Visual Discrimination and Short-Term Memory for Random Patterns in Patients with a Focal Cortical Lesion

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Visual discrimination and short-term recognition memory for computer-generated random patterns were explored in 23 patients with a postsurgical lesion in one of the cortical hemispheres. Their results are compared with those of 23 age-matched volunteers. In a same–different forced-choice discrimination task, *d′* and log beta (measures of sensitivity and bias), as well as reaction time (RT) were determined. All participants viewed patterns defined either by luminance contrast or isoluminant red–green color contrast, the amplitude of which was adjusted to be 10 times the respective detection threshold level. Block patterns consisting of a 6 × 6 matrix of light and dark (red and green) checks were randomly configured on each presentation. They were presented in pairs, randomly in two visual quadrants for a duration of 200 msec. Three presentation conditions were used: simultaneous presentation of reference and test stimulus, sequential presentation with a short delay (interstimulus interval, ISI = 3 s), and sequential presentation with a long delay (ISI = 6 s). The results indicate that patients with a lesion in the occipitotemporal cortex, the superior temporal cortex and the frontal cortex were significantly impaired on both luminance-contrast and color-contrast pattern discrimination. Patients with damage in the anterior inferotemporal cortex showed no overall impairment. The results suggest that performance in visual discrimination and recognition memory tasks rely on distributed neural processes with more than one neocortical location.

Introduction

There is now mounting evidence which suggests that several cortical areas in the human brain are involved in the processes underlying pattern discrimination and visual memory. This evidence comes from studies of regional blood flow using positron emission tomography (Corbetta *et al.*, 1991, 1993; Haxby *et al.*, 1991; Zeki *et al.*, 1991), from functional magnetic resonance imaging (McCarthy *et al.*, 1994; Sereno *et al.*, 1995), and from studies of patients with focal brain damage (Greenlee *et al.*, 1993, 1995a). The results from these different approaches to functional mapping of visual function indicate that several areas in extrastriate, associational and prefrontal cortex are activated during visual discrimination tasks.

Anatomical studies in nonhuman primates indicate the existence of a ventral pathway extending from primary visual cortex (V1), prestriate area (V2) to area V4 and from there to occipitotemporal and inferotemporal areas TEO and TE (for reviews see Ungerleider and Mishkin, 1982; Mishkin *et al.*, 1983; Van Essen *et al.*, 1991; Nakamura *et al.*, 1993). Single-unit recordings in area V4 suggest that this area is directly involved with the processing of color and form (Zeki, 1978; Desimone and Schein, 1987; Schein and Desimone, 1990). Lesions in area V2 lead to an impairment in pattern and texture discrimination (Merigan *et al.*, 1993), whereas those in V4 lead to an impairment in color discrimination and to a lack of perceptual constancies (Wild *et al.*, 1985; Heywood and Cowey, 1987; Schiller and Lee, 1991; Schiller, 1995). The response characteristics of cells in inferotemporal (IT) cortex have been demonstrated to be more complex than those at earlier levels in the visual pathway (Gross *et al.*, 1972; Desimone *et al.*, 1984; Sato, 1989; Tanaka *et al.*, 1991). Recordings in alert monkey performing delayed match-to-sample (DMS) tasks have demonstrated that stimulus-evoked responses persist during the delay period (Mikami and Kubota, 1980; Fuster and Jervey, 1982; Miyashita and Chang, 1988; Miller *et al.*, 1991, 1993; Quintana and Fuster, 1992), suggesting the involvement of this area in visual memory. The lateral intraparietal (LIP) area and area 7 (Andersen, 1989; Friedman and Goldman-Rakic, 1994), as well as the prefrontal areas to which they are connected (especially those in and around the principal sulcus) (Fuster, 1973; Rosenkilde *et al.*, 1981; Funahasi *et al.*, 1990, 1993; Wilson *et al.*, 1993; Friedman and Goldman-Rakic, 1994) have also been implicated in the neural processes underlying spatial working memory.

There is an extensive literature on the effects of lesions in temporal, parietal and prefrontal cortex on the monkey's performance in delayed pattern discrimination tasks (for a recent review see Fuster, 1995). Early studies produced evidence that IT cortex is important in various aspects of visual memory perforance (Mishkin, 1954; Iwai and Mishkin, 1969; Cowey and Gross, 1970; Dean, 1976). More recent studies have explored the effects of reversible cooling lesions in IT cortex on performance in tasks requiring visual memory (Fuster *et al.*, 1981; Voytko, 1986; Horel *et al.*, 1987). Such a reversible lesion in IT cortex impairs performance in a DMS task, although the effect of cooling is also evident for sequential discrimination without a delay (Horel and Pytko, 1982).

