Published in final edited form as:

Neuropsychology. 2008 September ; 22(5): 553–562. doi:10.1037/0894-4105.22.5.553.

DOES THE CLOCK DRAWING TEST HAVE FOCAL NEUROANATOMICAL CORRELATES?

D. Tranel^{a,*}, D. Rudrauf^{a,b}, E.P.M. Vianna^a, and H. Damasio^c

^a Division of Behavioral Neurology and Cognitive Neuroscience, Department of Neurology, University of Iowa

^b Laboratory of Computational Neuroimaging, Department of Neurology, University of Iowa

^c Dornsife Center for Cognitive Neuroimaging, Department of Psychology, University of Southern California

Abstract

The Clock Drawing Test (CDT) is widely used in clinical neuropsychological practice. The CDT has been used traditionally as a “parietal lobe” test (e.g., Kaplan, 1988), but most empirical work on the CDT has focused on its sensitivity and specificity for detecting and differentiating subtypes of dementia, and there are surprisingly few studies of its neuroanatomical correlates. We investigated the neuroanatomical correlates of the CDT, using a group of 133 patients whose lesions provided effective coverage of most of both hemispheric convexities and underlying white matter. On the CDT, 30 subjects were impaired and 87 were unimpaired (16 were “borderline”). Lesion analysis indicated that impairments on the CDT were most strongly associated with damage to right parietal cortices (supramarginal gyrus) and left inferior frontal-parietal opercular cortices. A follow-up analysis showed that visuospatial errors were predominant in patients with right hemisphere damage, whereas time setting errors were predominant in patients with left hemisphere lesions. These findings provide new empirical evidence regarding the neuroanatomical correlates of the CDT, and together with previous work, support the use of this quick and easily administered test not only as a screening measure but also as a good index of focal brain dysfunction (provided that error type is taken into account).

Keywords

lesion method; visuospatial cognition; neuropsychological tests; clock drawing; somatosensory cortex; basal ganglia

INTRODUCTION

The Clock Drawing Test (CDT) is widely used in clinical neuropsychological practice, and it invariably appears in top 40 or so of commonly used neuropsychological instruments (e.g., Rubin, Barr, & Burton, 2005). The test has been around more or less since the inception of

*Corresponding author: Daniel Tranel, Department of Neurology, Roy J. and Lucille A. Carver College of Medicine, 200 Hawkins Drive, Iowa City, Iowa, 52242, daniel-tranel@uiowa.edu, Phone: (319) 384-6050.

Publisher's Disclaimer: The following manuscript is the final accepted manuscript. It has not been subjected to the final copyediting, fact-checking, and proofreading required for formal publication. It is not the definitive, publisher-authenticated version. The American Psychological Association and its Council of Editors disclaim any responsibility or liabilities for errors or omissions of this manuscript version, any version derived from this manuscript by NIH, or other third parties. The published version is available at www.apa.org/pubs/journals/neu

clinical neuropsychology, and it was used originally as a probe of visuospatial neglect and inattention (Battersby, Bender, Pollack, & Kahn, 1956). The CDT actually makes demands on a wide range of cognitive abilities (Freedman, Leach, Kaplan, Shulman, & Delis, 1994), and this feature, together with its brevity and ease of administration, has helped the CDT become a popular screening measure for dementia (see review by Fischer & Loring, 2004). In fact, most published studies of the CDT have focused on its sensitivity and specificity with regard to detecting dementia (Dastoor, Schwartz, & Kurtzman, 1991; Esteban-Santillan, Praditsuwon, Ueda, & Geldmacher, 1998; Kirk & Kertesz, 1991; Kozora & Cullum, 1994; Libon, Swenson, Barnoski, & Sands, 1993; O'Rourke, Toukko, Hayden, & Beattie, 1997; Shulman, Gold, Cohen, & Zuccherro, 1993; Sunderland, Hill, Mellow, Lawlor, et al., 1989; Tuokko, Hadjustavropoulos, Miller, & Beattie, 1992; Wolf-Klein, Silverstone, Levy, & Brod, 1989) or differentiating different types of dementia (Blair, Kertesz, McMonagle, Davidson, & Bodi, 2006; Cahn-Weiner, Williams, Grace, Tremont, et al., 2003; Kitabayashi, Ueda, Narumoto, Nakamura, et al., 2001; Rouleau, Salmon, Butters, Kennedy, & McGuire, 1992). In addition, there is an extensive line of work that has been mostly concerned with developing various nuanced administration and scoring systems for the CDT (for reviews, see Fischer & Loring, 2004; Shulman, 2000).

Kaplan and colleagues (Borod, Goodglass, & Kaplan, 1980; Goodglass & Kaplan, 1983; Kaplan, 1988) used the CDT in their so-called “parietal lobe battery,” on the premise that the test was sensitive to parietal dysfunction, especially right-sided parietal dysfunction often associated with visuospatial neglect. Other work has shown that qualitative indices of CDT performance tend to be better predictors of localized brain dysfunction than quantitative indices (Freedman et al., 1994; Suhr, Grace, Allen, Nadler, & McKenna, 1998). For example, patients with right posterior lesions typically manifest spatial disorganization and inattention or neglect—e.g., leaving out numbers from the left side of the clock or bunching up all the numbers on the right side of the clock (Freedman et al., 1994). Surprisingly, though, especially in light of the overall popularity of the CDT in neuropsychological assessment, there are remarkably few studies that have looked carefully at the neuroanatomical correlates of CDT performance.

Suhr and colleagues (Suhr et al., 1998) studied CDT performance in stroke patients, but the focus of their study was on various scoring systems. The neuroanatomical precision was restricted to a “brain quadrant” approach (left versus right, anterior versus posterior) and distinguishing cortical versus subcortical, and a large number of patients in the study could not be defined even at those coarse-grain levels. The patients were studied in the acute phase of their illness, on average 26 days post stroke (the study does not mention when the neuroimaging data were collected). The main finding was that qualitative scoring approaches, unlike quantitative indices, were helpful in differentiating left versus right lesions and cortical versus subcortical lesions. One other study reported that CDT performances in stroke patients with right hemisphere lesions and left spatial neglect were influenced by verbal IQ, but the study did not include any other lesion comparison groups (Ishiai, Sugishita, Ichikawa, Gono, & Watabiki, 1993).

