

Use of Clock Drawing Test as a Screening Tool for Cognitive Status Evaluation in Middle-Aged Patients with Depressive Disorder

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ÖZET:

Depresif Bozukluğu olan orta yaşlı hastalarda saat çizme testinin kognitif durumu değerlendirmek için bir tarama testi olarak kullanılması

Amaç: Bu çalışmada, depresif bozukluğu olan orta yaşlı hastalarda saat çizme testi (SÇT) ile bilişsel işlevleri değerlendirmek amaçlanmıştır.

Yöntemler: Bu vaka-kontrol çalışmasına, 96 depresif bozukluk tanısı almış hasta ile 105 sağlıklı birey psikiyatri ve aile hekimliği polikliniklerinden ardışık olarak dahil edildi. Katılımcılara ilk önce sosyodemografik ve medikal özellikleri değerlendiren bir anket formu verildi. Daha sonra Mini Mental Test (MMT) ve Saat Çizme Testi (SÇT) uygulandı. Çizimler Manos, Shulman ve Sunderland skorlama yöntemlerine göre değerlendirildi. Depresyonun şiddeti Montgomery-Åsberg Depresyon Değerlendirme Ölçeği kullanılarak belirlendi.

Bulgular: Katılımcıların ortalama yaşı kontrol ve hasta grubunda sırasıyla; 52.45±5.16 ve 52.13±5.53 yıl olarak bulundu. Her iki grup yaş, cinsiyet, eğitim düzeyi ve komorbid hastalık yükü açısından farklılık göstermiyordu ($p>0.05$). Hastaların ortalama depresif hastalık süresi 63.41±86.42 aydı. Hastaların depresyon şiddet sırasıyla; 16 (%16.7) hastada hafif, 70 (%72.9) hastada orta ve 10 (%10.4) hastada ağır olarak tespit edildi. MMT skorları vaka ve kontrol grubunda sırasıyla 77 (%80.2) ve 101 (%96.2) hastada yüksekti (24-30); sırasıyla 19 (%19.8) ve 4 (%3.8) olguda ise düşüktü (≤ 23) ($p<0.01$). MMT skoru normal olan 101 sağlıklı katılımcının sırasıyla; 29 (%28.7), 28 (%27.7) ve 9 (%8.9)'unda Manos, Shulman ve Sunderland yöntemlerine göre anormal saat çizme skoru saptandı. MMT skoru normal olan 77 hastanın sırasıyla; 49 (%63.6), 28 (%36.3) ve 42 (%54.5)'sinde Manos, Shulman ve Sunderland yöntemlerine göre anormal saat çizme skoru bulundu. MMT skorlarının Manos, Sunderland ve Shulman yöntemlerine göre Pearson korelasyonu sırasıyla $r=0.52$, $r=0.48$ ve $r=0.53$ olarak tesbit edildi ($p<0.001$). Kontrol grubundaki tüm katılımcılar saat-okuma testinde gösterilen zamanı doğru okudular. Hasta grubunda ise, 96 hastadan 92'si gösterilen zamanı doğru olarak okudu. Demografik özellikler, komorbid hastalık yükü ve depresif hastalık süresinin SÇT performansı üzerinde bir etkisi tespit edilmedi.

Sonuç: Bilişsel işlevler, depresif bozukluğu olan orta yaşlı hastalarda SÇT kullanılarak taranabilir. SÇT depresif bozuklukta görülebilen kognitif bozukluğu saptamada yeterince duyarlıdır. Semptom şiddeti ile korele olduğu için bu testin depresif bozukluğu olan hastalarda kognitif durumun kabaca değerlendirilmesinde kullanılması yararlıdır (Shulman yöntemi; $r=0.26$, $p<0.05$).

Anahtar sözcükler: Orta yaşlı, depresif bozukluk, tarama, bilişsel yönlere, nörodavranışsal belirtiler

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ABSTRACT:

Use of clock drawing test as a screening tool for cognitive status evaluation in middle-aged patients with depressive disorder

Objective: The objective of this study was to evaluate the cognitive functions of middle-aged patients with depressive disorder by using the clock drawing test (CDT).

