

PAPER DETAILS

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ARAŞTIRMA / RESEARCH

Effectiveness of the clock drawing test in differentiating various types of dementia

Saat çizme testinin çeşitli demans tiplerini ayırt etmedeki etkinliği

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Abstract

Purpose: The aim of this study was to investigate the effectiveness of clock-drawing test (CDT) in differentiating dementia types.

Materials and Methods: 48 Alzheimer's disease (AD), 68 vascular dementia (VaD) and 13 frontotemporal dementia (FTD) patients were included in the study. Clock drawing test (CDT), mini mental state examination (MMSE) and other neurophysiological tests (back and forward numerical range, calculation test, abstraction test, word memory tests, boston naming test, word list recall and recognition tests) were applied to all patients. The scores of CDT and other neurophysiological tests were compared between the AH, VaD and FTD groups. The relationship between CDT and other neurophysiological tests was evaluated.

Results: There was no significant difference in CDT between the dementia groups. MMSE and back numerical range scores were statistically significant among dementia groups. A positive correlation was found especially in AD and VaD patients when MMSE and CDT tests were used together. In addition, a positive correlation was found between CDT and boston naming test for FTD type.

Conclusion: CDT is not a unique predictor to determine primary dementia type. However among the neurophysiological test batteries we used in the study, especially the combined use of MMSE and CDT and combined use of CDT with other tests have an important place in dementia differentiation.

Keywords: Clock-drawing test, dementia, visuospatial skills, assessment of cognition

Öz

Amaç: Bu çalışmanın amacı, demans tiplerini ayırt etmede saat çizme testinin (SÇT) etkinliğini araştırmaktır.

Gereç ve Yöntem: 48 Alzheimer hastalığı (AH), 68 vasküler demans (VaD) ve 13 frontotemporal demans (FTD) hastası çalışmaya dahil edildi. Tüm hastalara SÇT ile mini mental durum muayenesi (MMSE) ve diğer nörofizyolojik testler (ileri-geri sayım aralık, hesaplama testi, soyutlama testi, kelime hafıza testleri, boston adlandırma testi, kelime listesi hatırlama ve tanıma testleri) uygulandı. SÇT ve diğer nörofizyolojik testlerin skorları AH, VaD ve FTD grupları arasında karşılaştırıldı. SÇT ile diğer nörofizyolojik testler arasındaki ilişki değerlendirildi.

Bulgular: AH, VaD ve FTD grupları arasında SÇT testinin anlamlı bir fark olmadığı görülmüştür. Demans grupları arasında MMSE and geri sayım aralık skorları istatistiksel olarak anlamlı bulunmuştur. MMSE ve SÇT testlerinin birlikte kullanımında özellikle AH ve VaD hastalarında pozitif korelasyon saptanmıştır. Ek olarak FTD tipi için SÇT ve boston adlandırma testi arasında da pozitif bir ilişki saptanmıştır.

Sonuç: SÇT primer demans tipi belirlemede benzersiz bir öngörücü değildir, ancak çalışmada kullandığımız nörofizyolojik test bataryaları arasında, özellikle MMSE ve SÇT'nin birlikte kullanımı ve SÇT'nin diğer testlerle kombine kullanımının demans farklılaşmasında önemli bir yeri vardır.

Anahtar kelimeler: Saat çizme testi, demans, görsel mekansal beceriler, kognisyon değerlendirme

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INTRODUCTION

Dementia involves a series of lapses that are characterized by the progressive deterioration of cognitive functions, primarily memory that affects one's daily activities. Memory, perception, orientation, attention, judgment, visuospatial functions, executive functions and truth assessment are some cognitive functions that regress with dementia¹.

Dementia can be categorized as primary and secondary dementia in accordance with etiology. The major degenerative diseases that cause primary dementia include Alzheimer's disease (AD), vascular dementia (VaD), frontotemporal dementia (FTD), dementia with Lewy Bodies and Parkinson's Disease. The prodromal stages of these diseases may also cause primary dementia. AD is the most common cause of dementia worldwide, and VaD is the second most common cause of dementia².

