Original Paper

European Neurology

Eur Neurol 2005;53:140–145
DOI: 10.1159/000085832

Received: July 5, 2004
Accepted: March 9, 2005
Published online: May 17, 2005

Improvement Pattern in the Clock Drawing Test in Early Alzheimer's Disease

Jesús Cacho[a] Ricardo García-García[b,d] Bernardino Fernández-Calvo[a,b]
Silvia Gamazo[a] Roberto Rodríguez-Pérez[a] Aghostino Almeida[d]
Israel Contador[c]

[a]Section of Neurology, Salamanca University Hospital, [b]Department of Basic Psychology and Psychobiology, Salamanca University, and [c]Department of Personality, Evaluation and Psychological Treatments, Salamanca University, Salamanca, Spain; [d]Superior Institute of Maia (ISMAI), Porto, Portugal

Key Words
Clock drawing test · Improvement pattern · Early Alzheimer's disease

Abstract
Objective: The aim of this paper was to compare the performance of a group of patients with early Alzheimer's disease (EAD) against a control group of healthy control (HC) subjects in the Clock Drawing Test (CDT), i.e. verbal command versus copying of a clock model presented to the subject. ***Patients and Methods:*** The authors have studied 140 subjects; 70 patients with probable EAD, with a mean age of 76.4 ± 7.64 years and a clinical dementia rating stage 1 (mild dementia), and 70 HC with a mean age of 75.16 ± 6.34 years. ***Results:*** Patients in the EAD group obtained significantly higher scores on the copy command mode than on the verbal command mode ($Z = -7.129$, $p < 0.001$) – improvement pattern of the CDT – whereas no statistically significant differences were found in the HC group ($Z = -2.001$, $p < 0.080$). Within the group of EAD patients, we have noticed that there is a correlation between the copy command mode and the visual-constructive functions of the Cambridge Cognitive Examination (CAMCOG) ($r = 0.607$, $p < 0.01$), while the memory functions of the CAMCOG correlate with the verbal command mode ($r = 0.704$, $p < 0.01$). ***Conclusions:*** In our study, the EAD patients show an improvement pattern in the execution of the CDT copy command in comparison with the execution of the CDT verbal command, which we did not observe in the HC group. Such results might be associated with a greater deterioration of the memory functions when compared with the visual-constructive ones in the patients with EAD.

Introduction

The Clock Drawing Test (CDT) has achieved widespread clinical usage in recent years as a cognitive screening tool; a significant amount of the literature refers to its psychometric properties and clinical importance [1].

Up until now, different formats of presentation and scoring of the CDT have been published [1, 2]. Normally, this test is taken in two conditions: drawing the clock on verbal command or by asking the patient to copy it. Under the former, the patient is asked to draw 'by heart' (i.e. without having previous access to any model) an analog clock (including the numbers and the clock hands) showing a given time. Under the latter, the patient is asked to copy as exactly as possible the original drawing before

KARGER

Fax +41 61 306 12 34
E-Mail karger@karger.ch
www.karger.com

© 2005 S. Karger AG, Basel
0014–3022/05/0533–0140$22.00/0

Accessible online at:
www.karger.com/ene

Jesús Cacho Gutiérrez
Section of Neurology, Salamanca University Hospital
Paseo de San Vicente, 58–132
ES–37007 Salamanca (Spain)
Tel. +34 699 311 459, Fax +34 923 291 311, E-Mail lcacho@usal.es

him showing the same time as when he drew the clock on verbal command [1, 3].

The widest variations of application and scoring occur with regard to three aspects: (a) drawing the clock face either freehand or within a predrawn circle in response to a verbal command; (b) what time is to be set on the clock, and (c) whether the clock is drawn in two conditions (verbal command or copy) or in one condition only [3].

Most authors consider and score a single experimental condition, usually the verbal command mode [4, 13]. Few researchers assess and score both experimental conditions [3, 14–18], even though, as far as using the test as a screening device, they only take into account the verbal command condition. The fact that most published reports only consider the verbal command mode, with or without the predrawn circle, could in our opinion imply a loss of information since the functions evaluated in the CDT are different depending on whether the clock is drawn on verbal or copy command [19].