Methods: In this case control study, the data from 96 patients with depressive disorder and 105 healthy controls, who were recruited from the Psychiatry and Family Medicine clinics, were analyzed. Sociodemographic and medical questionnaires were completed by the participants. Thereafter, the Mini Mental State Examination (MMSE) and CDT (reading and drawing) were conducted. The drawings were rated according to the scoring methods of Manos, Shulman, and Sunderland. The severity of depression was assessed by the Montgomery-Åsberg Depression Rating Scale.

Results: The mean age of the participants were 52.45±5.16 and 52.13±5.53 years for control and patient groups, respectively. The two groups did not differ in age, gender, educational level, or history of comorbid conditions ($p>0.05$). The mean duration of depressive illness was 63.41±86.42 months. The severity of depression was rated as mild, moderate, or severe in 16 (16.7%), 70 (72.9%), and 10 (10.4%) of the patients, respectively. The MMSE scores were high (24–30) in 77 (80.2%) patients and 101 (96.2%) controls and were low (≤ 23) in 19 (19.8%) patients and 4 (3.8%) controls ($p<0.01$). Of the 101 controls with normal MMSE scores, 29 (28.7%), 28 (27.7%), and 9 (8.9%) had abnormal clock-drawing scores by the Manos, Shulman, and Sunderland methods, respectively. Of the 77 patients with normal MMSE scores, 49 (63.6%), 28 (36.3%), and 42 (54.5%) had abnormal clock-drawing scores by the Manos, Shulman, and Sunderland methods, respectively. The Pearson correlations of the MMSE with the Manos, Sunderland, and Shulman methods were $r=0.52$, $r=0.48$, and $r=0.53$, respectively and were all statistically significant ($p<0.001$). All participants in the control group read the indicated time correctly in clock-reading test. However, 92 out of 96 patients read the indicated time correctly. There was no impact of demographic characteristics, comorbid conditions, and duration of depression on the CDT performance of the subjects.

Conclusion: The cognitive functions of middle-aged patients with depressive disorder could be screened by the CDT. The fact that the CDT is sensitive enough to detect the cognitive impairment inherent in depressive disorder, as well as being correlated with symptom severity, makes this test useful in the assessment of cognitive status in depression (Shulman method; $r=0.26$, $p<0.05$).

Key words: Middle aged, depressive disorder, screening, cognitive aspects, neurobehavioral manifestations

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INTRODUCTION

There has been growing evidence of significant impairment in neurocognitive functioning in major depressive disorder. Depression-related disturbances of cognitive functions have been demonstrated in a range of domains, including attention (1,2), memory (3,4), executive functioning (5,6), and psychomotor functioning (7). Several neuropsychological studies in depression have showed cognitive deficits in young, middle-aged (8,9), or elderly (10,11) patients with depressive disorder.

There are detailed neuropsychological tests and more extensive bedside tests to specifically evaluate cognitive functions but most of them are impractical for screening in outpatient clinics. The clock drawing test (CDT) has become an integral part of several screening instruments for cognitive impairment. It is internationally valued by clinicians for both its quick and easy administration and its high acceptance among patients. The test is a valuable tool for quick investigation of several domains of cognitive functions (12). The usefulness of the CDT has been demonstrated in the evaluation of visuoconstructive ability, executive functions, and also both numerical and verbal memory (13-16). It may be administered as a verbal command (14,17,18) or as a copy command (19). The verbal command CDT simultaneously assesses a patient's language function, memory functions, and executive functions. The verbal command variations of the CDT are highly sensitive for temporal lobe dysfunction and frontal lobe dysfunction. The copy command clock drawing and reading tests are good for assessing parietal lobe lesions such as those that may result in hemineglect (15,20,21).

The value of the clock drawing test has been evaluated in elderly depressed patients but not in the younger group of depressed patients (18,22). To our knowledge there are no published data for middle aged depressive patients concerning CDT performance. The aim of this study was to evaluate the usefulness of the CDT as a screening tool for cognitive status in middle-aged depressive patients. In the present study, we compared the CDT performance of two groups: patients with depressive disorder living in the community and healthy controls.

METHODS

Study Sample

In this study we enrolled 201 individuals, 96 with a diagnosis of depressive disorder and 105 healthy controls, consecutively recruited from the outpatient clinics of Psychiatry and Family Medicine, in Kahramanmaraş Sutcu Imam University Hospital, Turkey between January and December 2007. Written informed consent was obtained from each patient before enrollment. This study was approved by the ethical committee of the School of Medicine of the previously mentioned university.