Against this background, the current study was designed to contribute novel empirical information about the neuroanatomical correlates of CDT performance. We took advantage of an opportunity afforded by a large database at the University of Iowa, which includes a sizeable number of patients with focal lesions and CDT performances (overall $N = 133$ for the current study). In order to perform analyses of lesion-deficit relationships, we first established that we had acceptable “effective statistical coverage” (statistical power) at a given threshold of significance for most of the convexities of the left and right hemispheres, as well as most of the underlying white matter, using a new method for establishing statistical coverage maps (Rudrauf et al., in press). Then, an empirical approach was utilized, building on the themes developed from the CDT literature reviewed above. First, we looked for focal and specific

lesion commonalities in patients with impaired CDT performances, i.e., lesion sites that were reliably and significantly associated with defective CDT performance. Second, we sought to determine whether different error patterns on the CDT would be reliably associated with different lesion sites. To shed light on possible causes of different error types, we also examined adjuvant neuropsychological test performances in subgroups of patients with different error patterns on the CDT.

METHOD

Participants

The participants were neurological patients with focal brain damage (overall N = 133; 77 men, 56 women), selected from the Patient Registry in the Division of Behavioral Neurology and Cognitive Neuroscience at the University of Iowa. Subjects were selected if they had (1) a CDT performance from the chronic epoch (defined as 3 months or more post lesion onset), and (2) a single, focal lesion in one hemisphere. All patients had provided informed consent in accordance with the Human Subjects Committee of the University of Iowa and federal guidelines. In connection with their enrollment in the Patient Registry, the patients have been extensively characterized neuropsychologically and neuroanatomically, using standard protocols of the Benton Neuropsychology Laboratory (Tranel, 2007) and the Human Neuroimaging and Neuroanatomy Laboratory (Damasio & Frank, 1992; Frank et al., 1997). All data, including the neuropsychological data and the neuroimaging data, were collected in the chronic epoch—as noted, we define “chronic” as 3 or more months post lesion onset.¹ Some of the patients with left hemisphere lesions were recovered aphasics, but none of them had residual aphasia so severe as to interfere with their basic comprehension of the neuropsychological tasks (i.e., they could follow the task instructions).

Neuropsychological Data Quantification

The CDT was administered according to standard procedures in the Benton Neuropsychology Laboratory (and adapted from Kaplan’s CDT administration procedure (Kaplan, 1988)). Patients were given a blank piece of white paper and a pencil, and instructed to, “Draw a clock with all its numbers, and set the time to twenty ‘til four.”² Scoring of the CDT was performed by a board-certified neuropsychologist who was not part of the current study, using a global rating system akin to that outlined by Shulman and colleagues (Shulman et al., 1993). Specifically, CDT performances were classified on a 1-2-3 scale where 1 indicates normal (non-impaired), 2 indicates borderline impaired, and 3 indicates impaired.³ For the purposes of the current study, we focused on the subjects who were classified into the non-impaired and impaired groups. Subjects who had borderline impaired scores, of whom there were 16, were not included in the data analysis. Therefore, data from 117 subjects were used in the final data analysis. Demographic characteristics of the sample of 117 are presented in Table 1. The lesion etiologies for this sample were as follows: cerebrovascular disease (N = 93), surgical treatment of benign tumor (N = 1) or arteriovenous malformation (N = 5), temporal lobectomy (N = 12), traumatic brain injury (N = 2), or infection (herpes simplex encephalitis, N = 2; meningioencephalitis, N = 1).

¹Chronicity data are provided in Table 1. We focused on the chronic epoch because the cognitive and neuroanatomical recoveries of brain-damaged patients have largely stabilized by then (3 months after lesion onset), at least in a general sense, and drawing inferences about brain-behavior relationships can be on more solid footing. We acknowledge that there can be other considerations that would make data from the acute epoch informative, but we did not collect data in the acute epoch so our study cannot speak to those issues.

²In 3 subjects, the instruction was to set the time to “three o’clock.”

³This scoring system has been in place for three decades in our Laboratory, and it is very familiar to our staff. Nonetheless, for the current study we selected a random subset of the CDT performances (n = 25) and had them scored by a second board-certified neuropsychologist in our Laboratory. The interrater reliability of the two scorers was .91, comparable to the interrater reliability of most scoring systems (see Fischer & Loring, 2004).

Neuroanatomical data quantification and analysis

The neuroanatomical analysis was based on magnetic resonance (MR) data obtained in a 1.5 Tesla General Electric Sigma scanner with a 3D SPGR sequence yielding 1.5 mm contiguous T1 weighted coronal cuts, or, in a few subjects in whom an MR could not be obtained, on computerized axial tomography (CT) data. Lesion mapping on a reference brain was performed according to MAP-3 lesion analysis methods, using the Brainvox programs (Damasio & Frank, 1992; Frank et al., 1997). This method entails a transfer of the lesion brain to a common space in a template brain (see Damasio et al., 2004). In order to facilitate reliable lesion transfer, all major sulci of the lesion brain were color-coded in the lesion brain and the template brain. Then, the template brain was oriented and resliced taking into account thickness of slices to match the lesioned brain. After this reslicing, the lesion of the subject on each slice was transferred manually to the corresponding slice in the template brain. This was done taking into consideration the distances between lesion borders and identifiable anatomical landmarks, such as color-coded gyri and subcortical structures. In all instances, a good match was assured by the inspection of the 2D images as well as the rendered 3D images. Each lesion was then entered into group lesion overlap analysis.