In our clinical practice, we noticed that when the CDT was used in the fashion presented in this paper, most subjects performed better on the copy command than on the verbal command mode, which we called 'improvement pattern' (IP) of the CDT. This is shown in the scores, which are higher for the copy command mode than for the verbal command mode. It is known that in early Alzheimer's disease (EAD) the visual-constructive functions are relatively intact, while, in contrast, memory and executive functions are already affected in the early stages of the disease [20–22]. Therefore, elderly subjects with EAD may be expected to more easily perform the CDT on copy than on verbal command. That is the reason why in this study the authors intended to establish whether patients with probable EAD performed better on the copy command as compared to the verbal command condition. The results were then compared with those obtained from a group of elderly healthy control (HC) subjects with the same age, sex and level of education. Our hypothesis was that the IP is present in a statistically significant fashion within the EAP group when compared to the HC group.

Patients and Methods

A total of 140 subjects were selected and evaluated at the Unit of Dementia and Memory of the Neurology Service of the Salamanca University Hospital (Salamanca, Spain), and all subjects gave their informed consent to participate in the study.

Selection of Elderly HC Subjects

This study included a total of 70 HC subjects (44 women and 26 men) with a mean age of 74.16 ± 6.01 years (range: 61–89 years) and a mean duration of schooling of 8.31 ± 3.65 years.

The HC group was formed by healthy, noninstitutionalized individuals leading an independent life, with intact activities of daily life, both basic and instrumental. Subjects with a history of psychiatric or neurological diseases or alcoholism were excluded, as were those subjected to psychopharmacological treatment. Elderly subjects scoring 2 or more points on the Lobo et al. [23] version of the Goldberg General Health Questionnaire (GHQ-28) were excluded. Cognitive impairment was determined using the Lobo et al. [23] version of the Mini Mental State Examination (MMSE) [24] and the Llinás et al. [25] version of the Cambridge Cognitive Examination (CAMCOG) leading to an average score of 28.37 ± 1.33 and 93.63 ± 4.83, respectively.

Selection of Elderly Subjects with EAD

The study included 70 patients diagnosed with probable AD (46 women and 24 men), with a mean age of 75.34 ± 6.81 years (range 64–89 years). The mean duration of schooling in this group was 7.29 ± 3.35 years. The mean score on the MMSE and CAMCOG was 23.01 ± 1.77 and 59.77 ± 13.02, respectively. The 70 patients in the EAD group were clinically diagnosed by the same neurologist (J.C.). The diagnosis of dementia was based on the DSM-IV criteria [26], and the diagnosis of AD on the NINCDS-ADRDA criteria [27]. All the patients meeting the criteria of 'probable' dementia of the Alzheimer type and mild dementia according to the clinical dementia rating (CDR stage 1) were included in this group [28].

Clinical Assessment

The patients and controls were subjected to the following intervention protocol: history (with the help of a relative or reliable caregiver), general and neurological clinical examination, and supplemental tests in the EAD group [complete blood count, general biochemistry, T4-TSH, vitamin B_{12} and folic acid, serologic testing for syphilis, apoE, a neuroimaging study (CT or MRI) and brain SPECT].

For the neuropsychological evaluation of the presence or absence of dementia, the MMSE [24] and CAMCOG [25] were used in all patients. When the EAD subjects were evaluated, none of them was taking a cholinesterase inhibitor.

CDT Application and Scoring

The CDT was performed on verbal command and on copy command. All subjects completed the two conditions in the same order: first on verbal command and then on copy command, in accordance with the instructions, criteria and scoring previously published [3]. The highest score possible in each of both conditions is 10.

Visual-Constructive Task

We applied the visual-constructive task of the CAMCOG, one of the sections of the praxis subscale, which consists in asking the subject to copy three geometric figures (two overlapping pentagons, a spiral and a three-dimensional house). The correct execution of each drawing scores 1 (maximum score: 3).