Case Group

Ninety-six patients aged between 45-64 years with a confirmed DSM-IV (23) diagnosis of major depressive disorder (single episode or recurrent) were recruited from the outpatient clinic of the department of Psychiatry. All patients met the criteria for unipolar depressive disorder. Patients were psychotropic-medication free for at least six weeks before the enrolment. Patients taking any other medication, which is active in the central nervous system or might influence cognitive functions, were excluded. Patients with comorbid psychiatric diagnosis, history of neurological diseases or major medical disorders likely to affect cognition and patients who had been given electro convulsive therapy in the past 12 months were also excluded. Additionally, being illiterate, having sight, language, or hearing impairment were other exclusion criteria for the case group. Based on self-report, patients with a current and/or past diagnosis of psychoactive substance abuse were not allowed to participate in the study. Severity of depression was assessed using the Montgomery-Åsberg Depression Rating Scale (MADRS) (24). Validity and reliability of the MADRS in a Turkish population has been demonstrated (25). Subjects with MADRS scores of 12 or more were included in the study (26).

Control Subjects

Control subjects were recruited from the healthy participants who applied for their annual check-ups at the Family Medicine outpatient clinic. One hundred and five healthy control subjects, who met the same inclusion criteria

as the patients with the exception of not having any current or past psychiatric disorder or treatment including depression, were enrolled in the study. Subjects with a history of comorbid psychiatric and/or neurological disease, or who were using a psychoactive substance or medication which might influence cognitive functions were excluded from the study. Additionally, being illiterate, having sight, language, or hearing impairment were exclusion criteria. The control group was selected to match the depressed patients as closely as possible for age, gender, years of formal education, and season of testing. The participants were interviewed and the “Primary Care Evaluation of Mental Disorders Device” (Prime MD) was applied to the control group in order to rule out any psychological disorder (27). The validity and reliability of the Prime-MD in Turkish population has been performed (28).

Procedures

The Sociodemographic and Medical Questionnaire were given to the participants to assess admission criteria and sociodemographic characteristics. Thereafter, the Folstein Mini Mental State Examination (MMSE) was conducted on all subjects to measure cognitive functions. The MMSE was designed to give a practical clinical assessment of change in cognitive status. It covers the person’s orientation to time and place, recall ability, short-term memory, and arithmetic ability. It may be used as a screening test for cognitive impairment or as a brief bedside cognitive assessment (29). The test can be completed in approximately 15 minutes and is suited as a routine test on admission to psychogeriatric wards. The highest possible score is 30 and scores lower than 25–23 indicate the presence of dementia or related syndromes. Test-retest reliability with a time interval of 24 h is 0.89 and the inter-rater reliability comes up to 0.82 (30). The external validity of the MMSE has been extensively investigated by comparison with EEG, CCT scans, or PET scans. Scores lower than 19 in the MMSE indicate a poor prognosis in dementia patients as approximately 50% of them die within two years (31). The MMSE score was determined according to the guidelines for the standardized MMSE (32).

For the CDT, each subject was given a pre drawn circle (to minimize the effect of educational level) and asked to “place the numbers on it to make it look like a clock.” Placement of the hands of the clock to read “10 past 11,”

which has been reported to be the most sensitive to neurocognitive dysfunction, was requested after the first task was completed to the best of the patient’s ability (33). Afterwards, a copy command clock-reading test (clock showing the time 10 past 11) was administered to the participants and they were asked to read the indicated time.

The CDTs were scored by means of three methods (14,17,34). The scoring method described by Manos (34) (referred in this article as the Manos method) is objective and based on dividing the clock into quadrants. This method takes digit positioning into account, not positioning of the hands of the clock. A score of less than 8 out of 10 in the clock test is considered abnormal. The method described by Sunderland and colleagues (17) (the Sunderland method) takes hand positioning into account and the score is determined using a 10-point scale (10 = perfect and 0 = very poor). In this scale scores of 6 or higher are considered normal. The Shulman14 procedure (referred in this article as the Shulman method) ranks clock drawings on a scale of 1 to 6, with 1 representing a “perfect” clock and thus minimal or no impairment and 6 representing the most severe degree of impairment.