The medical histories of patients with dementia and their relatives are crucial for the correct diagnosis of dementia. Moreover, neurological and complete physical examinations are necessary for the differential diagnosis of dementia. Neuropsychiatric tests, which enable the comprehensive evaluation of the neural network, including memory, attention, executive functions and visual-spatial functions, as well as language and daily life activities, are vital for diagnosis. Mini-mental state examination (MMSE), vocabulary counting tests for verbal learning, story reminding test, semantic fluency tests, Boston naming test, numerical range and tracking tests for attention and clock-drawing test (CDT) are some of the most commonly used neuropsychiatric tests worldwide¹.

The CDT is widely used as a cognitive screening tool in the clinical diagnosis of dementia. It has been used since the beginning of clinical neuropsychology and is a practical and facile test that can be used to diagnose patients with early-stage dementia^{3,6}. During the administration of the CDT, the patient is asked to draw a circle on a page and place the numbers and arrows on the "clock" to indicate the time given in the instructions^{4,5}. This exercise requires the use of a combination of numerous cognitive skills, such as visuospatial ability, executive functions, semantic knowledge and global cognitive capacity⁴. Although many studies involving the CDT have shown that cognitive function is influenced by dementia type, the specific cognitive function reflected by the results of

CDT remains unknown⁷.

In this study, we aimed to seek answers to the question of whether the CDT plays an effective test in the diagnosis of dementia type; AD, VaD, FTD. We investigated the role of combined use of CDT and neurophysiological tests in dementia type differentiation. There are many studies in the literature on the effectiveness of neuropsychological tests among dementia groups, we wanted to emphasize once again the importance of CDT in dementia type differentiation in this study together with literature data.

MATERIALS AND METHODS

Patient groups

The study recruited patients with dementia who consulted the Dementia Polyclinic of the Neurology Department at Mersin Medical Faculty over the period of 2014–2017. This patient group included individuals who were clinically diagnosed with AD in accordance with the criteria of the National Institute of Neurological and Communicative Disorders and Stroke-Alzheimer's Disease and Related Disorders Association and Diagnostic and Statistical Manual of Mental Disorders, 5th Edition. The patient group also included individuals who were diagnosed with VaD on the basis of NINDS-AIREN criteria and those who were diagnosed with FTD in accordance with the Frontotemporal Lobar Degeneration Clinical Diagnosis Consensus Criteria^{8,11}. The majority of patients involved in this study were diagnosed with VaD presenting with microvascular disease. The distribution of VD and FTD in the patient group was consistent with that in the overall population. Furthermore, VD and FTD are the two most common types of primary dementia syndromes after AD in our national population. Post hoc power analysis was performed for the smallest effect size (effect size=1.173) obtained in the study. Accordingly, the post hoc power of the study was calculated as 99.5% with GPower 3.1. After written approval of the ethics committee and of the institutions permission in which the study was to be performed were obtained the study started (decision no: 2013/340, date: October 10, 2013).

Among the 129 patients included in this study, 66 were male (51.2%) and 63 were female (48.8%). The mean age of the participants was 72 (min: 52, max: 90, SD: 7.8 years). The average educational background of the patients was 5 years (0–16 years).

The demographic information of the patients is summarized in Table 1. All patients were subjected to differential diagnosis. The patients underwent a neurological examination followed by the necessary laboratory procedures. Then, they received neuropsychological examination from the same psychologist. This retrospective study was conducted in accordance with the Helsinki Declaration.

Neuropsychological examination

The electronic data recording system in the electronic database of Turkish Alzheimer's Working Group, which was developed under the leadership, was used for neuropsychological evaluation.

MMSE

The MMSE is a simple and brief tool often used to assess various areas of cognition. The patient's performance was assessed with 30 maximum possible points that can be collected from the subtests of time–place orientation, recording, attention, calculation, recall, naming, repetition, three-step command, understanding, sentence building and figure copying. The Turkish adaptation of MMSE was developed by Gürgeç et al. (12) with the highest sensitivity (0.91) and specificity (0.95) scores ($\kappa = 0.86$) at a cut-off score of 23/24. In our study, we administered the MMSE-educated battery to individuals who received 5 years or more of formal education. We administered the MMSE-uneducated battery to the other participants.

