


Clock Drawing Test: Is It Useful for Dementia Screening in Patients Having Parkinson Disease With and Without Depression?

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Abstract

Despite the wide use of clock drawing tests (CDTs) for screening cognitive impairment, their use in patients having Parkinson disease (PD) with dementia has not been systematically investigated until date. In this cross-sectional study, neurological and neuropsychiatric statuses of 1449 outpatients having PD with and without dementia were comprehensively assessed. The CDT revealed cognitive impairment in 42.7% of the 1383 patients whose drawings were available. Overall, CDT sensitivity and specificity were 70.7% and 68.9%, respectively. The positive and negative predictive values were 48.0% and 85.3%, respectively. In patients with depression, CDT specificity dropped significantly to 55.8% (71.3% in nondepressed patients, $P < .001$). Classification performance was not impacted by motor symptoms. The estimated classification performances and predictive values correspond to those reported previously for non-PD populations. Our results indicate that CDT is a suitable screening instrument in patients with PD, but test results from patients with depression warrant careful consideration.

Keywords

clock drawing test, Parkinson disease, dementia, depression, screening, cognition

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Introduction

With demographic aging and migration, cognitive screening instruments that are largely independent of language and can be administered easily are becoming increasingly important. Among those, the clock drawing tests (CDTs) have become popular because of their brevity and comprehensibility.^{1,2} A number of CDTs are available with different ways to administer the test and to evaluate the results.³ Although the main task that involves drawing a clock face at a particular time usually remains the same, some variants recommend to present a pre-drawn circle to the patient, while others require that patients draw the circle on their own.^{4,5} In addition, more than a dozen scoring systems have been described, ranging from scoring on a 3- to a 33-point scale.^{6,7}

Initially developed to detect frontoparietal deficits,⁸ the CDTs are now widely used for screening of cognitive deficits in Alzheimer disease (AD) as well as in other disorders such as schizophrenia.^{9,10} The CDTs rely primarily on executive functions, and their completion require a number of cognitive domains including comprehension, visuospatial abilities and memory, programming and execution of motor action,

abstraction, concentration, and response inhibition.¹¹ These are impaired early on in patients having Parkinson disease (PD) and dementia or having dementia with Lewy bodies (DLB). Most studies on the psychometric properties in such patients have been conducted on small study samples and produced partly inconclusive results. Saka and Elibol reported differences in clock drawing performance of patients having AD and PD with dementia.¹² This was not replicated by Fukui and Lee who compared clock drawing performance between patients with AD and DLB.¹³ However, general differences in performance in drawing tasks between patients with AD and DLB

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have been discussed previously and are probably related to metabolic and structural abnormalities in the brain.¹⁴⁻¹⁶ However, to the best of our knowledge, comprehensive investigations on the utility of CDTs in outpatients having PD with and without depression have not been carried out to date.

We previously reported data from a large prevalence study on 1449 outpatients having PD with and without dementia and depression.^{17,18} Here, we discuss the utility of the CDT as a screening device in this patient population, describing the classification performance and predictive values for the CDT in our patient sample.

Methods

Study Design and Assessment

The German Study on the Epidemiology of Parkinson Disease with Dementia (GEPAD) was a cross-sectional study conducted within the German outpatient specialty care system. A representative nationwide sample of 315 office-based neurologists examined 1449 patients with PD and appraised their neurological and neuropsychiatric status with standardized instruments. For each patient, PD evaluation included the Hoehn and Yahr (HY) staging scheme and parts I, II, and IV of the Unified Parkinson Disease Rating Scale (UPDRS).^{19,20} Each patient was also comprehensively evaluated regarding the presence of cognitive impairment and dementia. Dementia was diagnosed using criteria of the *Diagnostic and Statistical Manual of Mental Disorders* (fourth edition, text revision [DSM-IV-TR]) during a structured clinical interview.^{21,22} For cognitive impairment screening, the Mini-Mental State Examination (MMSE) and the CDT (described in the next section) were applied.^{23,24} Moreover, each patient was screened for depression with the Montgomery-Asberg Depression Rating Scale (MADRS).²⁵ A cutoff score of ≥ 14 (out of 60 maximum) has been established as an indicator for the presence of depression in PD.²⁶ More comprehensive descriptions of the assessment and the study design were given in the previous publications.^{18,27}

