( $r=-0,386$ ,  $p=0,001$ ) puanları arasında istatistiksel olarak anlamlı negatif düşük düzeyli korelasyon olduğunu göstermiştir.

**Sonuç:** Bu çalışmanın sonuçları, DM'li hastalarda bilişsel rezervin (özellikle eğitimle ilgili bileşen) daha düşük olduğunu ortaya koymuştur. Ayrıca, DM'li bireylerde depresyon ve anksiyete sağlıklı kontrollere göre daha yüksekti. Depresyon, DM'li katılımcılarda bilişsel rezerv (boş zaman hariç) ile ilişkiliydi.

**Anahtar Sözcükler:** Anksiyete ve depresyon, Biliş, Psikolojik durum, Tip 2 diyabet

## INTRODUCTION

Diabetes mellitus (DM) is a common metabolic disease (1,2). In developed and developing societies, there is an increase in the prevalence of type 2 DM, mainly due to lifestyle changes (3). According to the results of the 7<sup>th</sup> Diabetes Atlas of the "International Diabetes Federation (IDF)", there were 412 million patients with DM in 2015 (4).

Cognitive impairment in individuals with DM may affect the management of the disease and lead to complications (5). People with both type 1 and type 2 DM have been shown to have a mild to moderate decrease in cognitive function compared to non-diabetic controls (6). Research suggests a link between DM and lower cognitive function, but the specific cognitive domains affected can vary. One study comparing elderly individuals with and without DM found that those with diabetes were more impaired in executive function (5). Another study showed that individuals with Type 2 DM were more affected in cognitive areas such as information processing speed, memory, attention and executive function than control groups (6). A lack of studies investigated cognitive function in DM (7).

In addition to being a metabolic disease, In addition to being a metabolic disease, diabetes can impact psychosocial and psychological well-being. The most common psychiatric conditions in diabetes are anxiety and depression (8). Studies have shown that factors such as gender, age, education, occupation, and longer duration of diabetes can increase the risk of anxiety and depression (9). No other studies have comprehensively investigated the cognitive reserve in patients with Diabetes Mellitus (DM). The purpose of the study was to demonstrate the comparison of cognitive reserve, depression and anxiety in patients with diabetes mellitus.

## MATERIALS and METHODS

### Study Design

A prospective cross-sectional study was conducted with 80 individuals (40 with DM and 40 with healthy controls) between December 2022 and May 2023. The study included patients admitted to the internal medicine outpatient clinic of Muğla Sıtkı Koçman Research and Training Hospital with

a diagnosis of type 2 DM.. Individuals were informed about the purpose of this study, and their consent was obtained. Participants were included if they met the following criteria: (1) a diagnosis of type 2 DM for at least six months, and (2) age between 18 and 65 years. Participants were excluded if they had any of the following: (1) hearing or speech problems, or (2) psychiatric problems that would prevent communication. The sample size was calculated using G\*Power software (10, 11) considering the effect size (Cohen's  $d = 0.80$ ) by Cohen's  $d$ -based classification (12). A total of 70 participants were calculated to be adequate with 95% power and 95% confidence level. It was determined that at least 35 cases were sufficient for both groups.

### Ethical Consideration

The study was conducted following the Declaration of Helsinki. Informed consent from the patients was obtained. The study was approved by the local ethics committee of Muğla Sıtkı Koçman University (No: 210022/13, Date: 03.12.2021).

### Data Collection

The Cognitive Reserve Index Questionnaire (CRI) was used to assess participants' cognitive reserve, while the Beck Depression Inventory (BDI) and Beck Anxiety Inventory (BAI) evaluated depression and anxiety, respectively. Permission to use the Turkish versions of the BDI and BAI was obtained from the researchers who established their reliability and validity.

**Cognitive Reserve Index Questionnaire:** The CRI assesses an individual's cognitive reserve by collecting information about his/her entire adult life (13,14). The Cronbach's alpha value of CRI was 0.62 in the development study and 0.78 in the Turkish version study (13).

**Beck Depression Inventory (BDI):** BDI is a self-assessment scale developed to determine the risk of depression (15).

**Beck Anxiety Inventory (BAI):** BAI is a self-assessment scale to measure the prevalence of anxiety symptoms (16).

### Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics (Version 25). Descriptive statistics were reported as

mean  $\pm$  standard deviation (SD) for continuous variables and percentages (%) for categorical variables. The significance level was set at  $\alpha = 0.05$ . One sample Kolmogorov-Smirnov test and Histogram were used to show the normality of the variables. Considering the normal distribution, the difference between the groups was analyzed by independent sample t-test. In addition, Pearson's correlation coefficient was used to analyze the relationships between the parameters.

