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Visual search and visual working memory in patients with chronic focal cortical lesions

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Abstract

Visually guided behavior is known to involve temporo-parietal, inferotemporal, and prefrontal cortex and each of these areas appears to contribute to visual working memory. We explored the extent to which chronic lesions in one of these cortical areas affect visually guided oculomotor performance. We also explore whether possible impairments become more pronounced with increasing memory load. With this aim we recorded saccadic eye movements in 19 patients with a chronic focal postsurgical lesion in either temporo-parietal, inferior temporal or prefrontal cortex. Their results are compared to those of 19 age-matched volunteers. The subjects performed three different visual search tasks with increasing memory load: Instructed search, cue-guided search and memory-guided search. In addition, the latter task was performed with a short (1 s) and a long (6 s) delay. All tasks required the subjects to make a saccade to a single target presented together with one or three distractors. The results indicate that patients with inferotemporal lesions make the most task-related errors. Saccadic reaction times (SRTs) were significantly prolonged in patients with temporo-parietal and prefrontal lesions, but were unaffected in the patients with lesions in the inferotemporal cortex. The spatial accuracy of saccades was lowest in patients with temporo-parietal lesions. An increase in memory load led to more errors, to longer reaction times and to lower saccadic precision. However, the effect was similar across the three patient groups and the controls. An error analysis indicated that both patients and controls tended to weight global (luminance contrast and form) features higher than local features (line-segment orientation) when making difficult perceptual decisions.

Keywords: Working memory; Visual search; Eye movements; Brain lesions

1. Introduction

Each time we move our eyes our visual cortex is confronted with an immense amount of information from the surrounding environment. The average fixation period between saccades lasts about 200–300 ms (Fischer, 1987; Schall, 1991; Carpenter, 1996), so that we can access different segments of visual scenes at rates up to three times per second. Foveal vision is uniquely capable of encoding object and scene information by means of a highly parallel, distributed representation in neocortex (van Essen & Zeki, 1978; Zeki, 1978a,b).

Exploration of the visual scene requires visual search and, if the visual response is to be delayed for a short time, visual working memory is also required. Visual search refers to the ability of subjects to find a target among simultaneously presented distractors (Treisman, 1982). Identification of a target among distractors not only requires fast visual processing, but also demands the accurate control of ballistic eye movements (i.e. saccades) that guide the fovea to the target location (Findlay, 1995, 1997). The role of visual working memory in the visual processing chain is to store, for short periods of time, information about objects and their location in space, which is needed for subsequent behavioral responses (e.g. executing the next saccade). Thus, the search for a target among distractors requires both efficient oculomotor scanning behavior and visual memory.

Abbreviations: F, prefrontal cortex; IT, inferotemporal cortex; ST/LP, temporo-parietal cortex.

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It is widely believed that, in addition to the occipital cortex, three cortical regions underlie the processes required for visual working memory: the temporal cortex for pattern recognition (Mishkin, 1954; Iwai & Mishkin, 1969; Gaffan & Weiskrantz, 1980; Fuster & Jervey, 1982; Sahgal, Hutchison, Hughes, & Iversen, 1983), the parietal cortex for spatial localization (Andersen, Essick, & Siegel, 1985; Quintana & Fuster, 1992; Friedman & Goldman-Rakic, 1994; Andersen, 1995) and the prefrontal cortex for retaining information over time (Fuster, Bauer, & Jervey, 1985; Lawler & Cowey, 1987; Funahashi, Bruce, & Goldman-Rakic, 1989, 1990, 1993a). Experiments in monkeys suggest that there exist two major intracortical streams that transmit information from posterior sites (the visual areas V1 and V2) to anterior areas. One projection system (the so-called ventral stream) passes through the inferotemporal cortex and deals with the identification of visual objects (the 'what' pathway), whereas the other (dorsal stream) passes via superior temporal areas to the parietal cortex and deals with spatial aspects (the 'where' pathway). There is anatomical and electrophysiological evidence (Funahashi et al., 1989, Funahashi, Chafee, & Goldman-Rakic, 1993b; Ungerleider, Gaffan and Pelak, 1989; Wilson, Scalaidhe, & Goldman-Rakic, 1993; Friedman & Goldman-Rakic, 1994) that these streams continue anteriorly to prefrontal areas, where a decision is made whether to attend to a given stimulus, whether to perform a response and when to start the response. It remains to be determined whether the domain specificity for 'what' and 'where' have separate prefrontal representations ('what' in ventrolateral and 'where' in dorsolateral prefrontal areas; see, Wilson et al., 1993) or whether the domains become merged in prefrontal cortex (Rao, Rainer, & Miller, 1997). Evidence that the two streams participate in visual working memory comes from animal studies in which transient cooling or experimental lesions affected performance in a delayed response or a delayed match-to-sample task (Fuster et al., 1985; Funahashi et al., 1993a). Also, neurons in the prefrontal, temporal and parietal cortex have been shown to maintain firing activity throughout the delay period (Mikami & Kubota, 1980; Fuster & Jervey, 1982; Miyashita & Chang, 1988; Funahashi et al., 1989; Tanaka, Saito, Fukada, & Moriya, 1991; Miller, Li, & Desimone, 1993).

Previous work suggests that the mechanism of retaining information over short periods of time is primarily a function of the prefrontal cortex, which feeds back task-related, sustained activity to the inferotemporal and the parietal cortex in a 'top-down' fashion. For instance, it has been shown in monkeys that the extent of neuronal activity during the delay period typically is larger in prefrontal than in inferotemporal regions and is less disturbed by other inputs (Miller et al., 1993, Miller, Erickson, & Desimone, 1996). Furthermore, deactivation by cooling of prefrontal cortex decreases the selectivity of delayed responses in inferotemporal neurons (Fuster et al., 1985). A similar interplay between prefrontal and parietal neurons has been reported for spatial working memory tasks (Chafee & Goldman-Rakic, 1998).

The basic principle of functionally specialized ventral and dorsal processing pathways for visual information can also be found in the human cortex. Occipitotemporal lesions in humans lead to agnosia of objects, faces, or color (Benson & Greenberg, 1969; Albert, Reches, & Silverberg, 1975; Damasio, 1985; Zeki, 1990), while occipitoparietal lesions lead to disturbances in motion and spatial perception, which is required to plan visually guided movements (Zihl, von Cramon, & Mai, 1983; Barton, Sharpe, & Raymond, 1995; Greenlee, Lang, Mergner, & Seeger, 1995; Greenlee & Smith, 1997).

We explored the extent to which cortical lesions have a specific and long-lasting effect on visual search and visual memory. Using visual search tasks, we investigated how chronic cortical lesions in temporo-parietal (ST/LP), inferotemporal (IT) and prefrontal (F) areas affect oculomotor performance during visually guided and memory-guided search tasks.