Statistical Analysis

Age, education and MMSE, CAMCOG and CDT scores of the two groups (HC and EAD subjects) were compared by means of the

Table 1. Mean and standard deviation (in parentheses) for the CDT measurements

Variable	HC group	EAD group
CDTCM	9.37 (0.91)	6.28 (1.05)
CDTCP	9.59 (0.78)	9.19 (0.95)
Memory (CAMCOG)	22.09 (2.58)	18.39 (4.01)
Copying (CAMCOG)	2.86 (0.35)	2.80 (0.40)

CDTCM = CDT command condition; CDTCP = CDT copy condition.

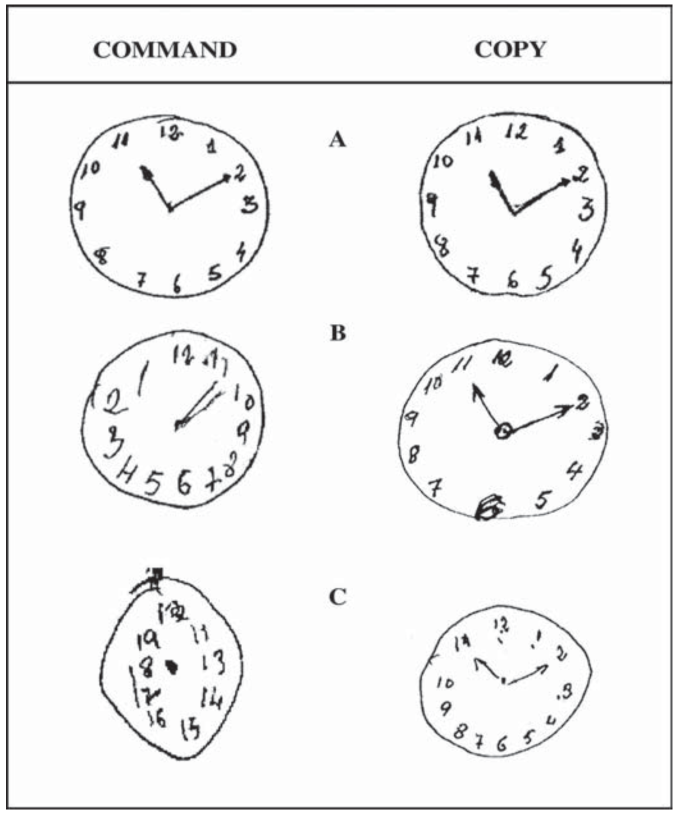

Fig. 1. A HC group: MMSE score = 30, complete primary education. **B** AD group (CDR stage 1): MMSE score = 24, minimum level of education. **C** AD group (CDR stage 1): MMSE score = 23, higher education.

Mann-Whitney U test. Comparisons within each group were made with the Wilcoxon two-sample test. The χ^2 test was used to compare nominal variables (for example, sex), and the Spearman correlational analysis to study the relationship between the variables was considered. In all tests, the significance level was $p < 0.05$.

Results

The EAD and HC groups did not differ in terms of age ($Z = 1.995$, $p = 0.079$), sex ($\chi^2 = 0.124$, $p = 0.724$), or years of schooling ($Z = -1.884$, $p = 0.065$). However, both groups differed in terms of degree of cognitive impairment as assessed by the MMSE (U = 112.500, $p < 0.001$) and CAMCOG (U = 128.000, $p < 0.001$).

Table 1 shows the mean scores of the HC and EAD groups for the verbal command and copy command conditions. The EAD patients scored significantly lower than the HC group in the verbal command (U = 1,334.00, p = 0.0001) and copy command (U = 1,717.50, p = 0.001) conditions. Moreover, significant differences between both groups in the CAMCOG memory task (U = 1,717.50, p = 0.001) were observed, while there were no significant differences (U = 2,310.00, p = 0.371) in the visual-constructive task of the CAMCOG.