In order to study lesion-deficit relationships at the group level, lesion proportion difference maps (what we call “proportional MAP3,” hereafter “PM3”) were computed. These are maps of the proportion of subjects with a lesion including a given voxel among the subjects with a deficit, minus the proportion of subjects with a lesion including that voxel among the subjects with no deficit (deficit, in the current context, referring to impairment on the CDT). A positive difference in proportions indicates a higher likelihood of having a lesion at the voxel in subjects with a deficit than in subjects with no deficit. These maps were thresholded using exact statistics involving a mixture of hypergeometric and binomial distributions based on the null hypothesis of statistical independence between lesion and deficit at the level of the parent distribution (i.e., population) (Rudrauf et al., in press).

Using this general framework, we first built “effective coverage maps” (ECMs) to delineate where significant effects at a given threshold could be detected, assuming the maximum lesion-deficit relationships allowed by the observed proportion of deficit in the sample and the number of subjects with a lesion at a given voxel. At the same time, these maps permit the identification of regions of the brain where nothing could be said even if lesion-deficit relationships were maximal, as a result of basic issues with statistical power. The issue of estimating statistical power is important for human lesion-deficit studies as statistical power is often low and highly heterogeneous (across different brain areas) in such studies (e.g., Rudrauf et al., in press). The ECMs maps provide a proxy for estimating statistical power at the voxel level. They are built by first constructing maps of the maximum lesion-deficit relationship permitted by the sample, as illustrated by the following example. In a hypothetical dataset of 100 subjects, in which 8 subjects had a deficit, if there were a voxel at which 10 lesions overlapped, the maximum permitted relationship at that voxel would be the case in which the 10 lesions corresponded to all 8 subjects with a deficit and 2 additional subjects without a deficit (e.g., $PM3 = 8/8 - 2/(100 - 8) = 0.98$). Maps of such maximally permitted statistics are then thresholded as described above to build the ECMs.

In the current study, at a threshold of $p < 0.05$ (uncorrected) the ECMs demonstrated effective coverage for most of the convexities of the left and right hemispheres, as well as most of the underlying white matter. We thus chose to use this threshold ($p < 0.05$, uncorrected) for further analyses of lesion-deficit relationships. This approach favors effective coverage and sensitivity over specificity, in keeping with the overall design of the study (in particular, our emphasis on looking at the whole brain insofar as possible).

PM3 maps were created and thresholded for the overall group of impaired subjects, and for subgroups of impaired subjects with different types of deficits on the CDT (see below). Specifically, we first grouped together all subjects who were impaired on the CDT, and calculated a PM3 map. Then, as a follow-up, we categorized subjects as belonging to either of two error patterns: (i) Spatial organization errors (including both spatial organization errors per se, and errors in the placement of clock numbers), (ii) Time setting errors. PM3 maps were calculated for each of these error type subgroups. (The error analysis is described in more detail below.)

All analyses were done using Matlab (MathWorks, Inc., Natick, MA).

RESULTS

Demographic results

Based on the overall “impaired” versus “non-impaired” classification described above, we ended up with 30 subjects in the impaired group and 87 in the non-impaired group (see Table 1). The two groups were not statistically different on any of the demographic parameters (per t-tests for Age ($t(115) = 1.94, p = 0.06$), Education ($t(115) = 0.76, p = 0.45$), and Chronicity ($t(115) = 0.15, p = 0.88$); per Chi Square tests for Sex ($X^2 = 0.04, p = 0.85$) and Handedness ($X^2 = 0.09, p = 0.77$)). The range for Chronicity was also similar between the two groups.

Statistical power

The results of the effective coverage maps (ECMs) are shown in Figure 1, broken down for the overall impaired group and for the two subgroups with specific error types. The maps differ slightly as statistical power does not depend only on lesion coverage (i.e., the number of subjects with a lesion at a given voxel), but also on the proportion of subjects counted as having a deficit in the sample, which varies across error types. In total, there were 64 subjects with left hemisphere lesions and 53 subjects with right hemisphere lesions, and it can be seen that at the selected threshold, effective coverage is adequate in the convexities of both hemispheres, and in the underlying white matter. However, there are some brain regions that are not covered adequately for any conclusions to be reached, and it is important to note that we simply cannot comment on these regions, one way or another, vis-à-vis their potential importance for CDT performance. Those regions include the mesial cortices of both hemispheres, and the very anterior prefrontal (mainly polar) cortices of both hemispheres. Some subcortical structures are not covered sufficiently to yield reliable conclusions, either.

Neuroanatomical correlates of impaired CDT performance

The thresholded PM3 map for the 30 impaired subjects versus the 87 non-impaired subjects is shown in Figure 2a. The map shows that subjects who were impaired were clustered in two groups: (1) Subjects with lesions overlapping in the right hemisphere, with foci in the right parietal cortices (mostly in the supramarginal gyrus), the middle and superior temporal cortices, the frontal operculum, and the insula and underlying subcortical structures (including anterior basal ganglia); and (2) Subjects with lesions overlapping in the left inferior frontal-parietal opercular cortices, with foci in the inferior frontal gyrus, the lower sector of the precentral and postcentral gyri, the anterior sector of the supramarginal gyrus, and the insula and underlying basal ganglia.

Error pattern analysis

We conducted analyses in which the neuroanatomical correlates of CDT performances were analyzed with an eye to the types of qualitative error patterns produced by subjects in the impaired group (given the emphasis on qualitative scoring approaches in previous studies, as

presented in the Introduction). A researcher blind to the lesions of the subjects (E.P.M.V.) classified CDT error types, using the methods suggested by Freedman et al. (1994). Of the 30 subjects with impaired CDT performance, it turned out that there were two predominant error patterns that characterized most of them (24/30): (1) impaired spatial organization, usually together with impaired number placement and/or omission of numbers ($n = 11$); and (2) impaired time (hand) setting, in the context of a relatively well drawn clock that had all the numbers in approximately the correct spatial locations ($n = 13$) (see Figure 3 for examples). (The remaining 6 subjects had various “other” types of errors, such as missing hands, distorted clock outlines, and mixed patterns that could not be readily classified into either of these error pattern types.) Following Freedman et al. (1994; see also Fischer & Loring, 2004), these two error patterns can be interpreted as impaired spatial analysis and spatial planning for the first type, and impaired linguistic and/or numeric processing in the second case, e.g., impaired comprehension of the time specifics in the clock drawing instructions.