Clock Drawing Test

In GEPAD, the CDT described by Shulman et al was applied.²⁸ Each patient was presented a predrawn circle (diameter: 3.9 inches) and instructed to draw the face of a clock by putting in all the numbers in their proper locations and to set the time at 10 past 11. The physicians rated the drawing on a scale ranging from 1 ("perfect") to 6 ("no recognizable clock"). Physicians were provided with formal descriptions and example drawings for each rating.³ Patients with a score ≥ 3 were classified to have cognitive impairment.²⁸ To ensure data quality, each drawing was independently reevaluated by 2 trained psychometricians (clinical psychologists) who were blinded to the physician's rating and the patient's dementia status. Patients without clock drawings ($n = 66$, see Results section) were eliminated from further analyses.

Statistics

We used the nonparametric Mann-Whitney test for continuously distributed data and the chi-square test for categorical variables to investigate the differences between the patient groups. Exact confidence intervals (CIs) were calculated for the proportion of dementia in subgroups.²⁹ The area under the receiver—operating characteristics curve (area under curve [AUC]) was estimated for evaluating classification performance of the CDT with respect to dementia. The accuracy of the prediction of dementia by the CDT was also investigated by the classification performance measures of sensitivity and specificity as well as by the positive and negative predictive values (PPV and NPV). The collinearities of the CDT with the MMSE and MADRS were determined with linear regression analyses. Statistical inference was based on a significance level of 5%. For standard errors, CI, and P values, the Huber-White sandwich estimator was implemented to consider the clustered sampling design.³⁰

Ethics

The study was approved by the local ethics committee (Technische Universität Dresden, August 11, 2005, no. EK140082 005). Written informed consent was obtained from all the participating patients or their caregivers.

Results

Clock Drawing Test Rating Distributions

The CDT ratings were distributed as follows: 1: $n = 445$ (30.7%), 2: $n = 350$ (24.2%), 3: $n = 309$ (21.3%), 4: $n = 192$ (13.3%), 5: $n = 64$ (4.4%), and 6: $n = 23$ (1.6%). Clock drawings were unavailable for 66 (4.6%) patients. These patients were of older age (74.9 vs 70.5 years, $P < .001$), had a higher mean HY score (2.4 vs 1.6, $P < 0.001$), a higher UPDRS II score (18.0 vs 8.9, $P < .001$), and were more often diagnosed with dementia (54.5% vs 28.9%, $P < .001$). Overall, 47.2% of all the patients were rated ≥ 3 on the CDT. Characteristics of the study sample with available CDT ratings ($n = 1383$) are shown in Table 1.

Patients with cognitive impairment according to the CDT differed from patients without impairment on all measures except for PD duration, which was similar in both the groups ($P = .500$).

Validity of the CDT for the Clinical Diagnosis of Dementia

The CDT cutoff correctly classified 70.5% of all patients with dementia according to DSM-IV and 68.9% of all patients without dementia. Thus, 29.5% of the patients with dementia were missed by the cutoff (false negative), and 31.1% were erroneously classified to have cognitive impairment (false positive). The CDT ratings significantly correlated with the dementia diagnosis (contingency coefficient: 0.343, $P < .001$).

Compared to patients with dementia, patients with a false-negative classification had a younger age of PD onset (63.6

Table 1. Patient Characteristics (for Whom Clock Drawings Were Available).