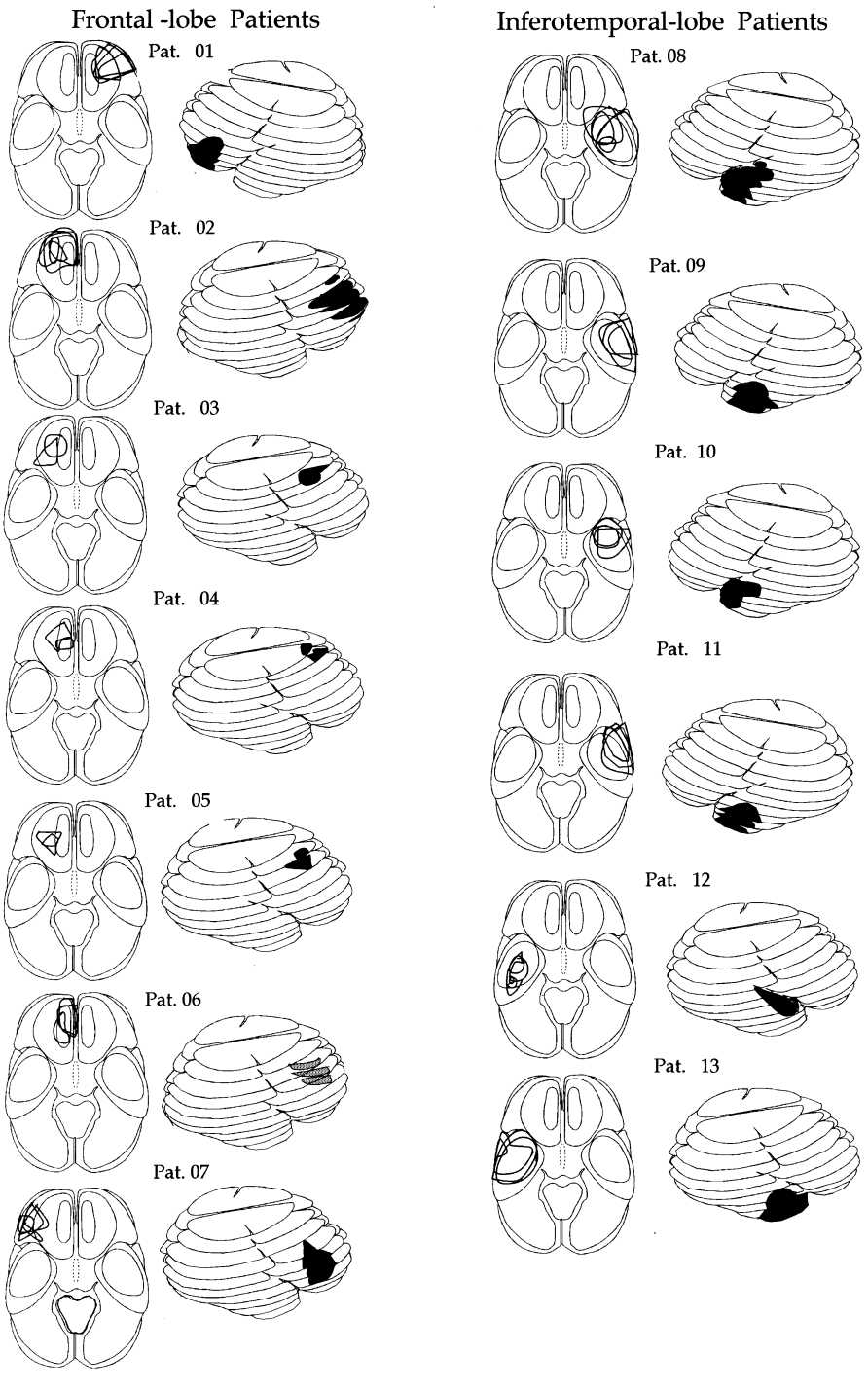
2. Methods

2.1. Subjects

Nineteen former patients were recruited from the clinical archives of the Department of Neurosurgery, University of Freiburg. The patients had a well-defined, unilateral lesion located either in the inferotemporal, temporo-parietal or prefrontal cortex, which resulted as a consequence of surgical resection of vascular malformations (three arteriovenous malformations, nine cavernous angiomas) or tumors (seven astrocytomas, low grade malignancy, without any signs of progression in follow-ups).

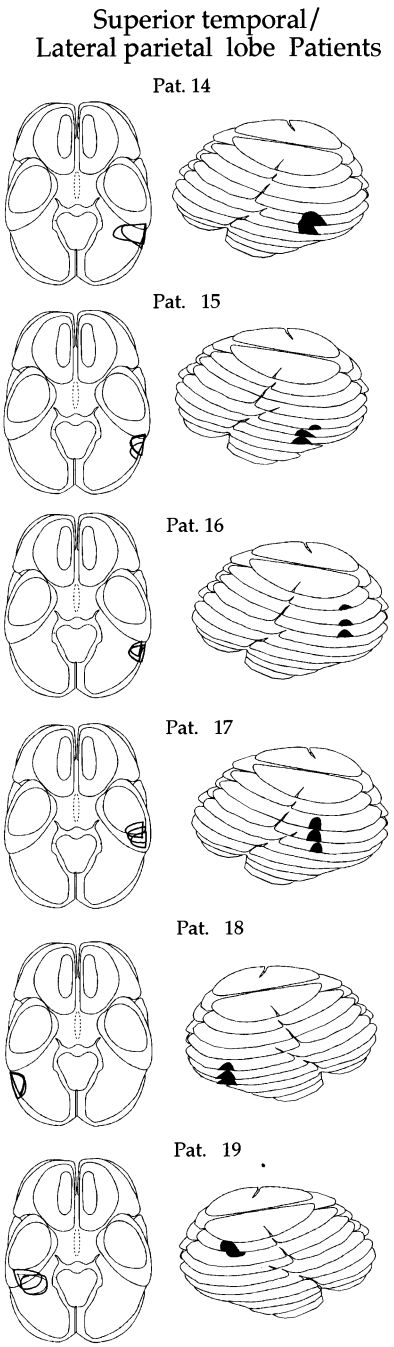
We excluded patients who were over the age of 60 years, those with multiple lesions or tumors of high-grade malignancy, and those receiving radiation therapy or high doses of anticonvulsant medication (>1000 mg/day). Patients were also excluded who showed substantial visual field defects (e.g. quadrant anopia, see below) or who exhibited established signs of visual neglect. Furthermore, we excluded patients with frontal lesions extending into the frontal eye field (FEF) and the supplementary eye field (SEF). The human FEF has been shown repeatedly in the past to be located in the precentral sulcus (BA 6; Sweeney et al., 1996; Petit, Clark, Ingeholm, & Haxby, 1997).

Surgical resections had been performed on average 56 months (range 1–84 months) prior to investigation. The patients' mean age was 37.5 years (range, 22–59 years); 14 male and five female patients participated. Four patients were left-handed (as determined by the Oldfield–Edinburgh Handedness Inventory; Bryden, 1982). Eight patients were receiving anticonvulsant medication (carbamazepine or phenytoin) at the time of study. Post-hoc analyses showed that the use of anticonvulsant medication had no significant effect on the experimental variables. Twelve patients were free of any neurological symptoms, one patient (PAT01, Fig. 1)



(a)

Fig. 1. Axial and lateral drawings of the computer-tomographic images revealing the location and extent of the cortical lesions (dark (light gray) shading in sagittal (medial) view, dark rings in axial view) in the patients under investigation.



(b)

Fig. 1. (*Continued*)

infrequently had mild seizures and two patients (PAT08, PAT10) exhibited a mild aphasia.

Prior to testing, all subjects performed two neuropsychological tests of short-term memory, i.e. Corsi Block Tapping (Milner, 1971) and Digit Span, digits forward (Wechsler, 1987). No significant difference was found between patients and controls on the Corsi Block Tapping test, whereas controls scored somewhat higher on the Digital Span test (mean score; controls = 8.8, patients = 7.6; $P < 0.05$). Visual fields were examined using automatic perimetry in cases where a field defect was suspected.

An equal number of control subjects, matched on age, gender and handedness, were recruited for the study and were paid a nominal fee for their participation. The control subjects had a mean age of 38.9 years (range, 22–58 years). Their ages did not significantly differ from those of the patient group.

2.2. Brain imaging

Computed tomographic (CT) and T1- and T2-weighted, magnetic resonance images (MRI) were acquired before and after surgery. Using standardized atlases of the human brain (Seeger, 1978; Talairach & Tournoux, 1988), we determined the extent and location of the cortical damage. The location and extent of the unilateral lesions are shown for each patient in Fig. 1. The patients were assigned to one of three groups depending on the focus of cortical lesion in either the left or right hemisphere. The lesions were located in seven patients in the prefrontal cortex (F), in six patients in the inferotemporal cortex (IT), and in six patients in the temporo-parietal cortex (ST/LP). Obviously the location and extent of lesions occurring within these three groups will vary to some extent. The patients have been grouped in a way as to maximize the similarity of location within each group. This method has been used in the past to determine the effects of brain lesions on psychophysical task performance (Greenlee, Rischewski, Mergner, & Seeger, 1993; Greenlee et al., 1995; Greenlee, Kössler, Cornelissen, Mergner, & Seeger, 1997; Greenlee & Smith, 1997).

2.3. Eye movement recording

The subject's horizontal and vertical eye movements were monitored with a head-mounted infrared recording system based on corneal reflection (IRIS, Skalar Medical, Delft, the Netherlands). The system derives eye velocity by on-line electronic differentiation of eye position. Position and velocity signals were sampled at 500 Hz and stored in a laboratory computer for off-line analysis. The spatial resolution was less than 0.5°. Calibration of eye position was made before and after each test condition. During each recording session, the subject rested his or her head on a chin-forehead rest, thereby assuring constant head position and viewing distance (57.4 cm).

Eye movement analysis was performed with the help of an interactive computer program. Saccades were detected by setting a velocity threshold of 30°/s. Artifacts resulting from blinks were detected and eliminated from further analysis. The method allowed us to estimate the saccadic reaction time (of the first saccade) and the subject's gaze errors. Central fixation had to be maintained prior to stimulus onset during the fixation period.

2.4. Stimuli and tasks

Texture stimuli were presented on a high-resolution color monitor (display subtending $30 \times 22°$) and were made up of 3×4 matrices of uniformly spaced slanted line segments (Fig. 2), each patch subtended $1.9 \times 2.7°$. The texture patches were defined by their luminance contrast with respect to the background ($\pm 12.5\%$ contrast, mean luminance = 8 cd/m^2), by their global form (vertical or horizontal rectangles) and by the local orientation of the line segments ($\pm 45°$). The patches were presented 5° eccentric of fixation (distance between fixation point and center of stimulus), one in each visual quadrant. These stimulus dimensions were selected to isolate global (luminance contrast, form) and local (line-segment orientation) processing components.

Four tasks were performed (Fig. 2).