Elderly HC subjects showed no significant differences between the scores obtained in the verbal command and copy command conditions ($Z = -2.001$, $p < 0.080$), whereas the EAD group showed a significant difference in the performance of the CDT on verbal command as compared to the copy command condition ($Z = -7.129$, $p < 0.001$). In other words, EAD patients showed a significantly better performance and score in the CDT when copying a clock model than when the clock was drawn on a verbal command; this is what we called IP (figure 1 shows some examples of IP).

Consequently, when we compared the presence of IP in both groups, we came to the conclusion that there was a significantly larger presence of IP in the EAD group than in the HC counterpart ($\chi^2 = 71.976$, $p < 0.001$; fig. 2).

Moreover, with regard to the MMSE and the presence or absence of IP, we have also noticed significant differences ($\chi^2 = 65.545$, d.f. = 2, $p < 0.001$), i.e. when the MMSE scores decreased (increase in cognitive impairment), the values of IP increased (fig. 3).

CDT and CAMCOG

The scores of both conditions of the CDT correlated significantly in the HC group ($r = 770$, $p < 0.01$) while not in the EAD group ($r = -0.039$, $p = 0.747$).

In the HC group, the scores of the CDT verbal command ($r = 0.401$, $p < 0.01$) and of the CDT copy command ($r = 0.445$, $p < 0.01$) correlated significantly with the score of the copying task of the CAMCOG. Moreover, the

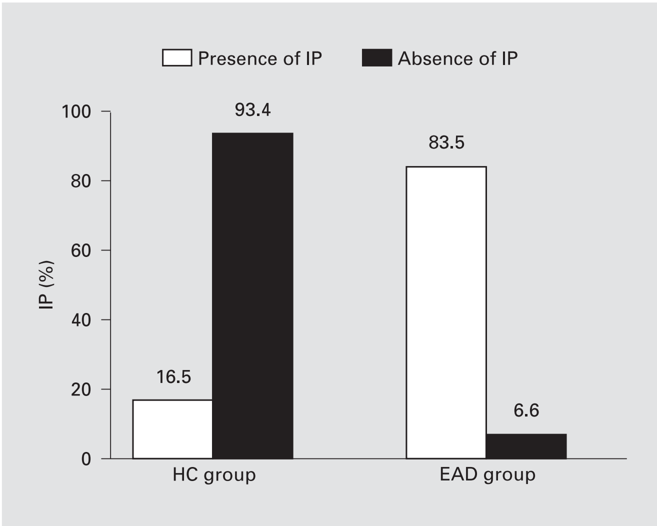

Fig. 2. Distribution of IP in the EAD and HC groups.

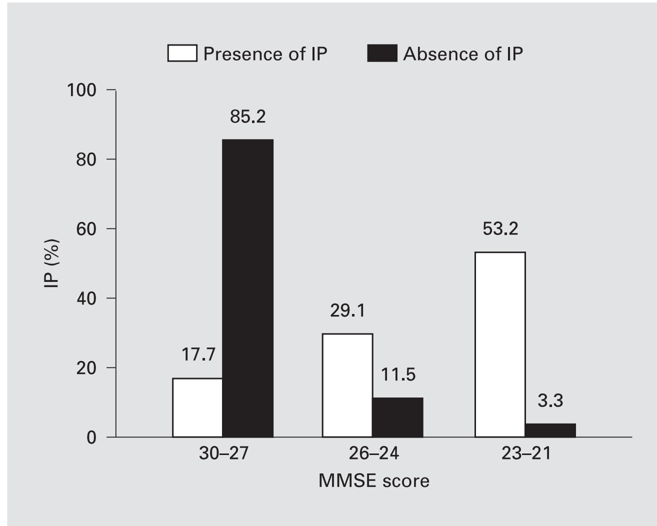

Fig. 3. IP and cognitive deficit.

scores of the CDT verbal command ($r = 0.781$, $p < 0.01$) and of the CDT copy command ($r = 0.415$, $p < 0.01$) also correlated significantly with the score of the memory subscale of the CAMCOG.