	CDT Score		P Value	Total
	≤2	≥3		
N (%)	793 (57.3)	590 (42.7)	—	1383 (100)
Sociodemographic				
Male: female (%)	64.1:35.9	55.6:44.4	<.01	60.4:39.6
Age, years (mean ± SD)	68.9 ± 8.6	72.6 ± 7.4	<.001	70.5 ± 8.3
Age groups (%)				
≤65 years	31.9	15.3	<.001	24.8
66—70 years	25.1	24.4		24.8
71—75 years	20.6	23.2		21.7
≥76 years	22.4	37.1		28.7
Neurological status				
Age of PD-onset, years (mean ± SD)	63.3 ± 9.7	66.7 ± 9.2	<.001	64.7 ± 9.2
PD duration, years (mean ± SD)	5.7 ± 5.2	5.8 ± 5.0	.500	5.7 ± 5.1
Hoehn and Yahr status				
Mild (stages I + II)	50.8	37.9	<.001	45.3
Moderate (stage III)	37.2	42.4		39.4
Severe (stages IV + V)	12.0	19.7		15.3
UPDRS I score (mean ± SD)	2.2 ± 1.9	3.3 ± 2.5	<.001	2.6 ± 2.2
UPDRS II score (mean ± SD)	7.8 ± 5.4	10.6 ± 6.6	<.001	8.9 ± 6.1
UPDRS IV score (mean ± SD)	2.5 ± 2.9	2.9 ± 3.3	<.05	2.7 ± 3.1
Neuropsychiatric status				
Dementia (%)	14.6	48.1	<.001	28.9
Depression (%)	18.6	34.5	<.001	25.4
MMSE score (mean ± SD)	28.4 ± 1.9	25.6 ± 4.1	<.001	27.2 ± 3.3

Abbreviations: CDT, clock drawing test; PD, Parkinson disease; UPDRS, Unified Parkinson Disease Rating Scale; MMSE, Mini-Mental State Examination; SD, standard deviation.

± 9.5 vs 68.1 ± 8.5 years, $P < .01$), lower scores on the UPDRS I (3.5 ± 2.0 vs 4.3 ± 2.6, $P < .01$) and UPDRS II (9.9 ± 5.0 vs 12.8 ± 6.9, $P < .01$), and a higher MADRS score (8.7 ± 6.7 vs 6.8 ± 6.5, $P < .01$). Compared to patients without dementia, false positives were older (71.0 ± 7.8 vs 68.6 ± 8.6 years, $P < .01$) and had a later onset of PD (65.3 ± 0.7 vs 63.3 ± 9.7, $P < .01$). The distribution of HY-stages did not differ between patients without dementia and false positives ($P = .659$), but there was a trend toward lower HY-scores in false negatives.

Table 2 compares the classification performances of the CDT with a cutoff ≥3 against the clinical diagnosis according to *DSM-IV* criteria in terms of sensitivities, specificities, PPVs, and NPVs.

All 4 measures varied considerably, and the highest sensitivity values were observed in older patients and at higher PD severity stages. Specificity was lowest in patients with depression, and younger patients exhibited the lowest sensitivity (48.9%) and highest specificity (77.3%) and NPV (90.5%). The lowest NPV was shown for patients with depression (65.4%). The differences in classification performance and predictive value are shown in Table 3.

Sensitivity and PPV significantly increased from the youngest to the oldest patients, while specificity and NPV showed significantly decrease. Increasing PD severity did not affect CDT specificity but was significantly associated with higher sensitivity and PPV and with lower NPV. The CDT had

significantly lower specificity, lower NPV, and higher PPV for patients having PD with depression than for those without depression.

Impact of Motor Impairment on CDT Validity

We tested the impact of motor impairment due to tremor on CDT validity using logistic regression analyses (data not shown). The odds ratio (OR) for the crude association between a CDT score ≥3 and the presence of dementia was 5.4 (95% CI: 4.2—7.0). This association remained significant after adjusting for tremor and micrography (“handwriting”) to the corresponding UPDRS II subitems (OR = 5.0; 95% CI: 3.8—6.5).

Collinearity Analyses

We next analyzed the dependencies of the MADRS and MMSE from the CDT (Figure 1).

There were moderate collinearities between the CDT and the MMSE ($r = -.52$, $P < .001$), and the MADRS had a small correlation with the CDT ($r = .21$, $P < .0001$).