2.4.1. Instructed search task (Fig. 2a)

The subject was informed at the beginning of the recording session which stimulus feature was of importance. Two test stimuli (200 ms duration) were presented on each trial, randomly in two of the four possible locations. The test stimuli differed only on the feature to be discriminated (e.g. luminance contrast). Over the trials the stimuli randomly varied with respect to the other two stimulus features. At the beginning of each measurement, the subject was instructed to make saccades to the center of the texture patch with the appropriate feature (e.g. 'Shift your gaze always to the bright target!'), as indicated by the virtual arrow (not present during the experiment). This condition assesses the ability of the patients to discriminate the stimuli and to make visually guided saccades without depending on memory. As such, it served as a screening test and was thus performed at the beginning in each subject.

2.4.2. Cue-guided search task (Fig. 2b)

A texture patch, serving as a cue, was presented centrally for 200 ms to be followed 1 s later by the simultaneous presentation of four test patches (stimulus duration 200 ms). The cue was identical on all three features to only one of the four test patches. The other three stimuli served as distractors and could differ from the cue on either one, two or all three features. The subject's task was to make saccades to the center of the target stimulus, i.e. to the test patch that was identical to the cue on all features. Target location was randomized over trials. This condition assesses cue-guided visual search performance for a target among distractors. The cue had to be remembered along all three dimensions so that the patient could find the target among the distractors.

2.4.3. Memory-guided search task (with short or long delay; Fig. 2c)

This task was similar to the previous task, except that the order of the cue and test stimuli was reversed. First, the four test patches were presented for 200 ms

and then, after a delay, the cue stimulus was presented for 200 ms. The delay between the offset of the test patch and the onset of the cue was either short (1 s) or long (6 s). The subject was now asked to make a saccade to the remembered location of the target stimulus. By presenting the four stimuli first and then after the inter-stimulus interval (ISI) the cue, we challenge most the short-term memory mechanism.

On all trials, the fixation point was extinguished 200 ± 50 ms prior to the onset of the test stimuli. Each subject performed 256 trials for each condition (total number of trials = 1280). Owing to the prolonged nature of the task, the memory-guided search task with the long delay was split into two blocks of 128 trials each. Adequate rest periods were given between measurement blocks. The instructions were given in a way to emphasise task accuracy, speed and saccadic precision equally. In all conditions, the subjects were instructed to make saccades to the centre of the selected target. They were informed that their errors, the latency and the saccadic accuracy were being recorded. The order of the four conditions was randomised over subjects, with the exception that the instructed search was performed first in all cases.

2.5. Error analysis

Trials were scored according to the final eye position with respect to the target/distractor location. The final eye position was defined as the position of gaze after a maximum of 3 saccades (the primary and two smaller correction saccades). We defined a time window that extended from 100 to 1500 ms, during which time the gaze should have come to rest at one of the possible target locations. A trial was judged as correct when the final eye position corresponded to the quadrant containing the target stimulus. The results of a trial were scored as a valid error if the final eye position was within the quadrant of one of the three distractors. Trials were scored as yielding invalid errors in cases where adequate fixation was not maintained prior to stimulus onset and/or where the final eye position fell either within a 2° zone along the vertical and horizontal midlines ($\pm 1°$ relative to the respective meridians) or beyond the stimulus display (see Fig. 2, inset).

During the response period, small (single pixel) white dots were presented at locations corresponding to the centre of the target or distractor stimuli. These dots were only visible when the subject's gaze fell within 1°

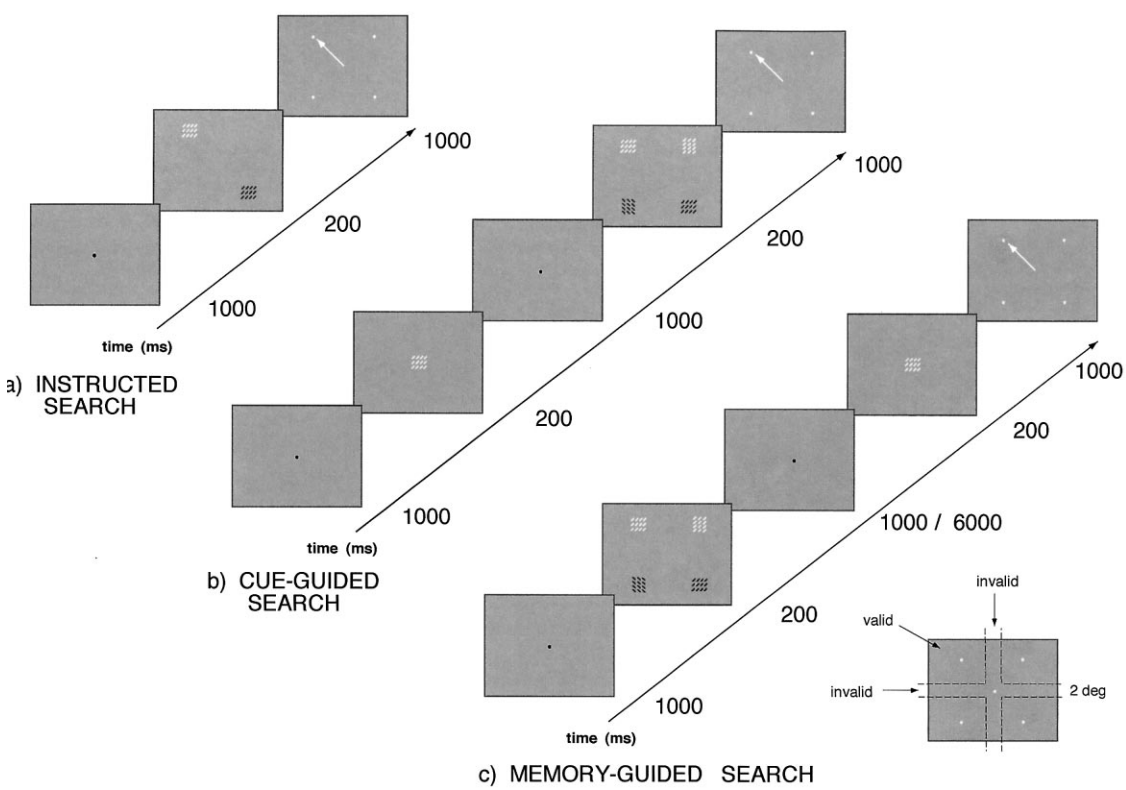


Fig. 2. Schematic illustration of the experimental paradigms employed in the present investigation. The texture patches were defined by their luminance contrast (bright versus dark), by their global form (vertical or horizontal rectangles) and by the line-segment orientation that make up the texture ($\pm 45°$). Three tasks were performed: instructed search (a), cue-guided search (b), and memory-guided search (c). In all tasks, the subjects were requested to make an eye movement to the target among distractors (as shown by virtual arrow). The small white dots (single pixel) were presented to provide information regarding the accuracy of the final eye position (only visible in foveal vision). The inset (lower right corner) illustrates the invalid and valid zones used to define the errors in final eye position.

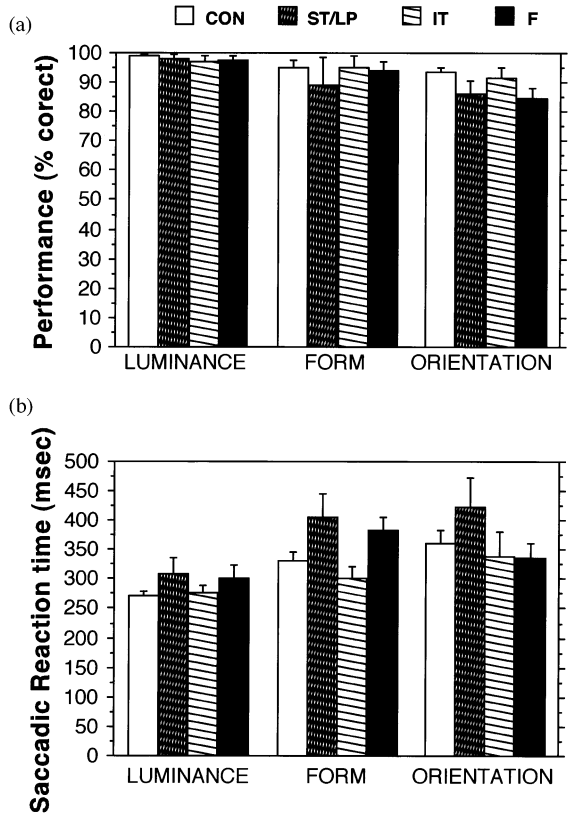


Fig. 3. (a) Probability of correct responses for the three patients groups and the control subjects for the instructed search task. The mean of these performance scores is shown for each of the three stimulus features. (b) The saccadic reaction times are shown for each stimulus feature (instructed search task) for the controls and the three patient groups.

of the dot. We informed subjects that the dots indicated the true centre location of the stimuli. The dots were provided as a form of visual feedback for the subjects, since the dot location could be used to assess the accuracy of each final eye position. The small fixation dot also helped the subjects to maintain their gaze long enough to establish the final eye position.

The distribution of errors was analyzed for all subjects by calculating the relative frequency of the different types of valid errors on the cue-guided and memory-guided tasks (errors in the instructed search task were analyzed separately). The errors were classified by comparing the distractor that was erroneously saccaded to with the target on all three stimulus features.