A common cause of impaired spatial organization in drawing tests is left-sided neglect, and it is relevant to ask whether this was a common finding in our sample of 11 participants with impaired spatial organization types of errors. In looking through the impaired clocks in this group, it seemed that there could have been subtle signs of neglect in some of the performances, but these were not unequivocal and really could not be rated reliably as spatial neglect. This is not surprising, given that our participants were studied in the chronic epoch, when major spatial neglect has typically dissipated (we return to this point in the Discussion). Also, to give a sense of the range of impaired CDT performances in our sample, Figure 4 has examples of the “best” and the “worst” clocks from participants in the impaired group (as judged by an expert blind to the current study hypotheses).

Using these different error patterns as a grouping variable, we analyzed the lesion commonalities in the subjects who comprised the two groups. This revealed the following results, depicted in the PM3 maps in Figures 2b and 2c:

- a. The first error pattern—the impaired spatial organization and number placement pattern—was much more frequent in subjects with right hemisphere lesions. In fact, all but one of the 11 subjects who produced this error type had right hemisphere lesions (Table 2). The PM3 map in Figure 2b indicates that the main areas of lesion overlap in these subjects were in the inferior frontal gyrus, with some effects in the middle frontal gyrus and in the ventral perirolandic region. There were also overlaps in the temporal lobe (mainly in the superior temporal gyrus), in the ventral occipitotemporal cortex (encompassing the posterior fusiform gyrus), and in the pericalcarine cortex. Also, there is significant lesion overlap in the insula, and in the anterior basal ganglia and white matter underneath the frontoparietal operculum.
- b. The second error pattern—the time setting error pattern—was much more frequent in subjects with left hemisphere lesions. Specifically, 11 of the 13 subjects who produced this error type had left hemisphere lesions (Table 2). The PM3 map in Figure 2c indicates that the main areas of lesion overlap in these subjects were in the inferior frontal gyrus, the ventral perirolandic region (with extensions along the postcentral gyrus), the anterior supramarginal gyrus, the insula, and the superior temporal gyrus.

Other neuropsychological test performances

It was of interest to compare the two impaired CDT subgroups and the non-impaired group on several other tests, in order to analyze possible causes behind and other correlates of the error patterns. Specifically, adjuvant neuropsychological tests were chosen in order to ascertain whether the differences between CDT performances were accompanied by differences in other cognitive domains, such as intellectual functioning, language, visuospatial performance, and

working memory, and to help substantiate our impression of why the different impaired CDT subgroups had failed the Clock Drawing Test. The data are presented in Table 3, and the groups were compared statistically with MANOVA. The groups did not differ on most of the WAIS-III scores, including overall Verbal IQ ($p = 0.05$), Performance IQ ($p = 0.15$), and the Digit Span subtest score ($p = 0.38$). However, the Impaired Time Setting group demonstrated lower performances on several language-related tests: Controlled Oral Word Association (COWA, $F(2,108) = 9.79$, $p = 0.000$, partial eta squared = 0.15; post-hoc analysis indicated that the Impaired Time Setting group was statistically different from the Non-impaired group ($p = 0.000$, 95% Confidence Interval for Difference = 6.4 to 24.5, Bonferroni adjusted)); Token Test ($F(2,108) = 21.25$, $p = 0.000$, partial eta squared = 0.28; post-hoc analysis indicated that the Impaired Time Setting group was statistically different from the Impaired Spatial Organization Group ($p = 0.000$, 95% Confidence Interval for Difference = 5.6 to 22.2, Bonferroni adjusted) and from the Non-impaired group, $p = 0.000$, 95% Confidence Interval for Difference = 10.1 to 22.1, Bonferroni adjusted)); Boston Naming Test ($F(2,108) = 24.40$, $p = 0.000$, partial eta squared = 0.31; post-hoc analysis indicated that the Impaired Time Setting group was statistically different from the Impaired Spatial Organization group ($p = 0.000$, 95% Confidence Interval for Difference = 13.9 to 34.9, Bonferroni adjusted) and from the Non-impaired group ($p = 0.000$, 95% Confidence Interval for Difference = 13.6 to 28.8, Bonferroni adjusted)). Subjects in the Impaired Spatial Organization group, by contrast, did not demonstrate defects on the language-related measures. Interestingly, though, the Impaired Spatial Organization group had lower scores on visuoconstruction and visuospatial tests, and the differences were statistically significant for the Block Design subtest from the WAIS-III ($F(2,108) = 4.59$, $p = 0.012$, partial eta squared = 0.08; post-hoc analysis indicated that the Impaired Spatial Organization group was statistically different from the Non-impaired group ($p = 0.021$, 95% Confidence Interval for Difference = 0.3 to 4.6, Bonferroni adjusted) and for the Facial Discrimination Test ($F(2,108) = 3.70$, $p = 0.028$, partial eta squared = 0.06; post-hoc analysis indicated that the Impaired Spatial Organization group was marginally different from the Non-impaired group ($p = 0.068$, 95% Confidence Interval for Difference = 0.2 to -6.8, Bonferroni adjusted)). The groups were not statistically different on the Judgment of Line Orientation Test ($p = 0.16$).

Overall, the findings support the notion that the CDT defects in the Impaired Time Setting group tended to be related to deficits in language processing (consistent with previous interpretations of this type of error pattern, e.g., Fischer & Loring, 2004), whereas CDT defects in the Impaired Spatial Organization group tended to be related to visuoconstructional and visuospatial processing defects. These findings are perhaps not surprising, but they help give a broader picture in which the nature of CDT performance impairments and specific error types in our patients can be situated.