## RESULTS

Demographic characteristics of the participants are presented in Table 1. The mean age of individuals with DM (53.8 $\pm$ 9.2 years) was significantly higher than those without DM (47.5 $\pm$ 13.4 years). Disease duration in the DM group was 7.6 $\pm$ 6.7 years.

Individuals with DM scored significantly lower on the CRI-total ( $p=0.009$ ) and the CRI-education ( $p=0.011$ ). In contrast, they had higher scores on the BDI ( $p=0.001$ ) and BAI ( $p=0.019$ ) compared to the healthy control group. Correlational analyses among participants with DM revealed a statistically significant negative low-level correlation between BDI scores and CRI-total ( $r=-0.373$ ,  $p=0.001$ ), CRI-education ( $r=-0.294$ ,  $p=0.008$ ), and CRI-work ( $r=-0.386$ ,  $p=0.001$ ) scores (Table 2).

The results of the correlational analysis also proved a statistically significant negative low-level correlation between BDI and CRI-total, CRI-education and CRI-work scores in individuals with DM. However, no significant correlation was found between BDI scores and the CRI-leisure subscale ( $p>0.005$ ). On the other hand, no significant correlation was observed between BDI and any score of CRI in individuals with DM ( $p>0.005$ ) (Table 3).

## DISCUSSION

The results of the present study revealed a lower cognitive reserve (particularly education-related component) in patients with DM. Besides, depression and anxiety were higher in individuals with DM than in healthy controls. Depression was associated with cognitive reserve (except leisure time) in participants with DM. Since the impairment of cognitive functions in individuals with DM is comprehended (5-7), further studies may elaborate on the current results with observational and qualitative research on the low cognitive status in individuals with DM. In addition, clinical studies should explore the potential reasons for the observed association between cognitive reserve and depression in this population.

Evidence demonstrates that cognition is reduced in individuals with diabetes (17). The prevalence of mild cognitive

**Table 1:** The baseline parameters of the groups.

Parameters	Cases with DM (n=40)	Cases without DM (n=40)	P
Age (years $\pm$ SD)	53.8 $\pm$ 9.2	47.5 $\pm$ 13.4	0.046
Gender, n (%)			
Women	22 (55)	23 (57.5)	0.051
Men	18 (45)	17 (42.5)	
Marital status, n (%)			
Married	35 (87.5)	30 (75)	0.152
Single	5 (12.5)	10 (25)	
Duration of DM (years $\pm$ SD)	7.6 $\pm$ 6.7	n/a	n/a
Comorbid disease, n (%)	27 (67.5)	12 (30)	0.001
Smoking, n (%)	11 (27.5)	7 (17.5)	0.156
Alcohol use, n (%)	7 (17.5)	4 (10)	0.550

SD: standard deviation, n: number of patients, DM: Diabetes Mellitus

**Table 2:** Comparison between the groups.

Indices*	Cases with DM (n=40)	Cases without DM (n=40)	P
CRI-total	78.8 $\pm$ 12.2	86.4 $\pm$ 13.2	<b>0.009<sup>a</sup></b>
CRI-education	91.0 $\pm$ 15.4	102.0 $\pm$ 20.1	<b>0.011<sup>a</sup></b>
CRI-work	92.8 $\pm$ 13.4	98.4 $\pm$ 12.6	0.059 <sup>a</sup>
CRI-leisure	67.4 $\pm$ 9.6	68.8 $\pm$ 8.8	0.501 <sup>a</sup>
BDI	17.6 $\pm$ 8.9	8.1 $\pm$ 5.6	<b>0.001<sup>a</sup></b>
BAI	30.9 $\pm$ 8.1	26.7 $\pm$ 7.4	<b>0.019<sup>a</sup></b>

Data were shown as "score $\pm$ standard deviation", **CRI-total:** Cognitive Reserve Index-total score, **CRI-education:** Cognitive Reserve Index-education score, **CRI-work:** Cognitive Reserve Index-work score, **CRI-leisure:** Cognitive Reserve Index-leisure score, **BDI:** Beck Depression Inventory, **BAI:** Beck Depression Inventory.