2.6. Data analysis

The task-related errors, saccadic reaction times (based on latency between stimulus onset and the beginning of the first saccade) and the saccadic accuracy (defined by the standard deviation of the final eye position in deg) were statistically evaluated with an analysis of variance for repeated measures (SuperANOVA and StatView 4.5, Abacus Concepts). The nonparametric contingency coefficient (c) was calculated to determine the χ^2-value of the observed error distributions. We tested the main effect of experimental group (patients versus controls) and the main effect of the task performed (instructed search, cue-guided search, memory-guided search with short and long delays). The effects of lesion location, lesioned hemisphere and relative position of target with respect to lesioned side (i.e. contralesional versus ipsilesional) were determined among the patients.

3. Results

An important prerequisite of performance on the cue- and memory-guided tasks is the ability to discriminate the stimuli along each of the three defining features, namely luminance contrast, form and line-segment orientation (see Section 2). Once this information has been encoded, it can be used to guide the subject's gaze to the target among distractors. As such, the instructed search task served as a screening test for both oculomotor control and visual discrimination. The results of the instructed search are shown in Fig. 3 with regards to the task performance (a) and saccadic reaction times (b) for the three patient groups and the controls. In this task the guessing level is at 50%, and the target and a single distractor always differed only on the instructed stimulus feature. In pilot experiments the stimuli were carefully designed so that discriminability across the features was approximately similar.

The findings related to percent correct, presented in Fig. 3a, indicate that both the control subjects and the patients were capable of making correct saccades to a target containing a predesignated feature in the presence of a single distractor. The overall difference between patients and controls with respect to valid errors (see Section 2) on the instructed search task was not significant (Contingency coefficient, $c = 0.028$). The effect of lesion location across patient groups was significant ($c = 0.138$, $P < 0.0001$). This difference arises mainly from the patients with F and ST/LP lesions, who made relatively more orientation errors, and form and orientation errors, respectively. However, the effect of lesioned hemisphere was not significant ($c = 0.019$). All subject groups had somewhat more difficulty discriminating between the line-segment orientation (40.4% of all valid errors) and the form of the texture patches (34.3%) than they did for stimuli that differed in luminance contrast (25.3%). Thus, the luminance contrast was the most predominant feature, followed by stimulus form and line-segment orientation.

As can be seen in Fig. 3b the saccadic reaction times for the correct responses were shortest for luminance

contrast as compared to form and line-segment orientation ($F_{2,6} = 8.5$; $P < 0.0003$). The longest latencies, on average, were found in the patients with ST/LP lesions, followed by patients with frontal lesions, while patients with IT lesions were similar to the controls ($F_{3,6} = 3.45$; $P < 0.02$).

3.1. Saccadic accuracy and final eye position

The results for the final eye position are shown in Fig. 4 for the three patient groups and the control subjects. The final eye position (correct trials only) is plotted on xy-coordinates for each of the four tasks performed. The mean values (patients, open symbols; controls, filled circles) show a slight hypometria with respect to the center of each target ($\pm 4°$ for x and y). Overall, there was no substantial difference for the mean final eye position across the subject groups. An index of variability is given in Fig. 4 by ellipses for the patients and by the crossbars for the controls (standard deviation averaged across subjects within each group). There was a slight tendency for the variability to be larger in the instructed search as compared to the cue-guided search, which we attribute to the fact that the former task always was conducted first. Interestingly, an analysis of variance with the standard deviation of the final eye position as the dependent variable revealed a significant difference between patient groups ($F_{2,16} = 9.89$; $P < 0.002$). This effect is related to the large variability shown by the patients with ST/LP lesions, as indicated by post-hoc pairwise comparisons (Bonferroni-Dunn; F vs. ST/LP, $P = 0.004$; IT vs. ST/LP, $P < 0.007$). The effect was especially prominent with the 6 s memory-guided search (F vs. ST/LP,

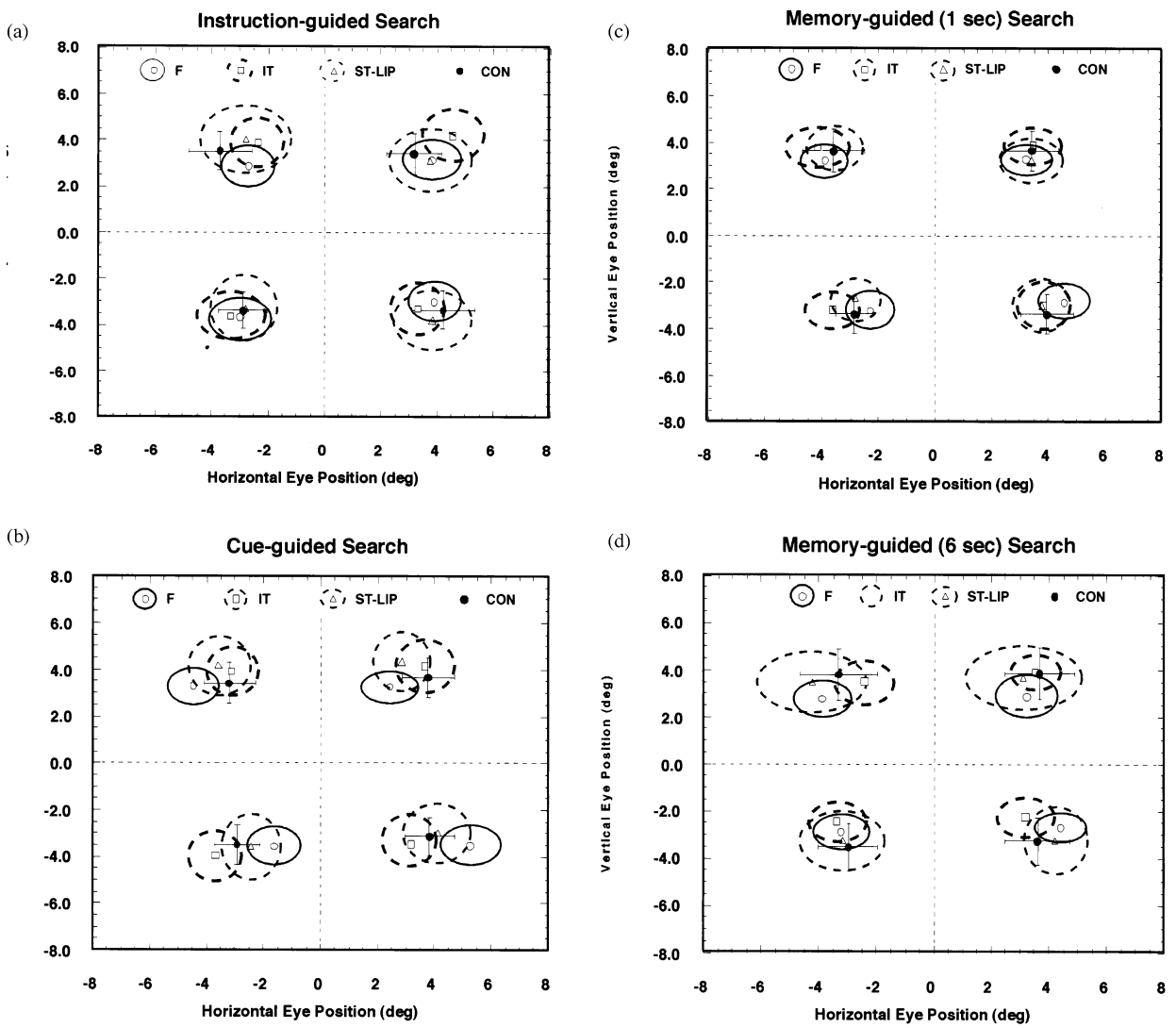


Fig. 4. Final eye position (symbols) and the variability of the final eye position (standard deviations shown by ellipses) for each patient group. Panels a–d present the results for the four different tasks performed. For comparison, the control results are presented by the filled circles and error bars give the average standard deviation.

