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Relation between the clock drawing test (CDT) and structural changes of brain in dementia

Ye-Sung Kim, Kyung-Mok Lee, Byung Hee Choi, Eun-Hee Sohn, Ae Young Lee*

Department of Neurology, Chungnam National University College of Medicine, University Hospital, 640 Daesa-dong, Junggu, Daejeon 301-721, South Korea

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ABSTRACT

The CDT is a useful screening instrument for assessing cognition. The aim of this study is to identify which structural change of the brain is related with the CDT performance. Eighty-four patients with memory impairment were enrolled. The Korean versions of the mini-mental state examination (K-MMSE) and the modified mini-mental state (3MS) test, and the Seoul Neuropsychological Screening Battery (SNSB) were given to every subject. Four CDT scoring methods were used. The cerebral white matter hyperintensity (WMH), cortical atrophy (CA), ventricular enlargement (VE), and medial temporal lobe atrophy (MTA) were rated by two neurologists who were kept "blind" to the clinical information. The cognitive and executive functions were significantly correlated with the CDT performance. The degree of WMH and MTA showed an inverse relation with the CDT performance. The periventricular WMH (PVH) contributed more to impairment of CDT, than that of the deep WMH (DWMH). This study suggests that a combination of executive dysfunction via the frontal-subcortical disruption due to the PVH and memory impairment due to the MTA might be responsible for further worsening on the CDT.

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1. Introduction

CDT has been regarded as a simple and useful screening tool for determining cognitive functioning in neurodegenerative disorders (Libon et al., 1996; Richardson and Glass, 2002; Cahn-Weiner et al., 2003; Lin et al., 2003). The diverse cognitive skills that are needed for the CDT operate in the different brain regions; these skills are verbal understanding, memory, spatially coded knowledge, abstract thinking, planning and visuo-constructive functions. The CDT also reflects deficits in the executive function, which are often overlooked by routine cognitive evaluations (Kitabayashi et al., 2001; Ino et al., 2003). However, little is known about the relation between the CDT and such structural cerebral changes as WMH or CA in dementia patients.

We expect that performance on the CDT may be influenced by frontal-subcortical circuits that have a role for the executive function. The purpose of the present study is to identify structural cerebral changes that might contribute to the results of the CDT taken by patients diagnosed with dementia.

2. Patients and methods

2.1. Participants

Eighty-four patients who were diagnosed with dementia were enrolled for this retrospective study. They attended the outpatient memory clinic of the Neurology Department at Chungnam University Hospital from January 2005 to April 2006 due to their cognitive impairment. Brain magnetic resonance imaging (MRI), laboratory studies and cognitive assessments, including the CDT, were given to all patients. Alzheimer's disease (AD), (n = 41) was diagnosed by the National Institute of Neurological and Communicative Disorders and the Stroke-Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA) criteria (McKhann et al., 1984). The diagnosis of vascular dementia (VaD), (n = 13) was made by using the National Institute of Neurological Disorders and Stroke and the Association Internationale pour la Recherche et l'Enseignement en Neuroscience (NINCDS-AIREN) criteria (Roman et al., 1993). The diagnosis of other types of dementia, including Parkinson's disease with dementia (n = 22), frontotemporal lobar degeneration (n = 3), progressive supra-nuclear palsy (n = 2), normal pressure hydrocephalus (n = 2), and corticobasal degeneration (n = 1) was made by using the individual criteria for each disease entity by an expert neurologist (Lee). Those patients with medical or neurological conditions and psychiatric illness that could have an effect on

^{*} Corresponding author. Tel.: +82 42 220 7801; fax: +82 42 252 8654. E-mail address: aelee@cnu.ac.kr (A.Y. Lee).

cognition were excluded, and drugs that possibly have an influence on cerebral function were not permitted.

2.2. Neuropsychological tests

The K-MMSE and the 3MS tests were given to all the patients to determine their general cognitive functioning. These tests which used widely at memory clinics in Korea have been validated reliability (Teng and Chui, 1987; Kang et al., 1997; Sohn et al., 2003). The SNSB, which is a structured neuropsychological battery for dementia evaluation, and frontal lobe function tests, like the contrast program, go-no-go, controlled oral word association test (COWAT) and Korean-color word Stroop tests (K-CWST) were also given. The SNSB includes about thirty tests evaluating attention, language and related functions, visuospatial functions, memory and frontal/executive functions. It also contains the K-MMSE, the Korean geriatric depression scale (K-GDS), the clinical dementia rating (CDR), and Barthel index for the activities of daily living (B-ADL). It is a battery, which provides in-depth evaluation for early and differential diagnosis of dementia. The subjects' cognitive function was evaluated by a neuropsychologist, who was not aware of the clinical or radiological information.