Statistical Analysis

Data were first analyzed for normality of distribution using the Kolmogorov-Smirnov test. The Manos, Shulman, and Sutherland scores did not follow a normal distribution. When comparing the differences between groups, the Mann–Whitney non-parametric test was used for non-normally distributed continuous variables. Also the Pearson Chi-square test was used for statistical analysis. Values were presented as mean \pm SD (standard deviation), medians (IQR) and as percentages. P values less than 0.05 (two-tailed) were considered to be statistically significant. The CDT scores were examined regarding the inter-rater reliabilities and inter-correlations of the scoring methods.

Inter-rater reliability and inter correlations

The drawings were rated independently by the third (MC) and fourth (HE) investigators according to the scoring methods of Manos and Wu (34), Shulman et al. (14) and Sunderland et al. without knowledge of the MMSE scores or the medical diagnoses of the patients/participants (17). Inter-rater reliabilities were calculated

using Spearman correlation coefficients. Additionally, we wanted to examine if two raters consistently judged the drawings as normal or abnormal. For this purpose, we dichotomized the scores into those to be considered normal and those to be considered abnormal and calculated agreement by means of Cohen's kappa (κ). Abnormal scores as suggested in the literature are <9 for the scoring Manos and Wu (34), >2 for Shulman et al. (14), and <6 for Sunderland et al. (17)

To see if the different rating systems mentioned above produce comparable results, we calculated the Pearson correlation coefficients between the clock test scores. We calculated the correlation separately for each one of the two raters. To examine if it is possible to come to consistent conclusions regarding the normality of a clock drawing when applying different rating systems, we used the cut off scores and calculated κ values separately for each of the two raters.

RESULTS

Sample

Ninety-six patients with depressive disorder and 105 healthy controls were enrolled in this study. The mean age was 52.45 ± 5.16 years for the control and 52.13 ± 5.53 years for the patient group. The two groups did not differ in age, gender, educational level, and history of comorbid diseases ($p > 0.05$). The mean duration of depressive illness was 63.41 ± 86.42 months (minimum 1 month – maximum 360 months). The demographic and medical characteristics of the study group are presented in Table 1.

Clock-drawing Scores

All of the participants in the control group read the indicated time in the copy command clock-reading test correctly. In the patient group, 92 participants out of 96

Table 1: Demographic and medical characteristics of the study group

Characteristics	Control group n (%)	Depressive Group n (%)	P value*
Gender			
Female	61 (58.1)	66 (68.8)	0.78
Male	44 (41.9)	30 (31.3)	
Marital Status			
Married	98 (93.3)	85 (88.5)	0.16
Single	7 (6.7)	11 (11.5)	
Educational level			
Primary school	39 (37.1)	47 (49)	0.28
Secondary school	11 (10.5)	10 (10.4)	
High School	22 (21.0)	19 (19.8)	
University	33 (31.4)	20 (20.8)	
History of Diabetes Mellitus			
Yes	14 (13.3)	10 (10.4)	0.330
No	91 (86.6)	86 (89.5)	
History of Hypertension			
Yes	24 (22.8)	30 (31.3)	0.23
No	81 (77.2)	66 (68.7)	
History of Cardiovascular Disease			
Yes	3 (2.8)	6 (6.3)	0.20
No	102 (97.2)	90 (93.7)	
Mini Mental State Examination score			
24-30	101 (96.2)	77 (80.2)	0.001
≤ 23	4 (3.8)	19 (19.8)	
Duration of depression (months)			
1-60	-	68 (70.8)	
61-121	-	12 (12.5)	
≥ 122	-	16 (16.7)	
MADRS score			
≥ 35	-	10 (10.4)	
18-34	-	70 (72.9)	
12-17	-	16 (16.7)	

*Pearson chi square

read the indicated time correctly. The distribution of clock drawing scores is shown in Table 2. There was no impact of demographic characteristics, comorbid diseases, and duration of depression on the CDT performance of the subjects. There was a significant association between the severity of depression and clock drawing scores with the Shulman method ($r=0.26$, $p<0.05$).

Inter-rater reliability and inter-correlations

Inter-rater reliabilities of different scoring methods ranged from $r=0.86$ to $r=0.97$ (Shulman et al. (14): $r=0.86$; Sunderland et al. (17): $r=0.95$; Manos and Wu (33): $r=0.97$) and were all highly significant ($p<0.001$). Kappa values for the consistency with which clock drawing was rated normal versus abnormal ranged from 0.83 to 0.90 (Shulman et al. (14): $\kappa=0.83$; Sunderland et al. (17): $\kappa=0.84$; Manos and Wu. (33): $\kappa=0.88$) and also proved to be highly significant ($p<0.001$).