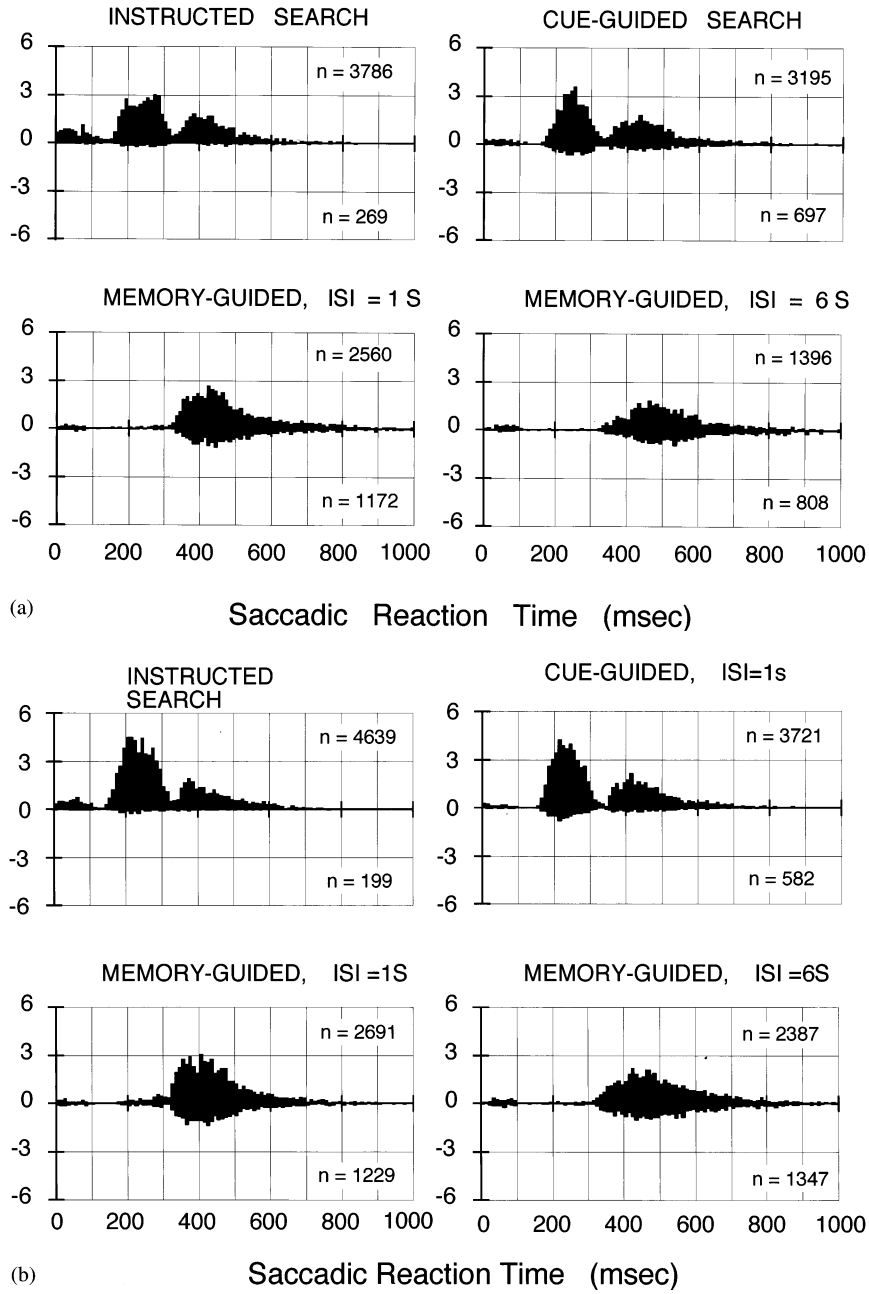


Fig. 5. Histograms depicting the relative frequency of saccades as a function of the saccadic reaction time (SRTs; zero corresponding to the time of test stimulus onset) for correct and incorrect trials, as shown by positive and negative percentages. The total number (n) of saccades are shown for correct trials (above abscissa) and for incorrect trials (below abscissa) summed over all subjects. (a) Presents the findings for the patients with a focal lesion on one cortical hemisphere and (b) gives the results for the 19 age-matched controls. The results for the instructed and cue-guided tasks are shown in the upper panels, those for the memory-guided search task for short (1 s) and long (6 s) delays in the lower panels, respectively. A trial was scored as correct when the final eye position (gaze location) was in the same quadrant as the target.

$P = 0.002$; IT vs. ST/LP, $P = 0.001$). Although there was a tendency for patients with left hemisphere damage to exhibit a slightly larger standard deviation in the final eye position (SD$x = 0.98$ vs. 0.81°; SD$y = 0.96$ vs. 0.95°), this difference was not significant. The joint effects of lesioned hemisphere and visual quadrant (i.e. ipsi- and contralesional) were negligible. This latter finding suggests that the effects of the lesions were not limited to the contralateral visual field.

3.2. Saccadic reaction time distributions

The distributions of the control subjects' and the patients' saccadic reaction times (SRTs) in the different tasks are shown in Fig. 5, panels a and b, respectively. The relative frequency of correct and incorrect trials, shown by positive and negative percentage values (ordinates), is plotted as a function of the latency of the first saccade for the four tasks performed. Trials were

scored as correct if the final eye position fell within the valid zone containing the target (see Section 2). In both normal subjects and patients a distinct bimodal distribution can be observed for the instructed and cue-guided tasks, showing maxima around 250 and 400 ms, respectively. In contrast, in the memory-guided tasks the early peak is no longer present, leaving a unimodal distribution with a maximum between 400 and 500 ms. Visual inspection of the distributions of SRTs indicated that these were comparable across the three patient groups.

Fig. 6a serves to facilitate comparisons between the three patient groups and controls, by plotting the mean SRTs for each of the performed tasks, separately for each group. Table 1 presents the portion correct and saccadic reaction times for each patient separately. Patients with inferotemporal (IT) lobe damage exhibit SRTs that are comparable to those of the controls (mean values are even slightly lower). Contrary to this, patients with damage in the ST/LP areas and the prefrontal cortex (F) show significantly increased SRTs under all conditions tested. Despite the non-normal distribution of the raw data of each individual subject, the mean SRTs across subjects were approximately normally distributed. We could thus apply parametric tests of significance to these mean values. An ANOVA for repeated measures revealed a significant main effect of lesion location ($F_{2,16} = 4.8$; $P < 0.02$), where patients with ST/LP and F lesions showed longer SRTs than the patients with IT lesions.

The experimental task had a highly significant effect on SRTs ($F_{3,111} = 133.1$; $P < 0.0001$), showing an increase in SRTs with increasing memory load (compare Fig. 6c). This task effect for SRTs was similar in both patient and control groups (as evidenced by a lack of a significant interaction term, group × task; $F_{3,111} = 0.36$). A post-hoc analysis also revealed a difference in the mean SRT for correct trials versus incorrect trials (mean SRT, correct trials = 446 ms; incorrect trials = 428 ms; $F_{1,37} = 16.9$, $P > 0.0002$). We attribute this effect to additional processing time required to perform the task correctly. The effect of damaged hemisphere (left vs. right) on SRTs was not significant, nor were any of the first and second-order interaction terms between the hemisphere and other variables significant. The lack of a hemifield-specific effect speaks for an impairment that is not tied to retinotopic coordinates.

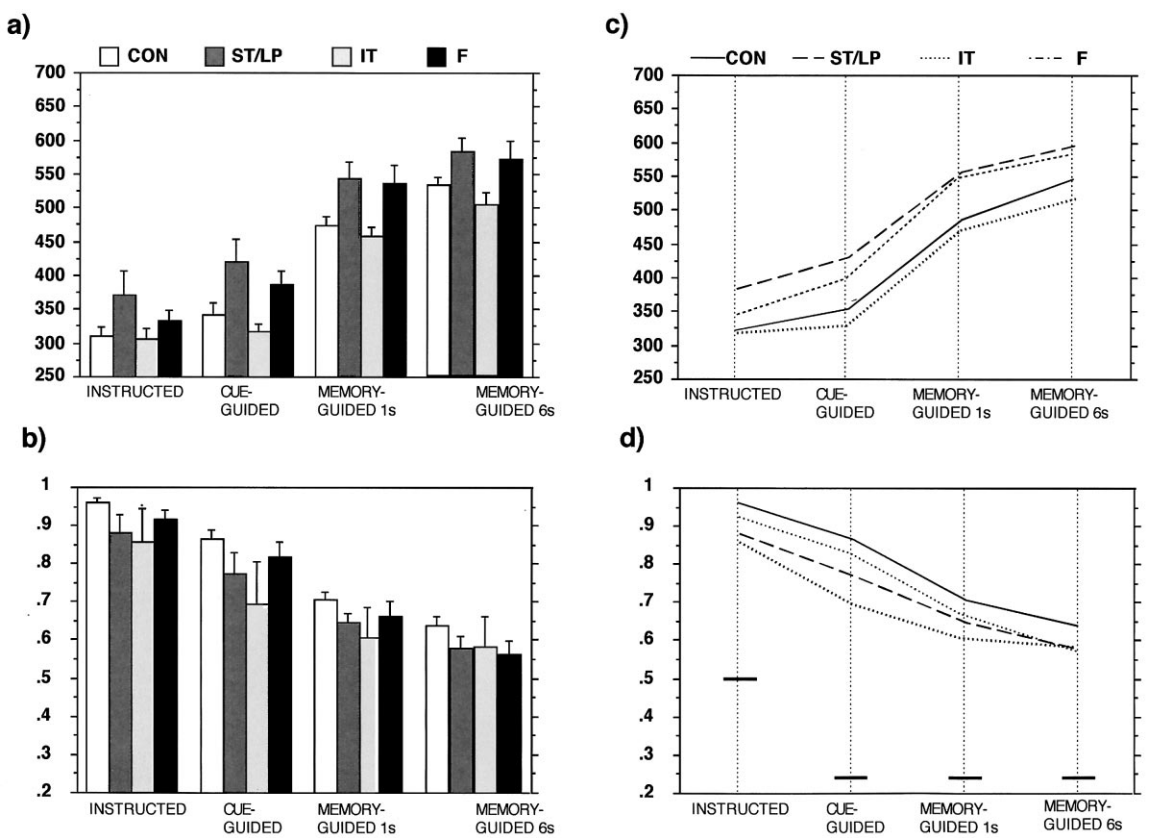


Fig. 6. Mean performance for the three patient groups and the controls for the four tasks. (a) and (c) show the mean saccadic reaction times (for SRTs > 80 ms, correct trials only as a function of the task. (b) and (d) present the probability of correct performance is shown as a function of the task performed. Error bars present 1 standard error of the mean values (a,b). Horizontal bars in panel d indicate the performance level expected by chance.