Numerical range

This test is administered for the clinical evaluation of attention, short-term memory and working memory. In the forward numerical test, the participant is required to repeat a series of progressively increasing numbers. In the backward numerical test, the participant repeats the numbers given by the practitioner in the reverse order, starting from the last one to the first. In both numerical range exercises, the maximum numbers repeated by the patient are recorded as scores. The dorsolateral prefrontal cortex is activated during the backward numerical performance, and the inferior prefrontal sulcus is highly activated during the forward numerical performance^{13,14}. These activation patterns show that the backward numerical range is associated with working memory, whereas the forward numerical range is associated with short-term memory. We used the following numerical sequences in our study:

28/51–372/494–5169/6294–83529/61074–285164/917203–4072916/3508172.

Calculation

This test is used to evaluate calculation skills. Arithmetic skills are connected to methods, such as shopping and organizing financial matters, that are frequently used in daily life. In this test, five simple mathematical problems were asked the participant. The minimum score was 0. The maximum score for the correct completion of all arithmetic tasks was 5. In our study, we applied the following calculation problems: $5 + 3.15 + 7$, 5×13 , $39/3$ and $31 - 8$.

Abstraction

Proverbs express short and abstract expressions and carry deeper meanings than their concrete meanings. Therefore, understanding proverbs requires the use of the basic features of spoken language and executive functions. In this study, we asked the participants to interpret three different proverbs. Each correct answer was worth 1 point. The proverbs used in this battery were “to be worn to the bone” (*Tur. lit. "Getting black water on my feet"*); “He that lies down with dogs will rise up with fleas” (*Tur. lit. "Grapes grow darker by facing each other"*) and “As the twig is bent so is the tree inclined” (*Tur. lit. "The tree is only bent when ripe"*). These were chosen among the most used Turkish proverbs.

Word Memory Test (WMS)

This test consists of learning experiments 1, 2 and 3 and the delayed recall and recognition subtests. In the learning experiments, the practitioner verbally presents a list of 10 words (oil, building, arm, beach, letter, cat, stick, ticket, grass and motor) with different sequences. All words are neutral nouns, and no adjective is given to avoid bias. After the presentation of the word set, patients are asked to count all the words they can remember from the list. One point is awarded for each correctly counted word. In the delayed recall stage, which is conducted after three tests following this test, the patient is asked to count the words they remember (recall). In the next step, a list of 20 words, including 10 new words of similar nature (mosque, five, mountain, string, coffee, lira, slippers, soldier, hotel and village) is given to the patient in mixed order. Then, the patient was asked to recognize previously learned words. At this stage, the total score that can be obtained for correct positive and false negative conditions is 20. When we administered this test, we

were careful to pause for a second before the next one and not to give feedback about the answers provided by the patient.

Boston Naming Test

This test evaluates the visual naming performances and lexicosemantic skills of the participants. The participants were shown a battery of 15 shapes that were drawn earlier. The participant was asked to name each shape (not their uses). The participant received 1 point for each correctly named object (maximum score is 15). This test is related with activity in the left inferior prefrontal and posterior temporal areas¹⁵.

CDT

The CDT is a simple pen-and-paper test. A piece of paper is given to the participant, who is wanted to draw a circle and to place numbers inside the circle to make it look like a clock. The patient is also asked to indicate a specific time on the clock (11:10 for this directive) without being asked to emplace the hour and minute hands. This test is important for the evaluation of the participant's understanding, planning, visual memory, imagery, visuospatial skills, motor programming, abstraction skills and executive functions¹⁶. The 10-point scoring scale used in this study is shown in Table 1¹⁷.