However, in the EAD group, the score of the praxis subscale CAMCOG correlated solely with the CDT copy command ($r = 0.607$, $p < 0.01$), whereas the CAMCOG memory subscale correlated with the CDT verbal command ($r = 0.704$, $p < 0.01$).

CDT and SPECT

Finally, we have found out using SPECT that 54.7% of the patients with EAD showed a pattern of hypoperfusion in the medial temporal left area, while 6.3% of the patients exhibited a pattern of hypoperfusion in the temporal-parietal right area. The rest of the patients with EAD (39%) exhibited other types of patterns of hypoperfusion (e.g. pattern of multifocal hypoperfusion).However, the type of hypoperfusion present in the EAD patients was not related with the presence or absence of IP ($\chi^2 = 3.538$, $p = 0.171$).

Discussion

The aim of the present study was to investigate whether the patients with probable EAD would perform better on the copy command mode of the CDT than on the verbal command mode, that is, whether the IP was proportionally more frequent in the EAD group than in the HC group. As a matter of fact, as we were able to demonstrate in our study, the IP allowed us to differentiate between the EAD group and the HC group.

The results obtained in our study showed that patients in the EAD group performed significantly better in the CDT when copying the clock than when drawing it on a verbal command, while elderly subjects from the HC group performed similarly well in both conditions.

Yet even if the IP is present both in the EAD patients and in the HC group, it was significantly more frequent in the EAD group. In fact, whereas in the HC group there was an IP in 17% of the cases, it was present in 83% of the EAD patients (fig. 2), that is, the IP is almost five times more frequent in the EAD group than in the HC group.

The reason for the existence of an IP in EAD appears to be the fact that the copy command condition mainly explores visual-constructive and perceptual functions [1, 3, 9], while the verbal command condition analyzes other functions such as receptive language, memory or certain executive functions [1, 3, 9, 15, 16]. In fact, it has recently been reported that the visual-constructive functions are relatively intact in the early stages of AD, and become impaired in later stages of the condition [19]. By contrast, the memory functions are affected already at the onset of the disease [21, 22, 29, 30].

In this sense, in our study, we have obtained a significant correlation between the memory subscale of the CAMCOG and the verbal command mode of the CDT in the EAD group, while, at the same time, we have observed a correlation between the visual-constructive task of the CAMCOG and the copy command mode of the CDT. Besides, when we compared both groups (EAD and HC), we have realized that the praxis subscale of the CAMCOG is preserved in both groups, whereas the memory subscale of the CAMCOG is solely altered in the EAD group.

We may therefore infer that the verbal command mode of the CDT implies a greater participation of the memory aspects (which is altered in our EAD group), while the copy command mode of the CDT implies a greater participation of the visual-constructive component (which is normal in our EAD group).

On the other hand, only one of the application conditions of the test, usually the verbal command condition, has generally been evaluated and scored [4–13]. Although some authors have noted an IP with the copy command as compared to the verbal command in the CDT, this fact may not have been sufficiently emphasized in the published reports [14, 16–18, 31]. For example, Rouleau et al. [16] compared the performance on the CDT (verbal command and copy command mode) of 25 AD patients, 25 equally demented patients with Huntington's disease, and 25 HC. They were able to demonstrate that, on the verbal command condition, both groups of patients performed equally well on the CDT, while significantly worse than the HC group. On the copy condition, however, patients with AD, but not Huntington's disease, evidenced a marked improvement in performance.

The fact that in our study the patients with AD were in the initial stage of the disease (CDR stage 1) could well explain the fact that they got a higher score in the copy condition in comparison with the patients studied by Rouleau et al. [16] (9.19 vs. 7.88). We could even state that the patients with a mild cognitive deficit exhibited a marked improvement when we compared their performance in the copy condition versus the verbal command condition. This possible effect of the mild cognitive deficit on the improvement in the patients' performance on the CDT, when both conditions were taken into account, remained reflected in our study in that when such cognitive deficit worsened, we noticed an improvement in the CDT performance on the copy condition compared to the verbal command condition (IP more frequent; fig. 3).