Human visual memory has been studied using alphanumerical stimuli, gratings and abstract patterns in healthy subjects (Phillips, 1974, 1983; Inui, 1988; Magnussen *et al.*, 1991) and in brain-damaged patients (Milner, 1968; Warrington and Weiskrantz, 1973; Greenlee *et al.*, 1993, 1995a). Studies on patients with focal brain lesions provide an important link between the results of functional imaging and psychophysical performance. If a specific cortical area is directly involved in the processes underlying visual discrimination and memory, then a lesion in that area should lead to an impairment in performance on tasks requiring higher-level processing and short-term storage of visual information. These considerations have motivated the present investigation.

We have studied the ability of observers to discriminate between two stochastic patterns, which are either presented simultaneously or with a delay. We compare the ability of healthy adults to that of a group of 23 persons who have a focal lesion in one cortical hemisphere. Using an approach based on signal detection theory, we explored whether there is a difference between these two groups in their ability to detect, to discriminate and to remember random block stimuli.

Table 1
Clinical data on the 23 patients who participated in the study

Patient	Sex	Age (years)	Lesioned side	Lesion location	Legion size (rank)	Diagnosis	Symptoms prior to surgery	Medication (possibly sedative) at time of study
PAT01	M	52	left	OT	8	cavernous angioma	GM 1983 and 1987	none
PAT02	M	57	left	OT	14	oligodendroglioma (WHO II)	GM 1989	none
PAT03	M	32	left	OT	1	cavernous angioma	psychomotor seizures	Tegretal® (carbamazepine)
PAT04	F	25	left	OT	6	arteriovenous malformation	headache	none
PAT05	F	33	right	OT	4	oligodendroglioma (WHO II)	partial seizures since 1985	none
PAT06	F	40	right	OT	19	cavernous angioma	one GM/year since 1980, increasing in frequency since 1985	none
PAT07	F	52	left	ST	20	cavernous angioma	1986 GM	Timonil® (carbamazepine)
PAT08	M	49	left	ST	17	arteriovenous malformation	acute migraines, transient hemiparesis right	Zentropil® (phenytoin)
PAT09	M	36	left	ST	15	arteriovenous malformation	focal seizures since 1985	Timonil® (carbamazepine)
PAT10	M	63	left	ST	11	arteriovenous malformation	seizures since 1982	Zentropil® (phenytoin)
PAT11	F	36	left	ST	5	cavernous angioma	1989 GM, headache	none
PAT12	F	63	right	ST	7	arteriovenous malformation	seizures	Mylepsinum® (primidon)
PAT13	F	35	left	IT_{ant}	12	cavernous angioma	psychomotor seizures since 1975	Timonil® (carbamazepine)
PAT14	M	32	left	IT_{ant}	18	astrocytoma (WHO II)	one GM1984, psychomotor seizures 1987–1988	none
PAT15	F	32	left	IT_{ant}	13	astrocytoma (WHO I)	seizures	none
PAT16	N	51	right	IT_{ant}	10	cavernous angioma	headache	none
PAT17	F	31	right	IT_{ant}	2	cavernous angioma	psychomotor seizures since 1990	none
PAT18	F	41	right	IT_{ant}	22	oligodendroglioma (WHO II)	focal seizures since 1989, one GM in 1990	Tegretal® (carbamazepine)
PAT19	F	56	left	F	21	cavernous angioma	focal seizures since age 27, with increased frequency prior to surgery	Zentropil® (phenytoin)
PAT20	M	39	left	F	9	cavernous angioma	headache	none
PAT21	F	77	left	F	16	intracerebral hemorrhage	headache	none
PAT22	F	44	left	F	3	cavernous angioma	headache	none
PAT23	F	17	right	F	23	arteriovenous malformation	two GM	Zentropil® (phenytoin)

GM, grand mal seizure.

