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Research report

The right hemisphere is dominant in organization of visual search—A study in stroke patients

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HIGHLIGHTS

- Search organization was studied in a large sample of stroke patients.
- Disorganized search (DS) was found in 22% of stroke patients.
- Lesions in right parietal, temporal and occipital areas were related to DS.
- These regions are associated with conjunctive search and spatial working memory.
- Spatial processes appear to be the key mechanisms, compared to frontal functions.

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ABSTRACT

Cancellation tasks are widely used for diagnosis of lateralized attentional deficits in stroke patients. A disorganized fashion of target cancellation has been hypothesized to reflect disturbed spatial exploration. In the current study we aimed to examine which lesion locations result in disorganized visual search during cancellation tasks, in order to determine which brain areas are involved in search organization. A computerized shape cancellation task was administered in 78 stroke patients. As an index for search organization, the amount of intersections of paths between consecutive crossed targets was computed (i.e., intersections rate). This measure is known to accurately depict disorganized visual search in a stroke population. Ischemic lesions were delineated on CT or MRI images. Assumption-free voxel-based lesion-symptom mapping and region of interest-based analyses were used to determine the grey and white matter anatomical correlates of the intersections rate as a continuous measure. The right lateral occipital cortex, superior parietal lobule, postcentral gyrus, superior temporal gyrus, middle temporal gyrus, supramarginal gyrus, inferior longitudinal fasciculus, first branch of the superior longitudinal fasciculus (SLF I), and the inferior fronto-occipital fasciculus, were related to search organization. To conclude, a clear right hemispheric dominance for search organization was revealed. Further, the correlates of disorganized search overlap with regions that have previously been associated with conjunctive search and spatial working memory. This suggests that disorganized visual search is caused by disturbed spatial processes, rather than deficits in high level executive function or planning, which would be expected to be more related to frontal regions.

Abbreviations: FDR, false discovery rate threshold; IFO, inferior fronto-occipital fasciculus; ILF, inferior longitudinal fasciculus; MMSE, Mini-Mental State Examination; MNI, Montreal Neurological Institute; PCA, posterior cortical atrophy; ROI, region of interest; SAN, Stichting Afasie Nederland; SLF, superior longitudinal fasciculus; VLSM, voxel-based lesion-symptom mapping.

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1. Introduction

Cancellation tasks are widely used for diagnosis of lateralized attentional deficits in stroke patients. In these tasks, multiple targets have to be found among distractors and crossed out. Additionally, cancelled targets should not be crossed out twice. An asymmetry in number of omitted targets between the left versus right half of the page is typically used as an indication for visuo-spatial neglect, an attentional disorder which is defined as the failure to orient, report or respond to visual stimuli toward the contralesional side of space [20].

Completing a cancellation task in an *organized* way requires a preconceived top-down strategy. Though it is achievable to cancel all targets without adopting a specific strategy, a disorganized fashion of target cancellation has been hypothesized to reflect a disorder in spatial exploration or planning [31]. For instance, stroke patients show less organized cancellation patterns compared to healthy control subjects [37,47]. Moreover, stroke patients with visuo-spatial neglect have an even less organized visual search pattern compared to stroke patients without neglect [7,37,43,47,53]. Even though the presence of visuo-spatial neglect seems a marker for a disorganized search pattern in stroke patients, the relation is not straightforward, and neglect and disorganized search seem to be distinct phenomena [31]. Disorganized visual search during cancellation might reflect a multitude of various deficits, such as disturbed executive function, spatial working memory disorder (remapping problems), deficient inhibition of return, loss of a strategy or plan to guide spatial search, difficulties with disengaging attention from already cancelled targets or a failure to inhibit stimulus-bound motor responses [31].

In this study, we aimed to investigate the anatomical correlates of visual search organization. A computerized version of a cancellation task was presented to patients with stroke and used to compute the amount of *intersections* with paths between previous cancelled targets [14,37,47,54]. This measure is thought to best depict organization of visual search in a stroke population [47]. We performed voxel-based lesion-symptom mapping (VLSM) and region of interest-based (ROI) analyses within grey and white matter to determine the anatomical correlates of visual search organization, and to learn about the various components of visual search.