2.3. The CDT

For the CDT, all the subjects were given a sheet of paper with a circle of 10 cm diameter on it. They were then asked to follow two-step instructions: "This circle represents a clock face. Please draw all the numbers on it and set the hands at '10 past 11'." We scored the result of the CDT using the methods of Wolf-Klein et al. (1989), Shulman et al. (1993) and Watson et al. (1993). The CDT scoring was independently done by two neurologists who were kept "blind" to the clinico-radiological information.

2.4. Visual rating of the structural changes on the brain MRI

All the brain MRIs of the patients were reviewed by two neurologists who worked independently to measure such possible structural changes, as WMH, CA, VE, and MTA. The inter-rater and intra-rater reliability were high (k = 0.89 and 0.95, respectively).

The WMH was measured by three different grading protocols, including the scale that was used in the Cardiovascular Health Study (CHS) (Manolio et al., 1994), the scale of Fazekas et al. (1987), and the modified scale of Wahlund et al. (2001). The WMH was divided into PVH and DWMH in the scale of Fazekas et al. (1987). Cortical regions were divided into the frontal, temporal and parieto-occipital areas, and the basal ganglia were included in the modified scale of Wahlund et al. (2001).

CA was measured by VE and sulcal widening (SW); this was graded from 0 to 9 (Manolio et al., 1994). In the protocol of Pasquier et al. (1996), the SW was rated at the frontal, temporal and parieto-occipital areas, and VE was rated at the frontal and temporal areas, the occipital horns of the lateral ventricle and the third ventricle in both hemispheres from 0 (absent) to 3 (severe). The sum of all scores related with the SW and VE was called the CA score (Pasquier et al., 1996).

The MTA was rated on the coronal images from 0 (no atrophy) to 4 (severe atrophy) in both medial temporal lobes and we took into account the width of the choroids fissure, the height of the hippocampus and the width of the temporal horn (Korf et al., 2004).

2.5. Statistical analysis

The Pearson's partial correlation coefficients with controlling for age and the education level were used to determine bivariate relationships among the continuous variables, including the CDT, MMSE, 3MS tests, the SNSB scores and visual rating scales of the structural change of the brain. Multiple regression analysis was used to analyze if the PVH or the DWMH contributed more to the CDT score. The significance level was set at p < 0.05. The data was analyzed using SPSS-PC-software for Windows Version 13.0.

3. Results

3.1. Sample characteristics

Table 1 shows the baseline characteristics of the study population. The mean age of the total sample was 69.4 years (range: 42–82 years). The mean scores of the MMSE and 3MS tests were 21.6 and 67.2, respectively.

3.2. Neuropsychological tests

The results obtained by the methods of Wolf-Klein et al. (1989) and of Manos and Wu (1994) had positive correlations with the MMSE/3MS tests. In contrast, the methods of Watson et al. (1993) and of Shulman et al. (1993) gave negative correlations with the MMSE/3MS tests. Performance on the CDT showed a significant relationship with the results of the contrasting program, the go-nogo test and the color reading of the K-CSWT on the SNSB (Table 2).

3.3. Neuroimaging evaluation

Table 2 shows the relations between results of the CDT and each radiological variable. The degree of the cerebral WMH and the MTA was highly related to the results of all scoring methods of the CDT performance. In contrast, CA and VE revealed no significant correlations with the CDT results. For the method of Fazekas et al. (1987), the degree of the PVH was more important for the performance on the CDT than that of the DWMH on the multiple regression analysis (Table 3).

Table 1 Baseline characteristics of all participants (n = 84)

Variables		$\text{Mean} \pm \text{S.D}$
Demographics		
Age (years)		69.4 ± 8.2
Gender (male/female)		1/1.5
Education (years)		7.3 ± 4.0
HT (%)		34.9
DM (%)		19.5
Cognition		
MMSE		21.6 ± 4.9
3MS		67.2 ± 15.9
CDT	Watson et al. (1993)	3.7 ± 3.0
	Shulman et al. (1993)	3.3 ± 2.0
	Wolf-Klein et al. (1989)	6.1 ± 3.4
	Manos and Wu (1994)	5.9 ± 4.0
Neuroimaging		
WMH	Manolio et al. (1994)	2.4 ± 2.0
	Fazekas et al. (1987)	2.2 ± 1.4
	Wahlund et al. (2001), modified	8.6 ± 7.2
CA	Manolio et al. (1994)	4.1 ± 1.4
	Pasquier et al. (1996)	$\textbf{7.1} \pm \textbf{4.1}$
VE	Manolio et al. (1994)	4.1 ± 1.7
	Pasquier et al. (1996)	$\textbf{7.9} \pm \textbf{5.8}$
MTA		2.6 ± 1.9

HT = hypertension; DM = diabetes mellitus.

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