Discussion

We investigated the sensitivity, specificity, PPV, and NPV of the CDT in a large sample of outpatients with PD and dementia.

Table 2. Classification Performance and Predictive Values of the CDT (Cutoff 2/3) Compared to the Clinical Diagnosis of Dementia.

	Dementia, % (95% CI)	Classification Performance			Predictive Value	
		AUC (95% CI)	Sensitivity, % (95% CI)	Specificity, % (95% CI)	PPV, % (95% CI)	NPV, % (95% CI)
Total sample	28.9 (26.5—31.3)	74.9 (72.0—77.7)	70.7 (65.9—75.1)	68.9 (65.9—71.8)	48.0 (43.9—52.1)	85.3 (82.6—87.7)
Gender						
Male	30.3 (27.2—33.4)	74.7 (71.1—78.3)	66.4 (60.2—72.2)	72.7 (68.9—76.3)	51.4 (45.8—56.9)	83.3 (79.7—86.4)
Female	26.7 (23.0—30.4)	75.8 (71.1—80.4)	78.1 (70.5—84.5)	63.3 (58.4—68.1)	43.7 (37.6—49.9)	88.8 (84.6—92.2)
Age group						
≤65 years	13.7 (10.1—17.4)	69.3 (61.1—77.4)	48.9 (34.1—63.9)	77.3 (72.1—81.9)	25.6 (16.9—35.8)	90.5 (86.2—93.8)
66—70 years	29.7 (24.9—34.6)	71.0 (64.9—77.1)	65.7 (55.6—74.8)	68.5 (62.2—74.3)	46.9 (38.5—55.4)	82.5 (76.5—87.5)
71—75 years	31.7 (26.4—37.0)	76.5 (70.8—82.2)	73.7 (63.6—82.2)	67.3 (60.4—73.7)	51.1 (42.4—59.7)	84.7 (78.2—89.8)
≥76 years	39.0 (34.2—43.9)	74.5 (69.6—79.4)	78.7 (71.4—84.9)	60.3 (53.9—66.5)	56.0 (49.1—62.7)	81.6 (75.1—87.0)
PD severity (Hoehn and Yahr)						
Mild (stages I + II)	18.4 (15.3—21.5)	70.0 (64.6—75.3)	60.4 (50.6—69.5)	70.4 (66.1—74.4)	31.5 (25.3—38.2)	88.7 (85.2—91.7)
Moderate (stage III)	33.3 (29.3—37.4)	72.7 (68.1—77.3)	69.1 (61.7—75.9)	66.6 (61.4—71.5)	50.8 (44.3—57.4)	81.2 (76.2—85.5)
Severe (stages IV + V)	47.5 (40.6—54.5)	79.0 (72.7—85.2)	81.3 (72.0—88.5)	68.9 (59.1—77.5)	70.3 (60.9—78.6)	80.2 (70.6—87.8)
PD duration						
≤5 years	25.1 (22.0—28.2)	75.9 (71.9—79.9)	70.7 (63.7—77.1)	70.3 (66.3—74.0)	44.3 (38.6—50.2)	87.8 (84.4—90.7)
6—10 years	32.7 (27.9—37.5)	75.6 (70.4—80.8)	72.7 (63.9—80.4)	67.1 (60.9—72.9)	51.8 (44.0—59.5)	83.5 (77.6—88.4)
≥11 years	32.8 (26.1—39.5)	70.0 (62.1—77.9)	61.9 (48.4—73.9)	71.3 (62.7—78.9)	51.3 (39.6—63.0)	79.3 (70.8—86.3)
Depression status						
No depression	22.8 (20.2—25.4)	74.5 (70.9—78.1)	69.6 (63.2—75.4)	71.3 (68.0—74.5)	41.8 (36.8—46.9)	88.8 (86.1—91.2)
Depression	50.5 (44.9—56.0)	72.0 (64.7—77.4)	72.3 (64.7—79.1)	55.8 (47.6—63.7)	62.5 (55.1—69.5)	66.4 (57.6—74.4)

Abbreviations: AUC, area under curve; PPV, positive predictive value; NPV, negative predictive value; PD, Parkinson disease; CDT, clock drawing test; CI, confidence interval.