Table 1
Portion of correct trials and saccadic reaction times during the four experimental tasks

Patient ID	Group	Instruction		Cue-guided		Memory (ISI = 1 s)		Memory (ISI = 6 s)	
		correct	SRT	correct	SRT	correct	SRT	correct	SRT
1	F	0.949	263.3	0.755	285.2	0.511	506.3	0.536	581.5
2	F	0.993	316.8	0.976	480.8	0.635	751.7	0.449	793.9
3	F	0.905	301.3	0.786	312.2	0.741	578.3	0.544	609.8
4	F	0.975	321.8	0.817	445.1	0.764	520.6	0.76	546.3
5	F	0.896	386.1	0.653	338.9	0.616	530.5	0.5	498.1
6	F	0.825	324.5	0.813	424.1	0.562	499.6	0.571	523.1
7	F	0.884	376.2	0.914	396.0	0.798	445.6	0.569	557.8
8	IT	0.955	280.1	0.403	354.2	0.402	477.8	0.361	562.7
9	IT	0.978	406.1	0.826	339.4	0.812	406.2	0.75	509.6
10	IT	0.996	250.6	0.936	252.2	0.587	483.2	0.552	516.1
11	IT	0.881	271.2	0.909	328.4	0.723	522.3	0.728	595.0
12	IT	0.91	371	0.78	352.8	0.769	400.9	0.761	438.9
13	IT	0.415	275.7	0.309	291.2	0.348	461.1	0.34	468.1
14	ST/LP	0.913	417.0	0.726	474.1	0.573	588.8	0.625	645.1
15	ST/LP	0.701	302.1	0.895	388.5	0.676	534.9	0.43	586.2
16	ST/LP	0.969	306.4	0.891	352.3	0.695	477.8	0.571	588.7
17	ST/LP	0.963	214.4	0.53	274.4	0.554	642.9	0.575	477.2
18	ST/LP	0.957	561.0	0.833	660.5	0.714	649.6	0.678	696.1
19	ST/LP	0.788	441.0	0.768	391.3	0.651	508.4	0.586	553.9

3.3. Task-related errors

The results obtained with respect to the error rates on each of the four tasks are shown in Fig. 6b in terms of 'probability correct'. The proportion of correct responses was significantly lower in the patients compared to controls ($F_{1,36} = 6.11$; $P < 0.02$). Patients with IT damage show a tendency to make more task-related errors (i.e. they more often made saccades to one of the distractors), followed by patients with ST/LP damage and those with F lesions. The effect of the experimental task (memory load; Fig. 6d) over all subjects was highly significant ($F_{3,111} = 118.9$; $P < 0.0001$). The interaction term between the experimental task and the experimental group (controls, IT, ST/LP, F lesion groups) was not significant, indicating that the effect of memory load was similar across groups.

3.4. Analysis of error distribution

Table 2 presents the relative error frequencies for the three patient groups and the control group. As described in Section 2, trials were classified as a valid error when the final eye position fell within the valid zone of a distractor. A trial was judged as invalid when the final eye position was outside the valid zone (see inset in Fig. 2). The error rates of the patients with prefrontal and IT lesions were not significantly different from those of the controls. However, there was a significant tendency for the patients with ST/LP damage to make more invalid errors (post hoc Bonferroni/Dunn, $P < 0.01$). This result suggests that these patients were more impaired with respect to their oculomotor control. Patients with right hemispheric damage also tended to make more invalid errors, on average in 29.7% of all trials, compared to patients with left hemispheric damage (17.8%).

As mentioned above, the results shown in Fig. 6b indicate that all subjects made more valid errors with increasing memory load. In a post-hoc analysis we analyzed the types of errors made by the subjects for the cue and memory-guided tasks for valid errors only. Since on any given trial the distractors could differ on any one, two or all three features, we could measure the relative frequency of the different error types. These relative error distributions are shown in Table 3. By way of example, if a subject made a saccade to a distractor that differed from the target only by the orientation of its line elements, then this trial was classified as yielding an orientation error. Accordingly, 52.4% of all errors were related to the line-segment

Table 2
Relative frequency (in %) of different error types (valid and invalid) in the three patient groups compared to the controls

	Group			
	F	IT	ST/LP	CON
Subjects (n)	7	6	6	19
Valid errors	17.0	15.5	15.4	17.4
Invalid errors	20.5	18.3	30.1	12.7
Sum	37.5	33.8	45.4	30.1

Table 3
Number of errors (column percentage in parentheses) is shown for the patients (PAT) and controls (CON), summed over all conjunctive search (cue- and memory-guided) tasks[a]

	Lesion Location			Totals		
	F	IT	ST/LP	PAT	CON	Totals
Subjects (n)	7	6	6	19	19	38
Orientation	607 (53.1)	518 (57.3)	436 (48.9)	1561 (53.1)	1887(51.9)	3448 (52.4)
Form	230 (20.1)	155 (17.1)	205 (23.0)	590 (20.1)	781 (21.5)	1371 (20.8)
Luminance contrast	64 (5.6)	50 (5.5)	19 (2.1)	133 (4.5)	123 (3.4)	256 (3.9)
Orientation and form	133 (11.6)	85 (9.4)	159 (17.8)	377 (12.8)	560 (15.4)	937 (14.2)
Orientation and LC	55 (4.8)	17 (1.9)	29 (3.3)	101 (3.4)	108 (3.0)	209 (3.2)
Form and LC	21 (1.8)	59 (6.5)	23 (2.6)	103 (3.5)	107 (2.9)	210 (3.2)
All wrong	33 (2.9)	20 (2.2)	20 (2.2)	73 (2.5)	72 (2.0)	145 (2.2)
Totals	1143	904	891	2938	3638	6576

[a] The effect of lesion location is shown separately (F, IT, ST/LP). The different rows give the number of valid errors related to the orientation of the line elements, the form of the stimulus, the luminance contrast of the stimulus or combinations of these features.

orientation (local processing), 20.8% of the errors were related to the form of the patch (global processing), and another 14.2% of errors were related to a combination of these two features. Only 3.9% of all errors were related to the luminance contrast of the target (global processing), whereas the remaining 8.6% of errors were related to combinations of these three features. Analyzed over all subjects, these trends were highly significant ($\chi^2 = 36.5$; $df = 12$; $P < 0.0003$). Interestingly, the error distributions were not statistically different between patient and controls groups, suggesting that, on average, both patients and controls used similar strategies to solve the search tasks.

A further analysis was conducted concerning the spatial location of the target on trials containing a valid error (upper versus lower quadrants; left versus right hemifields; ipsilesional versus contralesional hemifields). Patients with prefrontal lesions made more errors for contralesional targets (ipsilesional: 44% versus contralesional: 56%), whereas patients with ST/LP lesions made more errors for ipsilesional targets (54 vs. 46%). Patients with IT lesions showed no effect. The contingency coefficient was significant ($c = 0.083$; $P < 0.0001$). This trend in the error behavior was unexpected and eludes any simple interpretation.

4. Discussion

The present results support findings of previous studies, which indicate that focal lesions in the temporo-parietal, inferotemporal and prefrontal cortex lead to specific impairments in oculomotor performance in a visual search task. Before considering the effects of lesion location, we first discuss the general finding concerning the role of memory load on saccadic reaction times and task performance.

4.1. Saccadic reaction times and task performance

Saccadic reaction times demonstrate a clear bimodal distribution for each subject while he or she performs a visual search task. Two peaks can be resolved in the cumulative records in the instructed and cue-guided search tasks, the first with a maximum around 250 ms and a second with a maximum around 400 ms. An increase in the memory load, as represented by the transition from cue-guided to memory-guided search, has a substantial effect on the recorded SRTs. The early peak in SRTs is virtually absent leaving a single maximum around between 440 and 500 ms for the memory-guided tasks (Fig. 5a and b, lower panels, respectively). In these tasks, the subject must retain in memory the information about the four stimuli and their relative locations. At the time of cue presentation, this information must be retrieved and compared with the newly incoming information about the cue stimulus. This retrieval process obviously requires some time, as evidenced by the absence of saccades with latencies below 300 ms.