One aspect that seemed interesting to underscore was that the IP could be of clinical value in the screening for EAD thereby becoming an adequate neuropsychological tool for the evaluation of those subjects whose performance on the command condition is negative. Thus, in our study, of the 7 patients with EAD whose scores in the verbal command condition remained above the cutoff point (false-negative rate) 4 presented an IP. Similarly, of the 5 HC participants whose scores in the CDT verbal command condition were positive (false-positive rate) 3 did not show any IP.

Unfortunately, in our study, we were not able to explain the IP in association with a specific structural or functional alteration because the data we obtained through neuroimaging (be they structural or functional) did not allow us to establish a relationship between the hippocampus SPECT patterns and the presence or absence of IP, probably because the EAD group members are in the early stage of dementia (CDR stage 1) and the SPECT data reveal a very low sensitivity in the early stages of the disease [32].

This study has some limitations. (a) Only two groups of subjects (EAD and HC) were included. In order for the IP to have a more 'generalizable' value as far as screening for dementia is concerned, it would be advisable to conduct other studies including patients with other types of dementia (e.g. Parkinson with dementia, frontotemporal dementia, Lewy bodies disease). (b) There is no pathological confirmation of our cases, and the diagnosis of AD or the HC status cannot therefore be totally confirmed, though we have monitored the course of the patients for 24 months, and in all cases the diagnosis of probable AD or the HC status was confirmed before inclusion of the subjects in the study.

To summarize, a case-control study analyzing the behavior of two groups of elderly subjects (EAD and HC) in the performance of the CDT (verbal and copy command conditions) is reported. EAD patients showed significantly better performance in the copy command versus the verbal command condition. We have called this phenomenon the IP of the CDT, and suggest that it may be of diagnostic value in screening for EAD.