Table 3. Tests of Differences in Classification Performance and Predictive Values of the CDT (Cutoff 2/3) Compared to the Clinical Diagnosis of Dementia.^a

	Classification Performance			Predictive Value	
	Dementia χ^2 (df), P Value	Sensitivity χ^2 (df), P Value	Specificity χ^2 (df), P Value	PPV χ^2 (df), P Value	NPV χ^2 (df), P Value
Gender					
Male	Reference	Reference	Reference	Reference	Reference
Female	2.10 (1), .148	6.09 (1), .014	9.66 (1), .002	3.45 (1), .063	4.72 (1), .030
Age group					
≤65 years	Reference	Reference	Reference	Reference	Reference
66—70 years	25.74 (1), <.001	3.77 (1), .052	5.28 (1), .022	10.57 (1), .001	5.64 (1), .018
71—75 years	29.81 (1), <.001	8.52 (1), .004	6.13 (1), .013	14.65 (1), <.001	2.79 (1), .095
≥76 years	59.21 (1), <.001	15.78 (1), <.001	18.08 (1), <.001	23.64 (1), <.001	6.60 (1), .010
PD severity (HY)					
Mild (stages I + II)	Reference	Reference	Reference	Reference	Reference
Moderate (stage III)	33.21 (1), <.001	2.33 (1), .127	1.39 (1), .239	17.38 (1), <.001	7.65 (1), .006
Severe (stages IV + V)	67.38 (1), <.001	10.71 (1), .001	0.10 (1), .757	44.47 (1), <.001	5.80 (1), .016
PD duration					
≤5 years	Reference	Reference	Reference	Reference	Reference
6—10 years	7.23 (1), .007	0.14 (1), .706	0.84 (1), .360	2.41 (1), .121	2.16 (1), .141
≥11 years	4.69 (1), .030	1.71 (1), .191	0.05 (1), .817	1.19 (1), .275	6.41 (1), .011
Depression status					
No depression	Reference	Reference	Reference	Reference	Reference
Depression	88.45 (1), <.001	0.35 (1), .556	14.65 (1), <.001	21.37 (1), <.001	44.32 (1), <.001

Abbreviations: df, degrees of freedom; PPV, positive predictive value; NPV, negative predictive value; PD, Parkinson disease; CDT, clock drawing test; HY, Hoehn and Yahr.

^a Significant differences from the reference group are shown in bold.