Materials and Methods

Patient Selection

Twenty-three former patients were recruited from the clinical archives of the Department of Neurosurgery of the University of Freiburg. Table 1 presents a summary of the relevant clinical data on the patient group. We sought to find patients with a well-defined focal lesion, which was located either in the temporal, parietal or frontal cortex. These lesions resulted as a consequence of surgical resection of either a vascular malformation or a tumor. We excluded patients who were over the age of 78 years, those with multiple lesions or tumors of high malignacy, and those receiving radiation therapy or high doses of anticonvulsant medication. Patients were also excluded who showed subtantial visual field defects (large scotomas or quadrant anopia) or who had signs of visual neglect. The patients' results are compared to those of age-matched control subjects. The control subjects were recruited on a voluntary basis and were mostly in-patients from the Department of Neurology or the Department of Dermatology. These control patients had no signs of any central nervous disorder. The patients' mean age was 43.1 ± 14.1 years, whereas that of the controls was 40.5 ± 12.1 years [$F(1,44) = 0.45$, NS). Ten of the patients were recieving anticonvulsant medication at the time of study (Table 1). Eighteen patients were free of any neurological symptoms, two patients (PAT08, PAT19) infrequently had mild seizures, two patients (PAT09, PAT23) exhibited a brachiofacial hemiparesis, and one patient (PAT07) exhibited a mild aphasia.

The patients were studied, on average, 37 months after surgery (range 1–89 months). Prior to psychophysical 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)]. Patients were also tested using Ishihara pseudo-isochromatic plates to exclude subjects with obvious color discrimination deficiencies. Visual fields were examined using automatic perimetry in cases where a field defect was suspected.

Brain Imaging

Computed tomographic (CT) and magnetic resonance images (MRI) were made before and after surgery. Using standardized atlases of the human brain (Seeger, 1978; Talairach and Tournoux, 1988), we determined the extent and location of the cortical damage. Figure 1 show reconstructions of the lesioned area in each of the 23 patients. Sixteen patients had a lesion in the left hemisphere and seven patients had damage in the right hemisphere. Each patient was assigned to one of four groups depending on the location of the focus of the cortical lesion. Since the patients' lesions vary in extent and encroach on more than one cortical area, some patients were more difficult to classify than others. Our approach was to assign the patient to a group which best represented the focus of cortical damage. Six patients were assigned to the occipitotemporal (OT) group with lesions involving the ventrolateral part of area 37 (fusiform gyrus and posterior inferior temporal gyrus: PAT05, PAT06, PAT07), the ventromedial border region between areas 37 and 19 (PAT04) and between areas 31 and the 18/19 border (PAT12), as well as the posterior half of area 21 (middle temporal gyrus: PAT02). Six patients were assigned to the superior temporal (ST) group with lesions involving areas 39 and 40 (posterior superior temporal gyrus, angular gyrus or supramarginal gyrus: PAT10–12), areas 22 and 42 (anterior superior temporal gyrus: PAT07–09). Six patients were placed in the IT_{ant} group with lesions encorporating the anterior half of area 21 (inferior and middle temporal gyri: PAT13, PAT14, PAT16, PAT18) or the anterior area 20 and/or area 38 (temporal pole region: PAT15, PAT17). Finally, five patients made up the frontal lobe group with lesions in area 47 and/or area 10 (ventrolateral prefrontal cortex: PAT19, PAT21, PAT23), medial prefrontal area 9 (PAT22), as well as the ventromedial area 32 (PAT 20). Although some patients had lesions which straddled these different areas (especially the IT_{ant}–OT border regions), they were assigned to these groups based on the location with the most extensive grey matter damage. There was no significant difference in age between the four lesion groups [$F(3,19) = 1.05$; $P = 0.4$, NS).

Experimental Design

The stimuli were displayed on a color monitor (Eizo 661, 21 in.), the luminance gamma correction tables and spectral distributions of which were calibrated by a spectral radiometer (Spectra 705). The mean luminance of the display was 70 cd/m^2. The display was viewed from a constant distance of 114 cm. The observer was comfortably positioned in a chair and his/her head was supported by a head rest. A fixation cross