The results of the two scoring methods that correlated the least were those obtained with the Manos and

Sunderland methods ($r=0.84$). Also the judgement following the Manos and Sunderland methods were the most consistent ($\kappa=0.71$). The agreement of these methods for the depressive and control groups were $\kappa=0.82$ and $\kappa=0.53$, respectively. Inter correlations (r) between different scoring methods and agreement (kappa) on dichotomized scores are presented in Table 3.

The Pearson correlations of the MMSE with the Manos, Sunderland, and Shulman methods were $r=0.52$, $r=0.48$ and $r=0.53$, respectively and were all highly significant ($p<0.001$).

The three scoring methods with a normal MMSE

Out of the 101 healthy participants with a normal MMSE score (≥ 24), 29 (28.7%) had an abnormal clock-drawing score by the Manos method, 28 (27.7%) had an abnormal clock-drawing score by the Sunderland method, and 9 (8.9%) had an abnormal clock-drawing score by the Shulman method. Of the 77 patients with a normal MMSE score (≥ 24), 47 (61.03%) had an abnormal clock-drawing score by the Manos method, 28 (36.3%) had an abnormal

Table 2: The distribution of clock-drawing scores of the study group

Scoring method	Control	Depressed	P value*,**
Manos method			
mean \pm S.D.	8.77 \pm 1.82	6.88 \pm 2.80	0.001
median	10.0	7.0	
IQR	2	4.75	
9-10 (normal) n (%)	72 (68.6)	33 (34.4)	0.001
0-8 (abnormal) n (%)	33 (31.4)	63 (65.6)	
Shulman method			
mean \pm S.D.	1.45 \pm 0.72	2.21 \pm 0.98	0.001
median	1.0	2.0	
IQR	5	5	
1-2 (normal) n (%)	74 (70.5)	40 (41.7)	0.001
3-6 (abnormal) n (%)	31 (29.5)	56 (58.3)	
Sunderland method			
mean \pm S.D.	8.41 \pm 2.26	6.66 \pm 2.53	0.001
median	10.0	5.0	
IQR	1	2	
7-10 (normal) n (%)	95 (90.5)	57 (59.4)	0.001
0-6 (abnormal) n (%)	10 (9.5)	39 (40.6)	

*Mann-Whitney- U test and **Pearson-Chi square with continuity correction

Table 3: Intercorrelations (r) between different scoring methods and agreement (kappa) on dichotomized scores in the study group

Scoring method	Sunderland et al. (1989)		Shulman et al. (1986)	
	r	kappa	r	kappa
Manos and Wu (1994)	0.84	0.71	-0.84	0.47
Sunderland et al. (1989)			-0.87	0.56

clock-drawing score by the Sunderland method, and 42 (54.5%) had an abnormal clock-drawing score by the Shulman method.

DISCUSSION

The CDT is a reliable instrument and has been shown to have high sensitivity and specificity for the diagnosis of dementia in elderly patients (12,17-19,35,36). However, the value of the CDT in younger groups of patients has not been assessed. In this study we aimed to evaluate the performance of the CDT as a screening test for cognitive status in middle-aged depressive patients. In the past decade, a growing body of evidence has accumulated to suggest that patients suffering from depressive disorder present some cognitive disturbances, such as impairment in attention, working memory, and executive function, including cognitive inhibition, problem- and task-planning. Executive function refers to cognitive processes that control and integrate other cognitive activities such as episodic memory. These executive functions involve a set of cognitive behaviors which include: dealing with novelty, selecting strategies, inhibiting incorrect responses, monitoring performance and using feedback to adjust future responding. The CDT is thought to require the use of a variety of mental skills, visuo-perceptual and visuo-motor abilities to internally represent the clock face and to translate the mental representation into a motor program. In addition, visuo-perception also guides the ongoing layout of the clock and monitors the output. Hemi-attentional processes are needed to produce features on both sides of the space. The linguistic system must provide the graphomotor representation of numbers and executive function must coordinate the planning, organization and simultaneous processing. This includes corrections and inhibition of incorrect responses such as perseveration. Memory is needed to remember the instruction to set the time and retrieve it once the clock face is complete, and finally the time setting must rely on executive function (37,38,39). In our study, the performance of the control group was better than the patients on the verbal command CDT (time setting of 10 past 11) according to the three scoring methods. Additionally, all of the participants in the control group read the indicated time in the copy command clock-reading test correctly. However, only 95.8% of the patients read the indicated time correctly. In a study with