Overall the distributions of SRTs were comparable across patient and control groups, suggesting that both groups performed the tasks in a similar way (Fig. 5). Although the cue- and memory-guided tasks were difficult, the results clearly indicate that the patients were able to perform the task. Even though the patients did not perform as well as the controls, each patient's performance was clearly above that expected by chance (Table 1). The similar distributions of error types (Table 2) suggest that patients and controls used comparable strategies to solve the tasks.

4.2. Effect of lesion location on saccadic reaction times and task performance

4.2.1. Temporo-parietal lesions

The patients with damage in the parietal areas exhibited the longest saccadic reaction times (Fig. 6a and c) and made the most invalid errors (i.e. their saccades often fell outside of the spatial and temporal windows used; Table 2). Furthermore, the variability of their final eye position was largest and increased significantly with increasing task difficulty. Though based on only a few patients (Fig. 1, Table 1), these findings suggest that patients with parietal lesions had considerable difficulty in making saccades to the required location, in support of a role of the lateral parietal cortex in the control of saccades. In addition, the high variability of final eye position in ST/LP patients for the memory search task with a long delay (Fig. 4d) was only observed in this patient group.

The results provide further evidence that the human dorsal stream, having access to eye and head position information, is involved in the real-time and retrospective mapping of spatial coordinates. As such our results complement the single-unit data described in monkeys (Andersen et al., 1985; Andersen, 1995). Along similar lines, Constantinidis and Steinmetz (1996) found significant activity in parietal cells (area 7a) during the retention period of a delayed match to sample task. They relate this activity to short-term memory of stimulus spatial location.

Our results also are compatible with SRT studies in patients with parietal lesions and with recent functional imaging studies in humans. In the patient study of Pierrot-Deseilligny, Rivaud, Penet, and Rigolet (1987) lesions in the lateral parietal (LP) cortex affected both latencies and accuracy of memory-guided saccades. Similarly, in the study of Braun, Weber, Mergner and Schulte-Muenting (1992) parietal lesions led to more variable SRTs and more direction errors. The present findings extend these earlier observations with respect to the effect of memory load on SRTs (Fig. 6a and c), variability of final eye position (Fig. 4) and frequency of spatial (invalid) errors (Table 2) in cue-guided and memory-guided tasks. Recent fMRI studies confirmed a role of the lateral parietal cortex in saccade generation (Luna et al., 1998; Petit et al., 1997) and an interaction between the lateral parietal cortex and the FEFs was found in a comparison between saccadic tasks and covert shifting of attention (Corbetta, 1998).

4.2.2. Inferotemporal lesions

The patients with IT lesions exhibited normal saccadic latencies, but tended to make more errors related to pattern recognition in the visual search and working memory tasks (Fig. 6a and c). This trend is in accordance with a number of earlier studies (see Section 1) and recent studies in our laboratory which showed that patients with lesions in the posterior inferotemporal lobe have more difficulty discriminating between briefly presented grating and random block patterns (Greenlee et al., 1993, 1997). It is also in agreement with lesion studies in monkeys. As part of the ventral stream, neurons in macaque IT cortex have been shown to respond during the delay period of a delayed match-to-sample task (Fuster & Jervey, 1982; Miyashita & Chang, 1988; Miller, Li, & Desimone, 1991). Furthermore, reversible cooling lesions in IT cortex are associated with poorer memory performance (Fuster, Bauer, & Jervey, 1981; Horel, Pytko-Joiner, Voytko, & Salsbury, 1987). In the present study, chronic IT lesions lead only to a mild impairment in pattern discrimination (Fig. 6b and d).

4.2.3. Frontal lesions

The present results also indicate that patients with damage in the prefrontal cortex exhibit longer latencies when making a saccade to a target among distractors. The results of functional magnetic resonance imaging (McCarthy et al., 1994; Courtney, Ungerleider, Keil, & Haxby, 1997) and positron emission tomography (Swartz et al., 1995) of human cortex, acquired while subjects performed memory tasks, also point to a significant enhancement of activity in prefrontal cortex. It should be noted that the exact location of prefrontal damage will affect the nature of the perceptual and mnemonic impairment (compare Table 1 and Fig. 1).

It appears from behavioural work in monkeys that working memory is primarily a function of the prefrontal cortex and, if at all, sustained activity in the inferotemporal cortex seems to stem mainly from prefrontal projections (see Ungerleider, Courtney, & Haxby, 1998). Chronic focal lesions in prefrontal cortex, though significantly impairing performance in our tasks, did not selectively alter the visual working memory component of task performance. As a recipient of information from both the dorsal (location) and ventral (object) pathways (Ungerleider & Mishkin, 1982), the prefrontal cortex, acting as a central executive (Goldman-Rakic, 1988; Baddeley, 1992), appears to control oculomotor responses in visually mediated selection processes (Pierrot-Deseilligny, Rivaud, Gaymard, Muri, & Vermersch, 1995). In this framework, the posterior parietal cortex provides the spatial information required to program the saccade, while the inferotemporal cortex provides object-related information required for stimulus selection. Our results point to a distributed representation of spatial and object-related visual information in the three cortical regions studied.

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References

Albert, M. L., Reches, A., & Silverberg, R. (1975). Hemianopic colour blindness. *Journal of Neurology, Neurosurgery and Psychiatry*, *38*, 546–549.

Andersen, R. A. (1995). Coordinate transformation and motor planning in posterior parietal cortex. In M. S. Gazzanga, *The Cognitive Neurosciences* (pp. 519–532). Cambridge, MA: MIT Press.

Andersen, R. A., Essick, G. K., & Siegel, R. M. (1985). Encoding of spatial location by posterior parietal neurons. *Science*, *230*, 456–458.

Baddeley, A. (1992). Working memory. *Science*, *255*, 556–559.

Barton, J. J. S., Sharpe, J. A., & Raymond, J. E. (1995). Retinotopic and directional defects in motion discrimination in humans with cerebral lesions. *Annals of Neurology*, *37*, 665–675.

Benson, D. F., & Greenberg, J. P. (1969). Visual form agnosia: a specific defect in visual discrimination. *Archives of Neurology*, *20*, 82–89.

Braun, D., Weber, H., Mergner, T., & Schulte-Muenting, J. (1992). Saccadic reaction times in patients with frontal and parietal lesions. *Brain*, *115*, 1359–1386.

Bryden, M. P. (1982). *Laterality: functional asymmetry in the intact brain*. New York: Academic Press.

Carpenter, R. H. S. (1996). Eye movements and the mechanisms of accomodation and the pupil. In R. Greger, & U. Windhorst, *Comprehensive human physiology* (pp. 829–837). Heidelberg: Springer Verlag.

Chafee, M. V., & Goldman-Rakic, P. S. (1998). Matching patterns of activity in primate prefrontal area 8a and parietal area 7ip neurons during spatial working memory task. *Journal of Neurophysiology*, *79*, 2919–2940.

Corbetta, M. (1998). Frontoparietal cortical networks for directing attention and the eye to visual locations: identical, independent, or overlapping neural systems? *Proceedings of the National Academy of Science USA*, *95*(3), 831–838.

Constantinidis, C., & Steinmetz, M. A. (1996). Neuronal activity in posterior parietal area 7a during the delay periods of a spatial memory task. *Journal of Neurophysiology*, *76*, 1352–1355.

Courtney, S. M., Ungerleider, L. G., Keil, K., & Haxby, J. V. (1997). Transient and sustained activity in a distributed neural system for human working memory. *Nature*, *386*, 608–611.

Damasio, A. (1985). Disorders of complex visual processing: agnosias, achromatopsia, Balint's syndrome, and related difficulties of orientation and construction. In M. M. Mesulman, *Principles of behavioral neurology* (pp. 259–288). Philadelphia: Davis.

Findlay, J. M. (1995). Visual search: eye movements and peripheral vision. *Optometry and Visual Science*, *72*, 461–466.

Findlay, J. M. (1997). Saccade target selection during visual search. *Vision Research*, *37*, 617–631.

Fischer, B. (1987). The preparation of visually guided saccades. *Reviews in Physiology, Biochemistry and Pharmacology*, *106*, 1–35.

Friedman, H. R., & Goldman-Rakic, P. S. (1994). Coactivation of prefrontal cortex and inferior parietal cortex in working memory tasks revealed by 2DG functional mapping in the rhesus monkey. *Journal of Neuroscience*, *14*, 2775–2788.

Funahashi, S., Bruce, C. J., & Goldman-Rakic, P. S. (1989). Mnemonic coding of visual space in the monkey's dorsolateral prefrontal cortex. *Journal of Neurophysiology*, *61*, 331–349.

Funahashi, S., Bruce, C. J., & Goldman-Rakic, P. S. (1990). Visuospatial coding in primate prefrontal neurons revealed by oculomotor paradigms. *Journal of Neurophysiology*, *63*, 814–831.

Funahashi, S., Bruce, C. J., & Goldman-Rakic, P. S. (1993a). Dorsolateral prefrontal lesions and oculomotor delayed-response performance: evidence for mnemonic 'scotomas'. *Journal of Neuroscience*, *13*, 1479–1497.