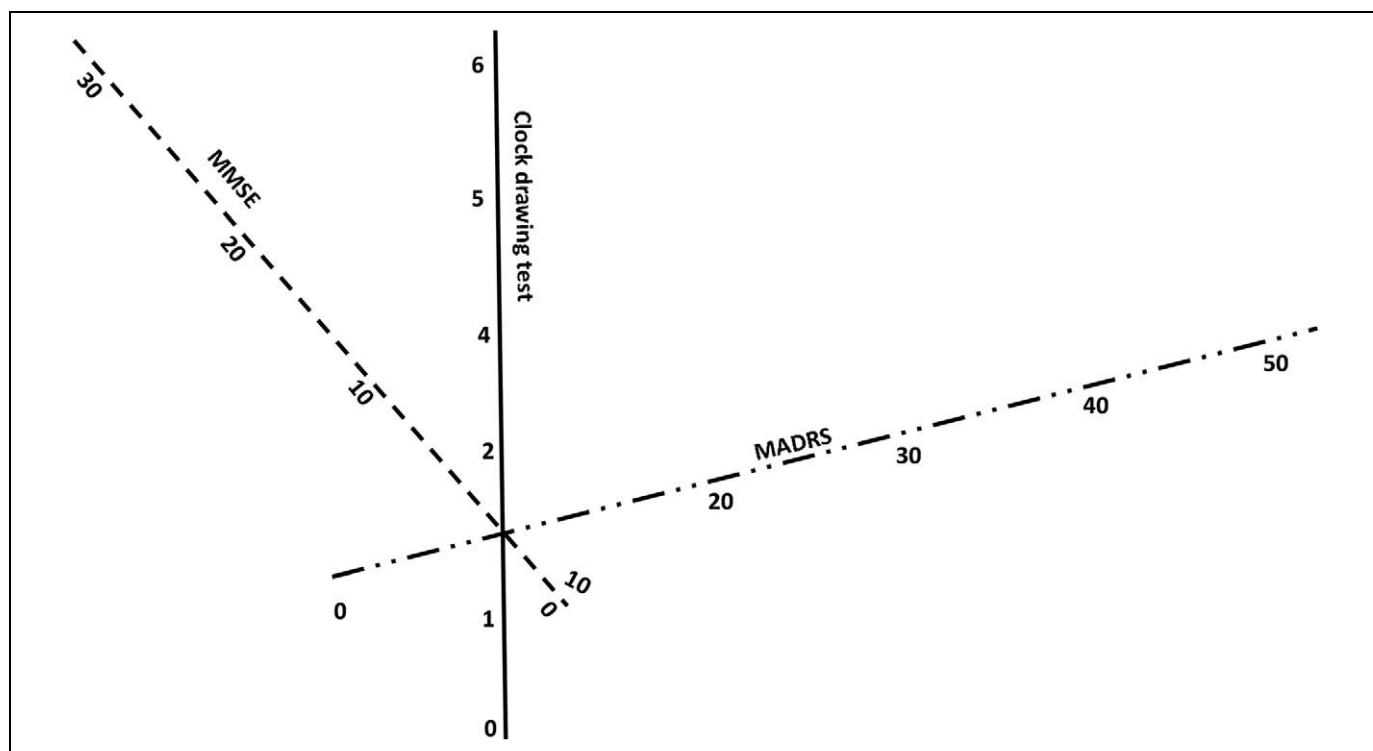


Figure 1. Collinearities among the clock drawing test (CDT), Mini-Mental State Examination (MMSE), and Montgomery-Asberg Depression Rating Scale (MADRS).

The sensitivities and specificities ranged from 48.9% to 71.3% and 55.8% to 77.3%, respectively. Classification performance and predictive value were significantly associated with gender, age, depression, and PD severity but not with duration of PD. Sensitivities were highest in female patients and patients of advanced age and PD stage and lowest in patients younger than 65 years old. Specificity was greatest in males and younger patients and lowest in patients who were older or depressed.

Overall, more than 4 of 10 patients were classified to have cognitive impairment when using the CDT cutoff proposed by Shulman et al.²⁸ These rates are clearly different from the low rates of cognitive impairment according to the MMSE (15.5%) that were previously reported in this patient population.¹⁸ On the other hand, the frequency of clinically diagnosed dementia according to *DSM-IV* criteria was substantially lower than that of cognitive impairment according to the CDT, which potentially could be explained by an influence of motor impairment on the clock ratings by the physicians (ie, patients without dementia were classified to have dementia due to the poor quality of their drawings rather than underlying conceptual errors). It should be noted, however, that the classification of patients according to the CDT was found to be robust against the presence of tremor and micrography. Although sensitivity was similar in patients with and without depression, CDT specificity dropped sharply from 71.3% to 55.8% in patients with a cutoff above 13 on the MADRS, indicating that almost every other patients with depression without dementia was erroneously

classified to have dementia using the CDT. This is partly due to the smaller number of nondemented patients among patients with depression (as also expressed by the reduced NPV). Moreover, this finding hints at the wide array of cognitive abilities needed for completing the CDT, some of which might also be impaired by depression (eg, concentration and planning).¹¹ Considering the specific deficits of executive functions that can occur in PD, it is possible that a CDT version laying more emphasis on executive abilities—such as the CLOX³¹—might have been more appropriate for this study population. However, when conceptualizing the GEPAD study, we deliberately decided to implement the CDT as described for 2 reasons. First, the CDT and the scoring system as used in this study are more common in neurologists' and psychiatrists' office, as the German National Guidelines for Dementia explicitly recommend the CDT for screening purposes, while the CLOX is less common in Germany. Second, we have already implemented a PD-specific screening instrument for cognitive impairment in the test battery, namely, the Parkinson Neuropsychometric Dementia Assessment (PANDA, data not reported here).^{17,18} So, in favor of a better data quality and higher participation rate among the study physicians, we decided to implement a CDT version they are probably familiar with.