elderly depressive patients the CDT score was found to be lower than the non-depressed seniors (16). However, to our knowledge there has not been any published data for middle aged patients with depressive disorder regarding CDT performance. Although the CDT scores have been associated with age and poor education in some of the studies (40,41), in our study there was no impact of demographic characteristics and educational level on the CDT performance of the subjects. Moreover, the CDT has been found to be relatively independent of culture, language, and education (12). In our study, there was no association between the duration of illness and the CDT performance. Although the participants had been drug free at least 6 weeks, the duration of previous antidepressant use and its possible influences on cognition should be kept in mind. The effect of severity of depression on neurocognitive task performance has been measured in many studies and findings have, however, been controversial (3,8,42,43). Nevertheless, a significant association was detected between severity of depression and clock drawing score according to the Shulman method in the present study. The findings of decreased performance in cognitive tasks in depressive patients compared to healthy controls agrees with the substantial literature (8,9,44,45) on the subject.

The MMSE scores of the patients with depressive disorder were lower than the healthy controls in the present study. The correlation of the three scoring methods with the MMSE was proven to be moderate and found to be concordant with the literature (46,47). In this study, we evaluated the CDT scores of patients with a normal MMSE score. When the MMSE score is abnormal, the suspicion of cognitive impairment is already raised. Yet, it might be difficult to screen the patients with normal MMSE scores in the presence of clinical concerns about the cognitive functions. When the CDT score is abnormal, it reinforces the suspicion of cognitive impairment. The CDT can be particularly useful to examine cognitive domains not evaluated by the MMSE (48).

Inter-rater reliabilities of the different scoring methods ranged from $r=0.86$ to $r=0.97$ in our study, and were accepted as sufficiently high. Kappa values for the consistency with which the clock drawing was rated normal versus abnormal ranged from 0.83 to 0.90. The results of the two scoring methods that correlated the least were those obtained with the Manos and Sunderland methods ($r=0.84$). Also the judgments following the Manos method and

Sunderland method were the most consistent ($\kappa=0.71$). The Pearson correlation coefficients and also κ values were proven to be relatively high. In a study by Seigerschmidt et al. (49), inter-rater reliabilities of the different scoring methods ranged from $r=0.82$ to $r=0.95$ for the Manos, Watson, Wolf-Klein, and Shulman methods of scoring the CDT. Scoring judgments using the Manos and Shulman versions were the most consistent among raters, while use of the Wolf-Klein and Shulman versions resulted in the most inconsistent judgments. The results of the two scoring methods that correlated the least were those obtained with Watson's and Shulman's version of the CDT ($r=0.42$). The highest correlation was found between Shulman's version and the Manos scoring system ($r=0.72$). In another study the Shulman, Sunderland, Wolf-Klein, Watson and Manos scoring methods of the CDT showed highly significant inter-rater reliability (0.82 to 0.94) (50,51).

Our study has certain limitations. The concurrent validity of the CDT with other widely used cognitive tests was not satisfactory in the present study. We decided to conduct the MMSE because it has high sensitivity and

specificity, and is widely utilized. The comparison of its psychometric properties to the clock data would be of interest. The CDT comfortably meets all criteria necessary for a cognitive screening instrument (47,52). An abnormal clock drawing may suggest executive cognitive dysfunction and should prompt further testing or referral.

In conclusion, of the 77 patients with a normal MMSE score, 47 (61.03%) had an abnormal clock-drawing score by the Manos method, 28 (36.3%) had an abnormal clock-drawing score by the Sunderland method, and 42 (54.5%) had an abnormal clock-drawing score by the Shulman method in the present study. The performance of the control group was better than the patients on the verbal command CDT according to the three scoring methods. Therefore, cognitive functions could be screened by using the CDT in conjunction with the MMSE in middle-aged patients with depressive disorder. However, further studies are needed to replicate our findings with a larger number of participants. Moreover, these studies could further delineate neuropsychological targets for future intervention studies aimed at improving the cognitive deficits relevant to functional decline.

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