The right parietal region and CDT performance

As indicated in the Introduction, there has been historically a strong emphasis on the CDT being related to right parietal function. Thus, it was of interest to explore in more detail the nature of lesion-deficit relationships for the CDT and the right parietal region in the current sample of patients.

To begin with, in the error analysis presented above, it appeared that neither spatial organization impairments nor time setting impairments were associated with significant lesion-deficit relationships in the right parietal cortex, contrasting with the effect in the right parietal cortex found for overall impairments irrespective of error type (compare 2b and 2c with 2a). As it turned out, the right parietal effects indeed did not appear to be specific to error types: among the 8 subjects with CDT impairments and lesions that involved the right parietal region, 4 had impairments in spatial organization (3 for spatial organization per se and 1 for number

placement), 2 had impairments in time setting, and 2 had other types of impairments (see Table 2).

We explored the relationship between CDT performance and the right parietal region in more depth, taking both a brain-to-behavior approach and a behavior-to-brain approach. In the brain-to-behavior case, we investigated the extent to which right parietal damage was predictive of CDT defects in our sample. An anatomical ROI comprising the supramarginal gyrus and angular gyrus was delineated on our reference brain. To have what we considered “substantial” right parietal damage, a lesion had to encompass at least 40% of the supramarginal gyrus or angular gyrus. Considering all such lesions, the likelihood of having defective CDT performance following substantial right parietal damage was 50%. Also, the odds of having a CDT deficit following substantial right parietal damage was 3.4 times greater than the odds of a CDT deficit following damage anywhere else in the brain (sampled in our study).

In the behavior-to-brain case, we investigated the question of whether subjects presenting with deficits on the CDT would turn out to have a right parietal lesion. In our dataset, the likelihood of having substantial right parietal damage (as defined above) when presenting with a deficit on the CDT was 17.9%, as only 17.9% of the entire set of subjects with CDT deficits had right parietal lesions. This means that the proportion of lesions elsewhere in the brain when presenting a CDT deficit has to be larger than that, which indicates that CDT deficits per se are not a good predictor of right parietal lesions. To put the formulation in terms of an odds ratio (following the standard definition of odds: $p/(1-p)$ for a given proportion p), the odds of having substantial right parietal damage when presenting with a deficit on the CDT were 38.3 times *smaller* than the odds of having damage elsewhere in the brain (as sampled in our study) when presenting a CDT deficit.

To summarize, we found overall a significant lesion-deficit relationship between impaired CDT performance and right parietal damage, but this relationship was not specific to error type. Also, our data suggest that having right parietal damage substantially raises the odds of performing defectively on the CDT, but having impaired CDT performance is not especially predictive of right parietal damage.

DISCUSSION

Using a neuropsychological approach, we identified brain regions where damage is reliably associated with impaired performance on the CDT, including the right parietal cortices and the left inferior frontal-parietal opercular cortices. These findings extend and sharpen previous work, which has hinted at similar neuroanatomical correlates for the CDT but has not provided systematic lesion-deficit mapping in a large cohort of patients with focal brain damage.

Given the emphasis on the right parietal region in previous work (e.g., Kaplan, 1988), the findings regarding the association between CDT performance and the right parietal region warrant discussion. Our data are consistent with the association between damage to the right parietal cortices and impairments in CDT performance, and suggest that those parietal regions, especially the supramarginal gyrus, are important for normal clock drawing performance. This is supported by the lesion-deficit analysis based on overall CDT impairments, and by the ROI analysis looking at the likelihood and relative odds of CDT deficits following right parietal damage. However, considering the lesion-deficit maps obtained for the different types of errors as well as the ROI analysis looking at the likelihood and relative odds of right parietal lesions when patients present with a CDT deficit, the presence of deficits in clock drawing in patients is not especially predictive of right parietal lesions, and is not specific to either of the error types we investigated. This suggests that the CDT is not a very specific test for right parietal functional patency, at least in the chronic epoch. Indeed, visuospatial neglect, which appears

to be a frequent factor in CDT failure in neuropsychological practice in in-patient settings (e.g., Kaplan, 1988) and which is frequently associated with right parietal lesions, typically occurs in the acute phase of brain injury, within hours or a few days of lesion onset, and then shows rapid recovery. In our sample, the subjects were studied in the chronic phase, and influences from neglect likely had dissipated. Thus in the acute phase impaired CDT performance might be a better predictor of right parietal dysfunction.

A high proportion of participants with lesions that included the right basal ganglia were impaired on the CDT (see Table 2, Figure 2b). The predominant error pattern in these participants was impaired spatial organization and defective number placement. The CDT places demands on planning and integrating spatial and motor components of drawing a clock. Harris et al. (2002) described a patient with a right basal ganglia lesion who demonstrated severe impairments on mental rotation tasks. Impairments in mental rotation have also been reported in Parkinson's disease patients (Amick et al., 2006; Cronin-Golomb and Amick, 2001) and Huntington's disease patients (Mohr et al., 1991), where basal ganglia dysfunction is a hallmark. Lesions in the basal ganglia disrupt several corticostriatal loops that would likely be involved in the coordination and planning of spatial tasks. The importance of the basal ganglia in the organization or planning of a task could be due to the converging information arriving from several areas such as the parietal cortex (the area most linked to visuospatial tasks) and motor cortex (Cavada & Goldman-Rakic, 1991; Harris et. al., 2002; Suvorov & Shuvaev, 2004).