References

1 Shulman KI: Clock-drawing: Is it the ideal cognitive screening test? Int J Geriatr Psychiatry 2000;15:548–561.
2 Brodaty H, Moore CM: The clock drawing test for dementia of the Alzheimer's type: A comparison of three scoring methods in a memory disorders clinic. Int J Geriatr Psychiatry 1997; 12:619–627.
3 Cacho J, García-García R, Arcaya J, Vicente JL, Lantada N: A proposal for the application and scoring of the clock drawing test in Alzheimer's disease (in Spanish). Rev Neurol 1999;28:648–655.
4 Goodglass H, Kaplan E: The Assessment of the Aphasia and Related Disorders. Philadelphia, Lea and Febiger, 1983.
5 Shulman KI, Shedletsky R, Silver IR: The challenge of time: Clock drawing and cognitive function in the elderly. Int J Geriatr Psychiatry 1986;1:135–140.
6 Sunderland T, Hill JL, Mellow AM, et al: Clock drawing in Alzheimer's disease. A novel measure of dementia severity. J Am Geriatr Soc 1989;37:725–729.
7 Mendez MF, Ala T, Underwood KL: Development of scoring criteria for the clock drawing task in Alzheimer's disease. J Am Geriatr Soc 1992;40:1095–1099.
8 Manos PJ, Wu R: The ten point clock test: A quick screen and grading method for cognitive impairment in medical and surgical patients. Int J Psychiatry Med 1994;24:229–244.
9 Freedman M, Leach L, Kaplan E, Winocur G, Shulman K, Delis DC: Clock Drawing: A Neuropsychological Analysis. New York, Oxford University Press, 1994.
10 Wolf-Klein GP, Silverstone FA, Levy AP, Brod MS: Screening for Alzheimer's disease by clock drawing. J Am Geriatr Soc 1989;37:730–734.
11 Watson YI, Arfken CL, Birge SJ: Clock completion: An objective screening test for dementia. J Am Geriatr Soc 1993;41:1235–1240.
12 Fujii DE: The clock drawing test as a screening measure for dementia of the Alzheimer type: Development and validation of the theoretically based scoring criteria. Diss Abstr Int 1993;53:2059.
13 Death J, Douglas A, Kenny RA: Comparison of the clock drawing with Mini-Mental State Examination as a screening test in elderly acute hospital admissions. Postgrad Med J 1993;69: 696–700.
14 Libon DJ, Swenson R, Barnoski E, Sands LT: Clock drawing as a assessment tool in dementia. Arch Clin Neuropsychol 1993;8:405–416.
15 Royall DR, Mulroy AR, Chiodo LK, Polk MJ: Clock drawing is sensitive to executive control: A comparison of six methods. J Gerontol B Psychol Sci Soc Sci 1999;54:328–333.
16 Rouleau I, Salmon DP, Butters N, Kennedy C, McGuire K: Quantitative and qualitative analyses of clock drawings in Alzheimer's and Huntington's disease. Brain Cogn 1992;18:70–87.
17 Albert MS, Moss M: Assessment of memory disorders in patients with Alzheimer′s disease; in Squire LR, Butters N (eds): Neuropsychology of Memory. New York, The Guilford Press, 1984.
18 Gnanalingham KK, Byrne EJ, Thornton A, Sambrook MA, Bannister P: Motor and cognitive function in Lewy body dementia: Comparison with Alzheimer's and Parkinson's diseases. J Neurol Neurosurg Psychiatry 1997;62: 243–252.
19 South M, Greve K, Bianchini K, Adams D: Interrater reliability of three clock drawing test scoring system. Appl Neuropsychol 2001;8: 174–179.
20 Cahn-Weiner D, Sullivan E, Shear P, Fama R, Lim K: Yesavage Jornal. Brain Structural and cognitive correlates of clock drawing test performance in Alzheimer's disease. J Int Neuropsychol Soc 1999;5:502–509.
21 Kertesz A, Mohs RC: Cognition; in Gauthier S (ed): Clinical Diagnosis and Management of Alzheimer's Disease, ed 2. London, Martin Dunitz, 2001, pp 179–196.
22 Perry RJ, Hodges JR: Attention and executive deficits in Alzheimer's disease. Brain 1999; 122:383–404.
23 Lobo A, Pérez Echevarria MJ, Artal J: Validity of the scaled version of the General Health Questionnaire (GHQ-28) in a Spanish population. Psychol Med 1986;16:135–140.
24 Lobo A, Ezquerra J, Gómez FB, Sala JM, Seva A: El miniexamen cognoscitivo. Un test sencillo y práctico para detectar alteraciones intelectuales en pacientes médicos. Actas Luso Esp Neurol Psiquiatr 1979;7:189–202.
25 Llinás-Reglá J, Vilalta-Franch J, López-Pousa S: CAMDEX. Examen Cambridge para trastornos mentales en la vejez (Roth-Huppert-Tym-Mountjoy). Adaptación y validación española. Barcelona, Ancora, 1991.
26 American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, ed 4. Washington, American Psychiatric Association, 1994.
27 McKhann G, Drachman D, Folstein M, Katzman R, Price D, Stadlan EM: Clinical diagnosis of Alzheimer's disease: Report of the NINCDS-ADRDA Work Group under the auspices of Department of Health and Human Services Task Force on Alzheimer's Disease. Neurology 1984;34:939–944.
28 Hughes CP, Berg L, Danziger WL, Coben LA, Martin RL: A new clinical scale for the staging of dementia. Br J Psychiatry 1982;140:566–572.
29 Royall DR: Comments on the executive control of clock-drawing. J Am Geriatr Soc 1996; 44:218–219.
30 Duke LM, Kaszniak AW: Executive control functions in degenerative dementias: A comparative review. Neuropsychol Rev 2000;10: 75–99.
31 Libon DJ, Malamut BL, Swenson R, Prouty Sands L, Cloud BS: Further analyses of clock drawing among demented and nondemented older subjects. Arch Clin Neuropsychol 1996; 11:193–205.
32 Jagust W, Thisted R, Devous MD SR, et al: SPECT perfusion imaging in the diagnosis of Alzheimer's disease: A clinical-pathologic study. Neurology 2001;56:950–956.