Statistical analysis

The patients demographic and test scores collected data were analyzed using IBM® SPSS® Statistics version 23.0 (IBM Corp, Armonk, NY). Descriptive statistics of mean, maximum, and minimum values were used to characterize continuous variables, and percentage values were used for qualitative variables. Shapiro–Wilk test was performed to determine if variables were normally distributed for CDT and other neurophysiologic tests. Score-type variables that did not follow a normal distribution were summarized as median [min–max], continuous

variables with normal distribution were given as mean \pm standard deviation (sd), whereas categorical variables were summarized on the basis of number and percentage. Kruskal-Wallis test was used for the comparison of the three groups because the data of the three groups were not normally distributed. Then Dunn test was used for pairwise comparisons as a post-hoc test. P value was adjusted by Bonferroni correction for multiple tests. Spearman correlation coefficient was used to examine the relationship between two score-type variables. $p < 0.05$ was accepted as the level of statistical significance.

RESULTS

This study involved 129 patients. The demographic and clinical features of these patients in accordance with diagnostic groups and genders are summarized in Table 1. In Table 2, CDT and other cognitive tests scores compare among each in AD, VaD and FTD patients groups. MMSE and backward numerical range scores are statistical meaningful low value ($p=0.002$, $p=0.027$). CDT scores is not meaningful value in between all groups ($p=0,04$).

In Table 3, we evaluated the correlation CDT and other neurophysiological tests each in AD, VaD and FTD groups. For AD and VaD patients groups, we found that between MMSE scores and CDT scores statistical meaningful, a moderate and positive correlation ($r=0,506$ $p<0,001$ - $r=0,599$ $p<0,001$)

For FTD patients groups, there is a statistically significant, positive and strong correlation between CDT score and boston naming scores in the FTD group. ($r=0,876$, $p<0,001$). CDT is not useful alone in the differential diagnosis between AD, VaD and FTD. However to use the combination CDT and MMSE the test CDT is beneficial in early diagnostic tools for AD and VaD. Differentiation between FTD Boston naming test and CDT are useful in clinical practice.

Table 1. The demographic and clinical features of the patients

	AD n=48 (%)	VaD n=68 (%)	FTD n=13 (%)
Gender (F/M)	30/18	26/42	7/6
Age (mean \pm SD)	74.60 \pm 7.097	73.56 \pm 7.195	62.92 \pm 7.182
Duration of disease (mean years, 25-75 percentils)	2.1-3.75	2.1-4	2.2-3
Marital status (married/single) n	27/20	49/18	10/2

AD: Alzheimer Disease, VaD: Vascular Demantia, FTD: Frontotemporal Demantia, F: Female, M: Male, SD: Standard Deviation, n:sample size

Table 2. Neuropsychological inventories differences between the patient groups

	Alzheimer Disease					Vascular Dementia					Frontotemporal Dementia					
	N		Median	Min	Max	N		Median	Min	Max	N		Media n	Min	Max	
	Valid	Missing				Valid	Missing				Valid	Missing				p
CDT Score	48	0	8.00	1	10	68	0	6.50	1	10	13	0	6.00	2	10	0.506
MMSE	46	2	27.00	12	30	67	1	26.00	11	30	13	0	17.00	6	29	0.002*
Forward numerical range	45	3	4.00	0	6	58	10	4.00	3	6	11	2	4.00	3	6	0.183
Back numerical range	44	4	3.00	0	5	58	10	3.00	0	5	11	2	2.00	0	4	0.027*
Calculation test score	44	4	5.00	0	5	58	10	5.00	0	5	9	4	5.00	0	5	0.593
Abstraction score	43	5	3.00	0	5	58	10	3.00	0	3	11	2	3.00	0	3	0.188
WMT-1	45	3	3.00	0	7	53	15	3.00	0	6	9	4	3.00	0	4	0.794
WMT- 2	45	3	4.00	0	9	53	15	4.00	0	7	9	4	4.00	0	5	0.838
WMT-3	44	4	5.00	0	10	53	15	4.00	0	8	9	4	4.00	0	5	0.342
BOSTON naming score	44	4	13.00	9	15	56	12	13.00	5	15	11	2	11.00	5	15	0.098
Word List Recall Score	41	7	1.00	0	8	52	16	2.50	0	7	9	4	2.00	0	5	0.760
Word List Recognition Score	41	7	16.00	0	20	52	16	16.00	0	20	9	4	18.00	4	20	0.301

CDT: Clock drawing test, MMSE: Mini-mental state examination, WMT: Word Memory Test, Min: Minimum, Max: Maximum, * p<0.05
**p<0.001