Funahashi, S., Chafee, M., & Goldman-Rakic, P. S. (1993b). Prefrontal neuronal activity in rhesus monkeys performing a delayed anti-saccade task. *Nature*, *365*, 753–756.

Fuster, J. M., Bauer, R. H., & Jervey, J. P. (1981). Effects of cooling inferotemporal cortex on performance of visual memory tasks. *Experimental Neurology*, *71*, 398–409.

Fuster, J. M., Bauer, R. H., & Jervey, J. P. (1985). Functional interactions between inferotemporal and prefrontal cortex in a cognitive task. *Brain Research*, *330*, 299–307.

Fuster, J. M., & Jervey, J. P. (1982). Neuronal firing in the inferotemporal cortex of the monkey in a visual memory task. *Journal of Neuroscience*, *2*, 361–375.

Gaffan, D., & Weiskrantz, L. (1980). Recency effects and lesion effects in delayed non-matching to randomly baited samples by monkeys. *Brain Research*, *196*, 373–386.

Goldman-Rakic, P. S. (1988). Topography of cognition: parallel distributed networks in primate association cortex. *Annual Review in Neuroscience*, *11*, 137–156.

Greenlee, M. W., Kössler, M., Cornelissen, F. W., Mergner, T., & Seeger, W. (1997). Visual discrimination and short-term memory for random block patterns in patients with unilateral brain damage. *Cerebral Cortex*, *7*, 253–267.

Greenlee, M. W., Lang, H.-J., Mergner, T., & Seeger, W. (1995). Visual short-term memory of stimulus velocity in patients with unilateral posterior brain damage. *Journal of Neuroscience*, *15*, 2287–2300.

Greenlee, M. W., Rischewski, J., Mergner, T., & Seeger, W. (1993). Delayed pattern discrimination in patients with unilateral temporal lobe damage. *Journal of Neuroscience*, *13*, 2565–2574.

Greenlee, M. W., & Smith, A. T. (1997). Detection and discrimination of first- and second-order motion in patients with unilateral brain damage. *Journal of Neuroscience*, *17*, 804–818.

Horel, J. A., Pytko-Joiner, D. E., Voytko, M. L., & Salsbury, K. (1987). The performance of visual tasks while segments of the inferotemporal cortex are suppressed by cold. *Behavioural Brain Research*, *23*, 29–42.

Iwai, E., & Mishkin, M. (1969). Further evidence on the locus of the visual area in the temporal lobe of the monkey. *Experimental Neurology*, *25*, 585–594.

Lawler, K., & Cowey, A. (1987). On the role of posterior and prefrontal cortex in visuospatial perception and attention. *Experimental Brain Research*, *65*, 695–698.

Luna, B., Thulborn, K. R., Strojwas, M. H., McCurtain, B. J., Berman, R. A., Genovese, C. R., & Sweeney, J. A. (1998). Dorsal cortical regions subserving visually guided saccades in humans: an fMRI study. *Cereb Cortex*, *8*, 40–47.

McCarthy, G., Blamire, A. M., Puce, A., Nobre, A. C., Bloch, G., Hyder, F., Goldman-Rakic, P., & Shulman, R. G. (1994). Functional magnetic resonance imaging of human prefrontal cortex activation during a spatial working memory task. *Proceedings of the National Academy of Science USA*, *91*, 8690–8694.

Mikami, A., & Kubota, K. (1980). Inferotemporal neuron activities and color discrimination with delay. *Brain Research*, *182*, 65–78.

Miller, E. K., Erickson, C. A., & Desimone, R. (1996). Neural mechanisms of visual working memory in prefrontal cortex of the macaque. *Journal of Neuroscience*, *16*, 5154–5167.

Miller, E. K., Li, L., & Desimone, R. (1991). A neural mechanism for working and recognition memory in inferior temporal cortex. *Science*, *254*, 1377–1379.

Miller, E. K., Li, L., & Desimone, R. (1993). Activity of neurons in anterior inferior temporal cortex during a short-term memory task. *Journal of Neuroscience*, *13*, 1460–1478.

Milner, B. (1971). Interhemispheric differences in the localisation of psychological processes in man. *British Medical Bulletin*, *27*, 272–277.

Mishkin, M. (1954). Visual discrimination performance following partial ablations of the temporal lobe. II. Ventral surface vs hippocampus. *Journal of Comparative and Physiological Psychology*, *47*, 187–193.

Miyashita, Y., & Chang, H. S. (1988). Neuronal correlate of pictoral short-term memory in the primate temporal cortex. *Nature*, *331*, 68–70.

Petit, L., Clark, V. P., Ingeholm, J., & Haxby, J. V. (1997). Dissociation of saccade-related and pursuit-related activation in human frontal eye fields as revealed by fMRI. *Journal of Neurophysiology*, *77*, 3386–3390.

Pierrot-Deseilligny, C., Rivaud, S., Penet, C., & Rigolet, M. H. (1987). Latencies of visually guided saccades in unilateral hemispheric cerebral lesions. *Annals of Neurology*, *21*(2), 138–148.

Pierrot-Deseilligny, C., Rivaud, S., Gaymard, B., Muri, R., & Vermersch, A. I. (1995). Cortical control of saccades. *Annals of Neurology*, *37*(5), 557–567.

Quintana, J., & Fuster, J. (1992). Mnemonic and predictive functions of cortical neurons in a memory task. *NeuroReport*, *3*, 721–724.

Rao, S. C., Rainer, G., & Miller, E. K. (1997). Integration of what and where in the primate prefrontal cortex. *Science*, *276*, 821–824.

Sahgal, A., Hutchison, R., Hughes, R. P., & Iversen, S. D. (1983). The effects of inferotemporal cortex lesions on Konorski delayed pair comparison in monkeys. *Behavioral Brain Research*, *8*, 361–373.

Schall, J. D. (1991). Neural basis of saccadic eye movements in primates. In A. G. Leventhal, *The neural basis of visual function*. London: MacMillan.

Seeger, W. (1978). *Atlas of topographical anatomy of the brain and surrounding structures*. Wien: Springer Verlag.

Swartz, B. E., Halgren, E., Fuster, J. M., Simpkins, F., Gee, M., & Mandelkern, M. (1995). Cortical metabolic activation in humans during a visual memory task. *Cerebral Cortex*, *3*, 205–214.

Sweeney, J. A., Mintun, A., Kwee, S., Wiseman, M. B., Brown, D. L., Rosenberg, D. R., & Carl, J. R. (1996). Positron emission tomography of voluntary saccadic eye movements and spatial working memory. *Journal of Neurophysiology*, *75*, 454–468.

Talairach, J., & Tournoux, P. (1988). *Co-planar stereotaxic atlas of the human brain*. Stuttgart: Thiema Verlag.

Tanaka, K., Saito, H. A., Fukada, Y., & Moriya, M. (1991). Coding visual images of objects in the inferotemporal cortex of the macaque monkey. *Journal of Neurophysiology*, *66*, 170–189.

Treisman, A. (1982). Perceptual grouping and attention in visual search for features and for objects. *Journal of Experimental Psychology*: *Human Perception and Performance*, *8*, 194–214.

Ungerleider, L. G., Courtney, S. M., & Haxby, J. V. (1998). A neural system for human visual working memory. *Proceedings of the National Academy Science USA*, *95*, 883–889.

Ungerleider, L. G., Gaffan, D., & Pelak, V. S. (1989). Projections from inferior temporal cortex to prefrontal cortex via the uncinate fascicle in rhesus monkey. *Experimental Brain Research*, *76*, 473–484.

Ungerleider, L. G., & Mishkin, M. (1982). Two cortical visual systems. In J. Ingle, M. A. Goodale, & R. J. W. Mansfield, *Analysis of visual behavior* (pp. 549–586). Cambridge: MIT Press.

van Essen, D. C., & Zeki, S. M. (1978). The topographic organization of rhesus monkey prestriate cortex. *Journal of Physiology*, *277*, 193–226.

Wechsler, D. (1987). *WMS-R: wechsler memory scale-revised manual* (p. 150). San Antonio, TX: The Psychological Corporation, Harcourt Brace Jovanovich.

Wilson, F. A. W., Scalaidhe, S. P. O., & Goldman-Rakic, P. S. (1993). Dissocation of object and spatial processing domains in primate prefrontal cortex. *Science*, *260*, 1955–1960.

Zeki, S. M. (1978a). The cortical projections of foveal striate cortex in the rhesus monkey. *Journal of Physiology*, *277*, 227–244.

Zeki, S. M. (1978b). Functional specialisation in the visual cortex of the rhesus monkey. *Nature*, *274*, 423–481.

Zeki, S. M. (1990). A century of cerebral achromatopsia. *Brain*, *113*, 1721–1777.

Zihl, J., von Cramon, D., & Mai, N. (1983). Selective disturbance of movement vision after bilateral brain damage. *Brain*, *106*, 313–340.