2. Material and methods

2.1. Procedure

The design of this study was retrospective. All clinical tests and imaging were conducted in the setting of standard clinical care. The research and consent procedures were performed in accordance with the standards of the Declaration of Helsinki.

2.2. Participants

Patients were selected from a cohort consisting of 357 stroke patients who were consecutive admitted to De Hoogstraat Rehabilitation center from November 2011 through February 2014. MRI or CT scans were administered in the hospital. At admission to the rehabilitation center, patients were screened for visuo-spatial neglect with a cancellation task as part of usual care within the first two weeks, if their condition permitted testing. A stepwise exclusion procedure was applied to these 357 patients according to the following criteria: (1) no data on the shape cancellation task (i.e., unable to understand instructions or unable to perform the task due to motor problems or fatigue; $n = 31$); (2) diagnosis other than ischemic stroke or delayed cerebral ischemia after subarachnoid haemorrhage ($n = 85$); (3) no delayed CT (i.e., performed >48 h after symptom onset) or MRI brain scan available for infarct segmentation ($n = 154$); (4) no infarct visible on post-stroke imaging ($n = 6$); and (5) insufficient quality of CT or MRI imaging ($n = 2$) (Supplementary Fig. 1).

2.3. Clinical characteristics

The following data were obtained on admission to the rehabilitation center: gender, age, time post-stroke, global cognitive functioning score (Mini-Mental State Examination, MMSE [17]), level of independence during daily live activities (Barthel Index [9]), strength in both upper and lower extremities (Motricity Index [8]), and presence of language communication deficits (Stichting Afasie Nederland, SAN score).

2.4. Shape cancellation task

The computerized shape cancellation task consisted of 54 small targets ($0.6^\circ \times 0.6^\circ$), 52 large distractors, and 23 words and letters (widths ranging from 0.95° to 2.1° and heights ranging from 0.45° to 0.95°). The stimulus presentation was approximately 18.5° wide and 11° high. Patients were seated 120 cm in front of a monitor and used a computer mouse. They were instructed to click all targets and tell the examiner when they had completed the task. No time limit was given. After each mouse click a small circle appeared at the clicked location and remained on screen, regardless whether a target, distractor, or location in between was clicked [51].

For each patient, all cancelled targets were connected in chronological order. Clicks at other locations were excluded from analyses. Targets that were revisited were included in analyses. The amount of crossings of paths between cancelled targets was computed (i.e., intersections). For each participant the *intersections rate* was computed with the CancellationTools software [14]. The intersections rate depicts the total amount of path intersections divided by the amount of cancellations that are not immediate revisits, resulting in a value ranging from 0 (no intersections) to 1 (maximum amount of intersections). An organized search pattern includes as few intersections as possible. That is, a high number of intersections would reflect less organized visual search [37,47]. See Fig. 1 for the target stimuli layout and examples of organized versus disorganized search. The convergent validity of the intersections rate was good, as observer ratings of disorganized search during a cancellation task were highly correlated with the intersections rate ($r = .87$ [54]).

In order to assess the robustness of the VLSM results with the intersections rate as continuous measure, we additionally performed VLSM using norm-based dichotomized performance on the shape cancellation task and a qualitative lesion subtraction analysis. In order to dichotomize the intersections rate, we used the scores of 37 healthy control subjects [47]. The threshold was set at their mean score plus 2.5 standard deviations. Stroke patients with an intersections rate above this threshold were assigned to the disorganized search group, whereas the other stroke patients were assigned to the organized search group.

2.5. Generation of lesion maps

The procedure for the generation of lesion maps has been previously described elsewhere and is only summarised here (for more details see Refs. [3–5]). Infarcts were manually segmented on transversal slices of either follow-up CT ($n = 49$), or on T2 FLAIR sequences of MRI scans ($n = 29$) by a trained rater who was blinded to the cancellation data (JMB). Infarct segmentations were transformed to the Montreal Neurological Institute (MNI)-152 template [18] using the following procedure. All registrations were performed with the elastix toolbox for registration [25]. An age-specific