Table 3. Correlation CDT and other neuropsychological inventories

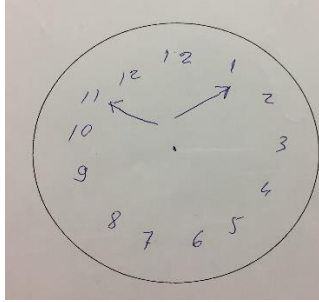
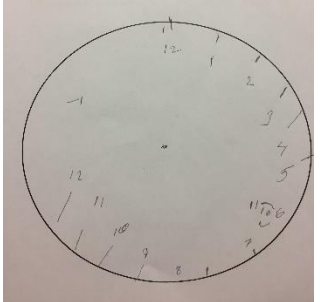
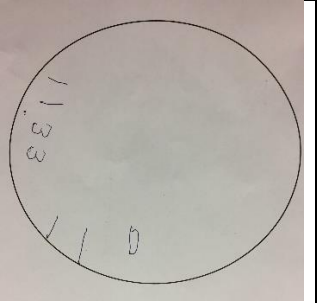
	Alzheimer Disease			Vascular Dementia			Frontotemporal Dementia		
	Spearman's rho			Spearman's rho			Spearman's rho		
	CDT Score			CDT Score			CDT Score		
	r	p	n	r	p	n	r	p	n
MMSE	0.506	.000	46	.559	.000	67	.536	.059	13
Forward Numerical range	.261	.084	45	.238	.072	58	.470	.145	11
Back Numerical range	.243	.112	44	.440	.001	58	.243	.472	11
Calculation score	.427	.004	44	.318	.015	58	.508	.162	9
Abstraction score	.154	.326	43	.159	.234	58	.326	.328	11
WMT- 1	.305	.042	45	.305	.027	53	.244	.528	9
WMT-2	.438	.003	45	.316	.021	53	.475	.196	9
WMT-3	.520	.000	44	.201	.149	53	.442	.233	9
BOSTON Naming score	.460	.002	44	.616	.000	56	.876	.000	11
Word List Recall score	.241	.129	41	.148	.295	52	.333	.381	9
Word List Recognition score	.595	.000	41	.306	.027	52	.223	.565	9

CDT: Clock Drawing Test, MMSE: Mini-mental state examination, WMT: Word Memory Test, *-1< r<1 p<0,05

As shown in Figure 1, CDT test score is low score of FDT and VaD even they preserved short time memory. On the other hand disturbed memory of

AD sufferers has preserved CDT test scores. VaD sufferers show proportionally deformation in CDT tests with memory function.

Figure 1. Samples of disrupted CDT patients in saved memory and attention in primary dementia patients

	AD n=48 (%)	VaD n=68 (%)	FTD n=13 (%)
CDT			
MMSE	28	21	27
WMT- 1	3	3	3
WMT- 2	3	0	3
WMT- 3	4	3	4
WLRS	0	2	1
WLRcS	12	13	16

AD: Alzheimer Disease, VaD: Vascular Disease, FTD: Frontotemporal Disease, CDT: Clock Drawing Test, MMSE: Minimal State examination, WMT: Word Memory Test, WLRS: Word List Recall Score, WLRcS: Word List Recognition Score

DISCUSSION

In this study, we evaluated the distinguishing role of the CDT together with a wide range battery and confirmed diagnostic tools of primary dementia patients. We identified CDT alone is not an early predictive test for dementia types. However, we found that MMSE and backward numerical range test scores are statistically meaningful results between in AD, VaD, and FTD. Even the CDT is not a unique predictors of primary dementia differentiation, it is a more effective test with combination MMSE and CDT among the batteries we used in the study. In addition, both of backward digit span and boston naming tests are another useful test in diagnosis of FTD especially with together using CDT. As expected not short-term memory batteries but recall tests using the pathways from the short-term memory to the long-term memory is another early predictor of AD in our data set.