**Table 3:** The comparison of cognitive reserve with depression and anxiety in patients with DM.

n:40	BDI (r, p)	BAI (r, p)
CRI-total	-0.373 (0.001)	-0.004 (0.975)
CRI-education	-0.294 (0.008)	0.085 (0.452)
CRI-work	-0.386 (0.001)	-0.133 (0.241)
CRI-leisure	-0.073 (0.519)	-0.004 (0.975)

\*r: Pearson correlation coefficient, n: number of patients, **CRI-total:** Cognitive Reserve Index-total score, **CRI-education:** Cognitive Reserve Index-education score, **CRI-work:** Cognitive Reserve Index-work score, **CRI-leisure:** Cognitive Reserve Index-leisure score, **BDI:** Beck Depression Inventory, **BAI:** Beck Depression Inventory<sup>b</sup>

impairment in individuals with type 2 DM is reported to be approximately 45% (18). A recent meta-analysis detailed the association between DM and cognitive impairment and dementia based on the results of 144 prospective studies. It has been established that biochemical indicators and pre-

dictors increase the incidence of cognitive impairment even in the early stages of pathology, including DM and prediabetes (19). Another recent meta-analysis emphasized that depression worsens cognition in individuals with DM and may even lead to the risk of dementia (20). Studies emphasize that depression and, thus, cognitive losses can be prevented by improving glycemic index control with exercise and different biological methods (21).

Cognitive reserve in individuals with DM has not been comprehensively addressed so far. Our study is unique in this regard. So far, many studies have shown the relationship between cognition and cognitive reserve. In older individuals, the relationship between age-related cognitive functions, particularly with the educational component of cognitive reserve, has been demonstrated (22). Although this result was obtained in community-dwelling older individuals, the study of cognitive reserve has evolved more critically due to the proof that cognitive impairment is observed in DM even at younger ages (23).

According to our results, lower cognitive reserve in individuals with DM compared to healthy controls was expected due to cognitive impairments in this case group. Our results confirmed that low cognition in elderly individuals is mainly related to the educational component of the CRI. Educational components such as years of education and vocational courses are lower in individuals with DM and should be investigated in more detail, together with cognitive capacity. Neurophysiological studies can further investigate the causality of academic life history on DM.

It has been observed that depression negatively affects cognition in individuals with DM. Our study determined that cognitive reserve based on work and education was more related to depression than leisure time. The relationship between work, education background, and depression compared to leisure time activities can be elaborated with qualitative research. The higher depression in individuals with low cognitive function may be related to the severity of the pathology of the disease. Consideration of DM tests, glycemic index, and other clinical parameters will increase the significance of the results (24).

Cognitive disorders in individuals with DM may affect their cognitive reserve capacity. Therefore, the follow-up of individuals with DM with cognitive behavioral training programme in clinical practice (25), especially with an educational component, may increase their cognitive capacity and thus improve both their physical and psychosocial conditions. Another hypothesis is that the predisposition of individuals with low cognitive reserves to the development of DM may be associated with unhealthy lifestyle and habits. However, our study cannot provide results that can

underline these hypotheses. Therefore, comprehensive research with causality and qualitative design studies should be provided.

### Limitations

The major limitation of our study is that the cognitive reserves of the participants were analysed without evaluating their cognitive levels. The Mini-Mental Test Examination or more advanced cognitive status assessment tools could have provided a broader spectrum of interpretation of our results (26). Secondly, we did not provide a clinical examination for depression and anxiety. Since patients with DM admitted to the internal medicine outpatient clinic were included in the study, we did not have access to these diagnostic testing facilities.

### Conclusion

The results of the present study revealed that patients with diabetes mellitus (DM) have lower cognitive reserve, particularly in the education domain, and experience higher levels of depression and anxiety compared to healthy controls. Furthermore, depression was associated with all aspects of cognitive reserve (except leisure time) in the diabetic group. Since the impairment of cognitive functions in individuals with DM is comprehended, further studies may elaborate on the current results with observational and qualitative research on the low cognitive status in individuals with DM. In addition, clinical studies on why cognitive reserve may be associated with possible depression may embellish our results.

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### Author Contributions

Conceptualization: **Fatih Özden, Serap Tuna**, Methodology: **Serap Tuna, Fatih Özden**, Formal analysis and investigation: **Serap Tuna, Fatih Özden**, Writing - original draft preparation: **Serap Tuna, Fatih Özden, Cem Şahin, Emine Neşe Yeniçeri**, Writing - review and editing: **Serap Tuna, Fatih Özden, Cem Şahin, Emine Neşe Yeniçeri**.

### Conflict of Interest

The authors report no conflicts of interest and certify that no funding has been received for this study and/or preparation of this manuscript.

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### Ethical Approval

The study was carried out in accordance with the ethical principles and the Helsinki Declaration. The study protocol was approved by the ethics committee of Muğla Sıtkı Koçman University (No: 210022/13, Date: 03.12.2021). Informed consent of the patients was obtained.

### Peer Review Process

Extremely peer-reviewed and accepted.

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