Overall, classification performance in our sample of outpatients with PD resemble data from Seigerschmidt et al who investigated a smaller sample of 238 community-dwelling patients without dementia.³² They reported a sensitivity and specificity of 66.7% and 65.5%, respectively, in patients with

questionable dementia (PPV 57.9%, 73.4%). It should be noted that their version of the CDT was slightly different from ours; their scoring system ranged from 1 to 10 instead of 1 to 6. However, they also analyzed concordance between different scoring systems and found high κ values between .76 and .91.

Nishiwaki and colleagues investigated CDT performance in a large sample of patients with cognitive impairments as determined by the MMSE.²⁴ They reported lower sensitivities (mean: 34.5%) and higher specificities (90.8%) but similar PPVs (43.9%) and NPVs (86.9%) in comparison to the values obtained for our sample. However, a direct comparison between these 2 studies is difficult, as our collinearity analyses showed only low-to-moderate correlations between the MMSE and the CDT ($r = -.52$, $r^2 = .28$ in a prediction model) and low correlations between the CDT and the MADRS. The latter can be regarded as highly desirable, because it indicates only small impacts of the presence of depression on cognitive performance. Yet, the former suggests that—at least in our sample of outpatients with PD—the MMSE and CDT appear to gauge different aspects of cognition. It is important to consider that both tests are subject to measuring errors. Thus, appraising the performance of CDT in patients classified to have cognitive impairment by the MMSE definitely warrants further investigation. In addition to the near independence between the CDT and the MADRS, the AUCs for the CDT were also similar in patients with and without depression. This may suggest that the CDT is potentially useful in patients having PD with depression, keeping the above-mentioned limitations of higher misclassification rates in mind.

To our knowledge, this study is the first comprehensive investigation of the classification performance and predictive value of the CDT in PD with dementia in a large representative sample of outpatients. The findings indicate that the CDT is a useful instrument for patients with PD, cognitive impairment, and depression. However, there are also serious limitations, some of which are inherent to the study design. First, it should be noted that 4.6% of the total sample was not included in the analyses due to missing clock drawings. These patients were older, more severely impaired by PD, and more often had dementia. Therefore, our results would have been altered if we had been able to include all patients. Second, the diagnosis of depression had to be based on a screening instrument with a PD-specific cutoff for depression rather than a comprehensive clinical evaluation, which could have provided more detailed information on the depression status (eg, duration and type of depression). This was implemented to keep the study protocol feasible for physicians during daily routine care. This objection also applies to the lack of the UPDRS motor subscale, which would have allowed a more finely graded analysis of motor impairment, especially type and laterality of tremors, which may have influenced CDT performance. Moreover, the diagnosis of dementia could have been partially influenced by the patient's CDT performance. We tried to minimize this bias by letting each drawing being rated by 2 trained clinical psychologists, who were blinded to the CDT rating by the physician as well as to the patient's dementia status. However,

the possibility of an interaction between both the sources cannot be totally eliminated.

Dementia is a complex syndrome. It is, therefore, important to point out that simply distinguishing between patients with and without dementia using screening instruments may not always be appropriate. Although it is acknowledged that the CDT relies on a wide range of cognitive domains,^{11,33} their individual contribution to test performance cannot be clearly quantified. Screening instruments, including the CDT, are not adequate substitutes for a comprehensive clinical diagnosis. In practice, the CDT is particularly useful for ruling out cognitive impairment rather than for detecting it.

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