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The anatomy of visuospatial construction revealed by lesion-symptom mapping

J. Matthijs Biesbroek [a,*], Martine J.E. van Zandvoort [b], Hugo J. Kuijf [c], Nick A. Weaver [a], L. Jaap Kappelle [a], Pieter C. Vos [c], Birgitta K. Velthuis [d], Geert Jan Biessels [a], Albert Postma [a,b], On behalf of the Utrecht VCI study group

[a] Department of Neurology, Brain Center Rudolf Magnus, University Medical Center Utrecht, PO box 85500, G.03.232, 3508 GA Utrecht, The Netherlands
[b] Experimental Psychology, Helmholtz Institute, Utrecht University, The Netherlands
[c] Image Sciences Institute, University Medical Center Utrecht, Utrecht, The Netherlands
[d] Department of Radiology, University Medical Center Utrecht, Utrecht, The Netherlands

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ABSTRACT

Visuospatial construction is a complex cognitive operation that is composed of a purely constructional component (visuoconstruction proper), and visuoperceptive, attentional, and decision-making components. The anatomical correlates of visuospatial construction and its cognitive subcomponents are poorly understood. The purpose of the present study was to determine the anatomical correlates of visuospatial construction by applying lesion-symptom mapping in a cohort of 111 patients with first-ever ischemic stroke. We employed the Rey–Osterrieth Complex Figure (ROCF) copy test and the Judgment of Line Orientation (JLO); both tests measure visuoperception, while only the ROCF has a constructional component. We first performed assumption-free voxel-based lesion-symptom mapping, which revealed large shared right hemispheric correlates for the ROCF and JLO in the frontal lobe, superior temporal lobe, and supramarginal gyrus. These shared anatomical correlates reflect the visuoperceptive component of the ROCF and JLO. Anatomical correlates were discordant in the right superior parietal lobule, and angular and middle occipital gyri: lesions in these regions were associated with poor performance on the ROCF, but not the JLO. Secondly, these findings were reproduced with a region of interest-based analysis that yielded a statistically significant correlation between infarct volume in the right inferior and superior parietal, angular and middle occipital cortices, and poor performance on the ROCF, but not the JLO. This discordance in anatomical correlates of the ROCF and JLO reflects the visuoconstructive component of the ROCF. These findings provide new insights in the anatomical correlates of the visuoperceptive and visuoconstructive components of the ROCF and provide evidence for a crucial role of the right inferior and superior parietal, angular and middle occipital gyri in visuoconstruction proper.

1. Introduction

Visuospatial construction can be defined as the ability to see an object or picture as a set of parts and then to construct a replica of the original from these parts (Mervis, Robinson, & Pani, 1999). Examples of visuospatial construction include drawing, buttoning shirts, constructing models, making a bed, and putting together furniture that arrives unassembled (Mervis et al., 1999). Deficits in visuospatial construction (also referred to as constructional apraxia) were first described by Kleist in 1934 as the inability of copying drawings in the absence of difficulties in making relevant individual movements (Kleist, 1934; Laeng, 2006; Trojano & Conson, 2008). Constructional apraxia is now known to be a common feature of many neurological disorders, including hemispheric stroke and neurodegenerative disorders such as Alzheimer's disease, Parkinson's disease with dementia and Lewy body disease (Nys et al., 2007; Trojano & Conson, 2008).

Importantly, visuospatial construction tasks depend not only on construction proper (the purely constructional component of visuospatial construction), but also on visuospatial perception, attention and executive functioning as well. The interplay between these cognitive components in the brain has been the topic of much discussion, but widely accepted theories regarding their neural bases and anatomical correlates are still lacking (Trojano & Conson, 2008).

Abbreviations: ADC, apparent diffusion coefficient; DSC, dice similarity coefficient; DWI, diffusion-weighted imaging; FDR, false discovery rate; fMRI, functional MRI; JLO, Judgment of Line orientation; MNI, Montreal Neurological Institute; ROCF, Rey–Osterrieth Complex Figure copy test; VLSM, voxel-based lesion-symptom mapping

* Corresponding author.
E-mail address: J.M.Biesbroek@umcutrecht.nl (J.M. Biesbroek).

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Roncato, Sartori, Masterson, and Rumiati (1987) presented a propositional model of drawing based upon isolated cognitive components (exploration and encoding; activation of motor patterns; comparison between drawing and model) and tested this model in three patients with brain lesions. Due to this limited sample size they could not arrive at specific anatomical correlates for these components. Several fMRI studies have suggested that visuoperception depends on bilateral occipito-temporal and parieto-frontal structures and that visuoconstruction depends on bilateral occipito-parietal, frontal and cerebellar structures (Ino, Asada, Ito, Kimura, & Fukuyama, 2003; Makuuchi, Kaminaga, & Sugishita 2003; Kesler et al., 2004). However, fMRI studies do not prove that activated structures are actually essential to the task. As such, these findings should be confirmed with lesion studies in order to demonstrate a direct causal relation between damage in specific brain regions and loss of function (Rorden & Karnath, 2004). Previous lesion studies on visuospatial construction have demonstrated that constructional apraxia can occur after both left and right hemispheric occipito-parietal, occipito-temporal, and frontal lesions (Black & Bernard, 1984; Grossi, Calise, Correra, & Trojano, 1996; Kirk & Kertesz, 1993; Trojano & Conson, 2008; Villa, Gainotti, & De Bonis, 1986). However, these lesion studies have an important methodological limitation: they used traditional lesion scoring methods which are helpful in differentiating left versus right, and cortical versus subcortical, but provide very low spatial resolution (i.e. by classifying lesion locus as parietal, temporal, frontal, etc.). A recent study attempted to overcome from this limitation by performing voxel-wise analyses to relate lesion location to dichotomized performance on a clock drawing task, resulting in right parietal and temporo-frontal, and left parieto-frontal correlates (Tranel, Rudrauf, Vianna, & Damasio, 2008). However, these results were not corrected for multiple testing, which raises concerns regarding the specificity of these findings (correction for multiple testing increases specificity at the cost of decreased sensitivity). Furthermore, none of these previously performed lesion studies have attempted to isolate the purely visuoconstructive component of the applied drawing tests from the visuoperceptive component. Therefore, direct evidence from lesion-symptom mapping studies for a crucial role of occipito-parietal and frontal regions in visuoconstruction proper is lacking.