It was interesting that our data yielded a strong finding in the left inferior frontal-parietal opercular region, where damage was consistently associated with impaired CDT performance and with a specific error pattern (impaired time setting). This finding puts some empirical teeth in the long-standing clinical lore that patients can fail the CDT secondary to impaired comprehension of the linguistic and numeric information required by the task (e.g., Fischer & Loring, 2004; Kaplan, 1988). And the finding gains credence from the adjuvant neuropsychological data, which showed that the impaired time setting participants also were impaired on several language tests, namely COWA, Token Test, and Boston Naming Test.

An open question in this context is whether instructions for different time settings might influence the nature of the relationships we uncovered (we used "twenty minutes 'til four"). In fact, Fischer and Loring (2004) pointed out that a number of different time settings have been used in clock drawing instructions (with "10 minutes past 11" being the most popular), but it turns out that the exact instructions do not seem to matter much (see also Shulman, 2000). What does matter is that instructions to set a specific time are actually provided (Kaplan, 1988), rather than just an open-ended "draw a clock." Thus, we suspect that our findings would generalize to other time settings, but of course this is an empirical question and one that could be addressed with further research using different time settings.

A limitation of our study is the lesion sampling. As noted earlier, there are brain regions that are not sampled by the lesions included in this study, and we simply cannot comment on these regions, one way or another, vis-à-vis their possible role in CDT performance. For some of these regions, e.g., superior dorsolateral and high mesial prefrontal cortices (where we had virtually no patients with lesions in this sample), it seems unlikely that the areas would turn out to play any significant role in CDT performance, based on what is known about the functions of these areas and what has been published previously regarding neuroanatomical correlates of CDT performance. But for regions like the superior parietal lobule, a role in CDT performance is more plausible, and our study is necessarily silent on the issue due to low lesion sampling.

Another issue concerns the administration and scoring systems we used for the CDT, which are not as elaborate as many in the literature (cf. Fischer & Loring, 2004; Shulman, 2000). However, Fischer and Loring (2004) pointed out that essentially all of the systems tend to yield neuropsychologically meaningful data. The critical factor seems to be the distinction between qualitative and quantitative scoring approaches, where it has been consistently shown that qualitative approaches are more effective when using the CDT to detect focal brain dysfunction (e.g., Freedman et al., 1994; Kaplan, 1988; Suhr et al., 1998). Our results are quite consistent with this line of thinking. On balance, it seems unlikely that a more elaborate scoring system would change appreciably the main conclusions from our study.

The multifaceted demands of the CDT likely contribute to its success as a dementia screening instrument: the task requires a variety of cognitive skills, and can be failed for multiple reasons. The current study suggests that the CDT also has reliable neuroanatomical correlates, especially in the right parietal region and left inferior frontoparietal opercular region.

Acknowledgments

Supported by NINDS P01 NS19632 and NIDA R01 DA022549

We thank Ken Manzel for careful assistance with the neuropsychological data and statistical analyses. This work was supported by NINDS P01 NS19632 and NIDA R01 DA022549.

References

- Adolphs R, Damasio H, Tranel D. Neural systems for recognition of emotional prosody: a 3-D lesion study. *Emotion* 2002;2:23–51. [PubMed: 12899365]
- Amick MM, Schendan HE, Ganis G, Cronin-Golomb A. Frontostriatal circuits are necessary for visuomotor transformation: Mental rotation in Parkinson's disease. *Neuropsychologia* 2006;44:339–349. [PubMed: 16061263]
- Battersby WS, Bender MB, Pollack M, Kahn RL. Unilateral “spatial agnosia” (“inattention”) in patients with cerebral lesions. *Brain* 1956;79:68–93. [PubMed: 13342276]
- Blair M, Kertesz A, McMonagle P, Davidson W, Bodi N. Quantitative and qualitative analyses of clock drawing in frontotemporal dementia and Alzheimer's disease. *Journal of the International Neuropsychological Society* 2006;12:159–165. [PubMed: 16573849]
- Borod JC, Goodglass H, Kaplan E. Normative data on the Boston Diagnostic Aphasia Examination, Parietal Lobe Battery, and the Boston Naming Test. *Journal of Clinical Neuropsychology* 1980;2:209–216.
- Cahn-Weiner DA, Williams K, Grace J, Tremont G, Westervelt H, Stern RA. Discrimination of dementia with lewy bodies from Alzheimer disease and Parkinson disease using the clock drawing test. *Cognitive and Behavioral Neurology* 2003;16:85–92. [PubMed: 12799594]
- Cavada C, Goldman-Rakic PS. Topographic segregation of corticostriatal projections from posterior parietal subdivisions in the macaque monkey. *Neuroscience* 1991;42:683–696. [PubMed: 1720224]
- Cronin-Golomb, A.; Amick, MM. Spatial abilities in aging, Alzheimer's disease, and Parkinson's disease. In: Boller, F.; Cappa, S., editors. *Aging and Dementia*. 2. Vol. 6. Elsevier; Amsterdam: 2001.
- Damasio, H. *Human brain anatomy in computerized images*. 2. New York: Oxford University Press; 2005.
- Damasio H, Frank R. Three-dimensional in vivo mapping of brain lesions in humans. *Archives of Neurology* 1992;49:137–143. [PubMed: 1736845]
- Damasio H, Tranel D, Grabowski T, Adolphs R, Damasio A. Neural systems behind word and concept retrieval. *Cognition* 2004;92:179–229. [PubMed: 15037130]
- Dastoor D, Schwartz G, Kurtzman D. Clock drawing: An assessment technique in dementia. *Journal of Clinical and Experimental Gerontology* 1991;13:69–85.