CDT is an easy and speedy test as well as independent of culture, language and education¹⁸. Thus, the CDT has an important place in the diagnosis of dementia. It requires the activation of

numerous cognitive functions and is effective even in the diagnosis of early-stage dementia^{10,19}. We found that the clock drawings produced by patients with early-stage FTD were the most distorted, followed by those produced by the VaD group. The clock-drawing function was relatively maintained in the AD group. AD primarily affects the medial temporal lobe, temporal limbic areas and reciprocal corticolimbic areas, which are associated with recording memory. Impairment in these areas causes regression in the long-term recording of information in memory and in information recall²⁰. In the CDT, executive functions and visuospatial functions that are primarily affected in the FTD and VaD groups are more active than memory. The CDT scores of patients with AD, which is characterized by memory deterioration, were although it tends to be higher than those of patients with other types of dementia but there isn't statistical meaningful differences in each dementia groups. In a similar study, Sallam et al. reported that when the CDT scores of a general group comprising participants with AD, VaD and other types of dementia were compared with those of a control group, participants with AD had the lowest CDT scores²¹. It is suggested that this difference may

have been caused by our battery and sample numbers are larger than Sallam's study and there is methodological differences and the characteristics of the patients groups.

The low CDT averages of patients with VaD and FTD, which are predominated by the deterioration of executive functions and visuospatial skill functions, indicate that the CDT is more closely associated with these functions. The average CDT scores of patients with AD, which is primarily characterized by memory impairment, are higher than those of patients with other types of dementia. This study provides further evidence that CDT does not assess short-time memory²². In addition, identifying whether CDT reflects visuospatial function or executive function to a larger extent is complicated. The function reflected by CDT can only be identified through a study that is designed to identify error types and by using different methodology. In a study that categorized error types, more spatial and planning errors were seen in patients with VaD than in patients with AD²². The administration of CDT helped identify the type of dementia suffered by the patients in the three different groups by illustrating the compromised cognitive function of the patients. However depending on early impairment in FTD patients, supported that executive dysfunction is more important than visuospatial dysfunction in our data set.

Comparing CDT with other cognitive tests revealed a statistically significant and positive relationship between CDT and MMSE. The combined use of MMSE and CDT provides high specificity and sensitivity in the diagnosis of dementia^{21,23}. A study involving a four-point scoring system, 125 patients with AD, 75 patients with VaD and a cognitively normal group of 25 individuals revealed that the CDT has 100% sensitivity and 70% specificity in distinguishing patients with dementia from the normal population. However, CDT does not help distinguish between patients with AD and VaD²⁴. Our data have shown that in community-based studies or in cases where an assessment of dementia is required within a limited time, the use of CDT in addition to MMSE test would significantly increase diagnostic sensitivity, especially for AD and VaD types.

The most important disadvantage of this study is its inability to identify the errors made by patients in CDT and to determine the types of errors that are prevalent in each type of dementia. Kitabayashi et al.

stressed that the type of the error made by the patient, such clock size and graphical difficulties, is indicative of defective warning-based response and conceptual, spatial and planning deficits (18). This study also did not consider the decrease in scores attributed to the lack of education and the failure to classify the patients in accordance with dementia stages. We supported the idea of CDT which is among the most useful tests in lower educated population.

Our study presents an authentic methodology for the comprehensive neurological assessment of the most common primary dementia syndromes and comparatively analyses the significance of CDT within a wide range of neuropsychiatric tests. We also open a discussion a perfect algorithm in differential early diagnosis of primary dementia syndromes in a short time visits in outpatients without specific biomarker.

In conclusion, CDT is a simple test with a high diagnostic value given that but alone CDT is not a predictive test for dementia types. The combination of CDT and MMSE, commonly used tests and more effective combination for the early diagnosis of the most common primary dementia syndromes (AD, FTD and VaD).

Yazar Katkıları: Çalışma konsepti/Tasarımı: AÖ; Veri toplama: MŞ, GGY; Veri analizi ve yorumlama: GGY, KK; Yazı taslağı: GGY; İçerğin eleştirel incelenmesi: AÖ; Son onay ve sorumluluk: GGY, AÖ, MŞ, KK; Teknik ve malzeme desteği: MŞ; Süpervizyon: AÖ; Fon sağlama (mevcut ise): yok.

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