In the present study, we aimed to further reveal the anatomical correlates of visuospatial construction and the interplay between visuoperception and visuoconstruction proper in the human brain by employing an advanced lesion-symptom mapping approach. We used the Rey–Osterrieth Complex Figure copy test (ROCF) to assess visuospatial perception and construction (Osterrieth, 1944). This test is very popular for cognitive assessment because it is easily administered, yields reproducible results, and has high sensitivity for detecting brain damage, which is due to the fact that performance depends on many cognitive abilities. Performance on the ROCF depends not only on visuospatial perception and visuoconstruction proper, but also on spatial attention, and executive functioning as well. The high sensitivity of the ROCF makes it a valuable tool for clinical and research purposes, but the fact that performance depends on many cognitive abilities complicates the study of the neural basis of its subcomponents. One way of overcoming this limitation would be to determine and compare the anatomical correlates of the ROCF with another visuospatial test that does not have a visuoconstructive component. An example of such a test is the Benton Judgment of Line Orientation (JLO) in which the subject is confronted with two stimulus lines positioned above 11 reference lines and asked to select the two reference lines that have the same orientation as the stimulus lines (Benton, Sivan, Hamsher, Varney, & Spreen, 1994). The ROCF and JLO therefore both have a visuoperceptive component, while only the ROCF additionally has a visuoconstructive component (Strauss, Sherman, & Spreen, 2006).

In order to perform lesion-symptom mapping, both the ROCF and the JLO were administered in a cohort of patients with first-ever ischemic stroke. We first performed voxel-based lesion-symptom mapping (VLSM), thus relating lesion location to performance on the ROCF copy test and the JLO. This assumption-free VLSM analysis was of an exploratory nature, meaning potential involvement of regions anywhere in the brain was assessed. By comparing the anatomical correlates of these tests, we aimed to isolate the visuoconstructive component of the ROCF and determine its anatomical substrate. Secondly, we assessed whether the findings of the VLSM analyses could be reproduced using a region of interest-based analysis in which we additionally adjusted for total infarct volume, in order to rule out method-dependent false negative findings. The current study is the first to apply these advanced lesion-symptom mapping methods to determine the anatomical substrates of these visuospatial tests, and to decompose the ROCF in order to isolate the anatomical substrate for its visuoconstructive and visuoperceptive components.

2. Materials and methods

2.1. Subjects

A flowchart of the inclusion of patients for the current study is provided in Supplementary Fig. 1. From a prospectively collected database of patients who were admitted with ischemic stroke to our service, we retrieved data on all 111 patients who were admitted from November 2005 to December 2012 and who fulfilled the inclusion criteria for the current study: (1) first-ever ischemic stroke; (2) an infarction on follow-up CT or MRI; (3) complete data on the Rey–Osterrieth Complex Figure copy test (ROCF) or the Judgment of Line Orientation test (JLO). Patients with pre-existent neurologic conditions that might interfere with cognition were excluded history of cognitive impairment ($n=7$), traumatic brain injury ($n=5$), brain tumor ($n=4$), epilepsy ($n=1$), multiple sclerosis ($n=1$), moyamoya disease ($n=1$), or severe cerebral small vessel disease, reflected in large confluent lesions on CT/MRI (i.e. Fazekas grade 3; see Fazekas, Chawluk, Alavi, Hurtig, and Zimmerman, 1987; $n=7$). Patients with old brain infarcts ($n=30$) or recurrent stroke between imaging and neuropsychological examination ($n=2$) were excluded. Lesion locus and cognitive performance were no criteria for inclusion: patients with lesions anywhere in the brain, both with and without cognitive impairments were included. Due to the applied inclusion criteria, the prevalence of cognitive impairment in the study group might not reflect the prevalence in the overall stroke population. However, this was not considered to be a concern for the current study because we did not aim to assess the prevalence and severity of cognitive impairment following ischemic stroke. Instead, we aimed to determine the anatomical correlates of visuospatial construction by relating lesion location to variance in visuoconstructive abilities within the study group. The current study was approved by the institutional review board of the University Medical Center Utrecht.

2.2. Neuropsychological assessment

Neuropsychological assessment was performed in the setting of standard clinical care within one month after ischemic stroke (mean 7.6 days, range 1–30 days). We have previously demonstrated that the applied cognitive assessment battery is feasible and reliable in the acute stage (first days to weeks) of ischemic stroke (Nys et al., 2005). To perform the ROCF copy test, the figure was placed in front of the subject who was requested to copy the figure as accurately as possible (Osterrieth, 1944). The ROCF