- Esteban-Santillan C, Praditsuwan R, Ueda H, Geldmacher DS. Clock drawing test in very mild Alzheimer's disease. *Journal of the American Geriatrics Society* 1998;46:1266–1269. [PubMed: 9777909]
- Fischer, JS.; Loring, DW. Construction. In: Lezak, MD.; Howieson, D.; Loring, DW., editors. *Neuropsychological assessment*. 4. New York: Oxford University Press; 2004. p. 531-568.
- Frank RJ, Damasio H, Grabowski TJ. Brainvox: an interactive, multimodal visualization and analysis system for neuroanatomical imaging. *NeuroImage* 1997;5:13–30. [PubMed: 9038281]
- Freedman, M.; Leach, L.; Kaplan, E.; Shulman, KI.; Delis, DC. *Clock drawing: A neuropsychological analysis*. New York: Oxford University Press; 1994.
- Goodglass, H.; Kaplan, E. *Assessment of aphasia and related disorders*. 2. Philadelphia: Lea and Febiger; 1983.
- Harris IM, Harris JA, Caine D. Mental-rotation deficits following damage to the right basal ganglia. *Neuropsychology* 2002;16:524–537. [PubMed: 12382991]
- Ishiai S, Sugishita M, Ichikawa T, Gono S, Watabiki S. Clock drawing test and unilateral spatial neglect. *Neurology* 1993;43:106–110. [PubMed: 8423871]
- Kaplan, E. A process approach to neuropsychological assessment. In: Boll, T.; Bryant, BK., editors. *Clinical neuropsychology and brain function: Research, measurement, and practice*. Washington, D.C: American Psychological Association; 1988.
- Kirk A, Kertesz A. On drawing impairment in Alzheimer's disease. *Archives of Neurology* 1991;48:73–77. [PubMed: 1986729]
- Kitabayashi Y, Ueda H, Narumoto J, Nakamura K, Kita H, Fukui K. Qualitative analyses of clock drawings in Alzheimer's disease and vascular dementia. *Psychiatry and Clinical Neurosciences* 2001;55:485–491. [PubMed: 11555344]
- Kozora E, Cullum CM. Qualitative features of clock drawings in normal aging and Alzheimer's disease. *Assessment* 1994;1:179–187. [PubMed: 9465148]
- Libon DJ, Swenson RA, Barnoski EJ, Sands LP. Clock drawing as an assessment tool for dementia. *Archives of Clinical Neuropsychology* 1993;8:405–415. [PubMed: 14589710]
- Mohr E, Brouwers P, Claus JJ, Mann UM, Fedio P, Chase TN. Visuospatial cognition in Huntington's disease. *Movement Disorders* 1991;6:127–132. [PubMed: 1829137]
- O'Rourke N, Toukko H, Hayden S, Beattie BL. Early identification of dementia: Predictive validity of the Clock Test. *Archives of Clinical Neuropsychology* 1997;12:257–267. [PubMed: 14588418]
- 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 and Cognition* 1992;18:70–87. [PubMed: 1543577]
- Rubin LA, Barr WB, Burton LA. Assessment practices of clinical neuropsychologists in the United States and Canada: A survey of INS, NAN, and APA Division 40 members. *Archives of Clinical Neuropsychology* 2005;20:33–65. [PubMed: 15620813]
- Rudrauf D, Mehta S, Bruss J, Tranel D, Damasio H, Grabowski T. Thresholding lesion overlap difference maps: Application to naming and recognition deficits in various categories of concrete entities. *NeuroImage*. (in press).
- Shulman KI. Clock-drawing: Is it the ideal cognitive screening test? *International Journal of Geriatric Psychiatry* 2000;15:548–51. [PubMed: 10861923]
- Shulman KI, Gold D, Cohen C, Zuccherro C. Clock-drawing and dementia in the community: A longitudinal study. *International Journal of Geriatric Psychiatry* 1993;8:487–496.
- Suvorov NF, Shuvaev VT. The role of the basal ganglia in organizing behavior. *Neuroscience and Behavioral Physiology* 2004;34:229–234. [PubMed: 15151175]
- Suhr J, Grace J, Allen J, Nadler J, McKenna M. Quantitative and qualitative performance of stroke versus normal elderly on six clock drawing systems. *Archives of Clinical Neuropsychology* 1998;13:495–502. [PubMed: 14590633]
- Sunderland T, Hill JL, Mellow AM, Lawlor BA, Gundersheimer J, Newhouse PA, Grafman JH. Clock drawing in Alzheimer's disease: A novel measure of dementia severity. *Journal of the American Geriatrics Society* 1989;37:725–729. [PubMed: 2754157]

- Tranel, D. Theories of clinical neuropsychology and brain-behavior relationships: Luria and beyond. In: Morgan, JE.; Ricker, JH., editors. Textbook of clinical neuropsychology. New York: Taylor and Francis; 2007. p. 27-39.
- Tuokko H, Hadjistavropoulos T, Miller JA, Beattie BL. The clock test: A sensitive measure to differentiate normal elderly from those with Alzheimer disease. *Journal of the American Geriatrics Society* 1992;40:579–584. [PubMed: 1587974]
- Wechsler, D. Manual for the Wechsler Adult Intelligence Scale-III. New York: Psychological Corporation; 1997.
- Wolf-Klein GP, Silverstone FA, Levy AP, Brod MS. Screening for Alzheimer's disease by clock drawing. *Journal of the American Geriatrics Society* 1989;37:730–773. [PubMed: 2754158]

Figure 1.

Effective Coverage Maps (ECMs) for the Clock Drawing Test. The ECMs show regions of the brain, in red, where significant effects of lesion-deficit relationships could be found at a threshold of $P < 0.05$ (uncorrected), if lesion-deficit relationships were maximal, given the observed lesion coverage and proportion of subjects with impairments in the sample. Three series of maps are shown: (a) ECMs for overall impairment on the CDT (irrespective of error type); (b) ECMs for impairments in spatial organization and number placement; and (c) ECMs for impairments in time setting. For all three ECMs, left and right lateral hemispheres are shown on the left side of the Figure, and coronal slices at the levels indicated by 1–6 (on the left and right hemispheres in (a)) are shown on the right side of the Figure (the left hemisphere is on the right in the coronal slices).

Figure 2.

Lesion-deficit relationships for the Clock Drawing Test. The Maps show regions of the brain, in red, where significant effects of lesion-deficit relationship were found at a threshold of $P < 0.05$ (uncorrected). Three series of maps are shown: (a) Maps for impairments irrespective of error type; (b) Maps for impairments in spatial organization and number placement; and (c) Maps for impairments in time setting. For all three Maps, left and right lateral hemispheres are shown on the left side of the Figure, and coronal slices at the levels indicated by 1–6 (on the left and right hemispheres in (a)) are shown on the right side of the Figure (the left hemisphere is on the right in the coronal slices).

A. Impaired spatial organization and number placement

A.1*

A.2

B. Impaired time setting

B.1

B.2

Figure 3.

Examples of Clock Drawing.

* Note: The patient in example A1 was asked to set the time to 3 o'clock; in the other 3 examples, the patients were asked to set the time to "20 'til 4."

A. “Best” impaired clock (the number “12” missing; slight misplacement of numbers)

B. “Worst” impaired clock (multiple severe errors)

Figure 4.

Examples of “best” (A) and “worst” (B) impaired Clock Drawing Test performances from the sample of 30 participants with impaired clock drawing tests.

Demographic characteristics of the participants, broken down as a function of performance (Impaired v. Non-impaired) on the Clock Drawing Test.

Table 1

Group	N	Age	Gender	Education	Chronicity	Handedness
Impaired	30	54.9 (10.1)	13 W; 17 M	12.3 (1.8)	1.7 (2.3) Range: .3 – 9.9	29 RH; 1 LH
Non-impaired	87	48.7 (16.5)	36 W; 51 M	12.7 (2.3)	1.8 (2.1) Range: .3 – 11.7	83 RH; 4 LH
Overall	117	50.3 (15.3)	49 W; 68 M	12.6 (2.2)	1.7 (2.1) Range: .3 – 11.7	112 RH; 5 LH

N, number of participants; W, women, M, men; RH, right-handed; LH, left-handed. For Age, Education, and Chronicity, the data indicate the means (in years) and standard deviations (in parentheses).

Table 2

Clock Drawing Test error types and associated lesion sites.

Subject	Error Type	Lesion Site
1103	Impaired number placement	Right occipital, posterior IT, and mesial temporal cortices
1300	Impaired number placement	Right basal ganglia, and right frontal operculum, temporal and insular cortices
1359	Impaired number placement	Left frontal operculum
1620	Impaired number placement	Right basal ganglia, and right frontal operculum, parietal and insular cortices
1680	Impaired number placement	Right mesial occipital cortex
1725	Impaired spatial organization	Right basal ganglia, and right frontal operculum, SI, MI, insular, and parietal cortices
1932	Impaired number placement	Right temporal lobe
1969	Impaired spatial organization	Right basal ganglia, and right frontal operculum, SI and insular cortices
2236	Impaired number placement	Right basal ganglia
2746	Impaired spatial organization	Right parietal, MI, SI, insular and prefrontal cortices
2825	Impaired spatial organization	Right parietal and insular cortices
0868	Impaired time setting	Left parietal, SI/insula, frontal operculum
1195	Impaired time setting	Left MI, parietal cortices
1312	Impaired time setting	Left occipital cortex
1392	Impaired time setting	Right superior parietal cortex, SI, MI
1760	Impaired time setting	Left frontal operculum, SI, MI, insular and parietal cortices
1808	Impaired time setting	Left posterior inferior temporal cortex
1848	Impaired time setting	Left parietal, SI, insular cortices
1978	Impaired time setting	Left SI, MI, frontal operculum, SMA, insular cortices
2054	Impaired time setting	Left frontal operculum, SI, insular cortices
2382	Impaired time setting	Right parietal cortex
2762	Impaired time setting	Left parietal and temporal cortices
2906	Impaired time setting	Left parietal cortex
2927	Impaired time setting	Left posterior, SI, MI cortices
0983	Other type of errors	Left occipital and mesial temporal cortices
1422	Other type of errors	Left SI and insular cortices
1648	Other type of errors	Left underlying white matter of parietal cortex, and left SI and insular cortices
1683	Other type of errors	Right parietal cortex
2174	Other type of errors	Right parietal, frontal, SI and MI cortices
2611	Other type of errors	Left parietal cortex

MI: primary motor cortex; SI: primary somatosensory cortex; IT: inferotemporal cortex; SMA: supplementary motor area.

Table 3

Comparison of CDT subgroups on IQ and other neuropsychological variables (means, standard deviations in parentheses).

GROUP	N	WAIS-III VIQ	WAIS-III PIQ	WAIS-III Digit Span	WAIS-III Block Design	COWA	Token Test	Boston Naming Test	Facial Discrimination Test	Judgment of Line Orientation Test
Impaired Spatial Organization	11	94.3 (10.9)	90.2 (7.0)	8.3 (1.6)	7.6 (2.4)	27.8 (10.8)	38.3 (8.0)	54.5 (3.3)	41.2 (4.1)	22.5 (5.0)
Impaired Time Setting	13	90.9 (11.4)	94.9 (8.3)	8.2 (2.7)	8.8 (2.8)	20.5 (11.8)	24.4 (14.3)	30.1 (19.4)	42.2 (5.6)	23.2 (7.0)
Non-impaired	87	98.9 (11.9)	98.1 (14.1)	9.0 (2.5)	10.1 (2.8)	36.0 (12.8)	40.5 (7.1)	51.3 (9.3)	44.5 (4.3)	25.0 (4.4)

WAIS-III (Wechsler Adult Intelligence Scale-III) VIQ is Verbal IQ, PIQ is Performance IQ, Digit Span and Block Design data are age-corrected scaled scores. Data for the COWA (Controlled Oral Word Association Test), Token Test, Boston Naming Test, Facial Discrimination Test, and Judgment of Line Orientation Test are raw scores. The results in **bold** indicate statistically significant between-group differences (see text for details).

Neuropsychology. Author manuscript; available in PMC 2010 March 8.