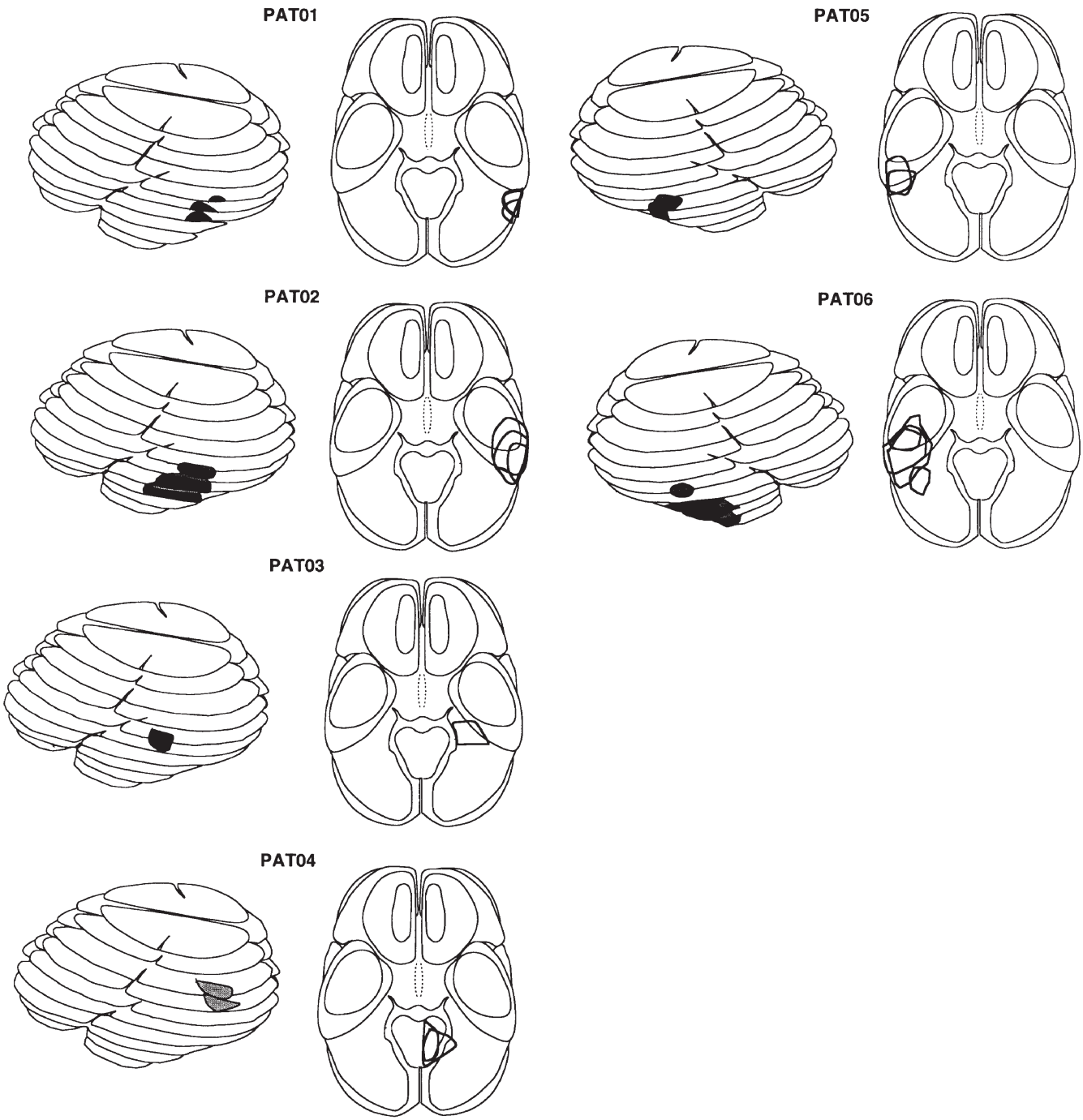


Figure 1. Lateral and axial views of the cortical lesions (based on the computed tomograms) of 23 patients who participated in the study. The schematic brain images are grouped according to lesion location with six patients forming the occipito-temporal (OT) group, six patients making up the superior temporal (ST) group, six patients in the anterior inferotemporal (ITant) group, and five patients in the frontal lobe (F) group. Left hemisphere lesions are shown on the left. The darkened regions indicate the extent and location of the lesions, black signifying lateral and grey medial lesions. The patient identifier numbers are used in Table 1 and in Figure 5.

was displayed in the center of the display. Its bars were 2 pixels wide and 20 pixels long.

Two procedures were performed. The first procedure determined the ability of the patients and control subjects to detect the presence of a centrally presented random block pattern. The second procedure measured the ability of the subjects to discriminate the pattern configurations of two block patterns presented in different visual quadrants.

Detection thresholds were determined for block patterns using a temporal, two-alternative forced choice paradigm. The stimuli were 2 × 2 matrices of randomly arranged blocks, whose contrast was defined by luminance or color differences. A low-contrast block pattern was

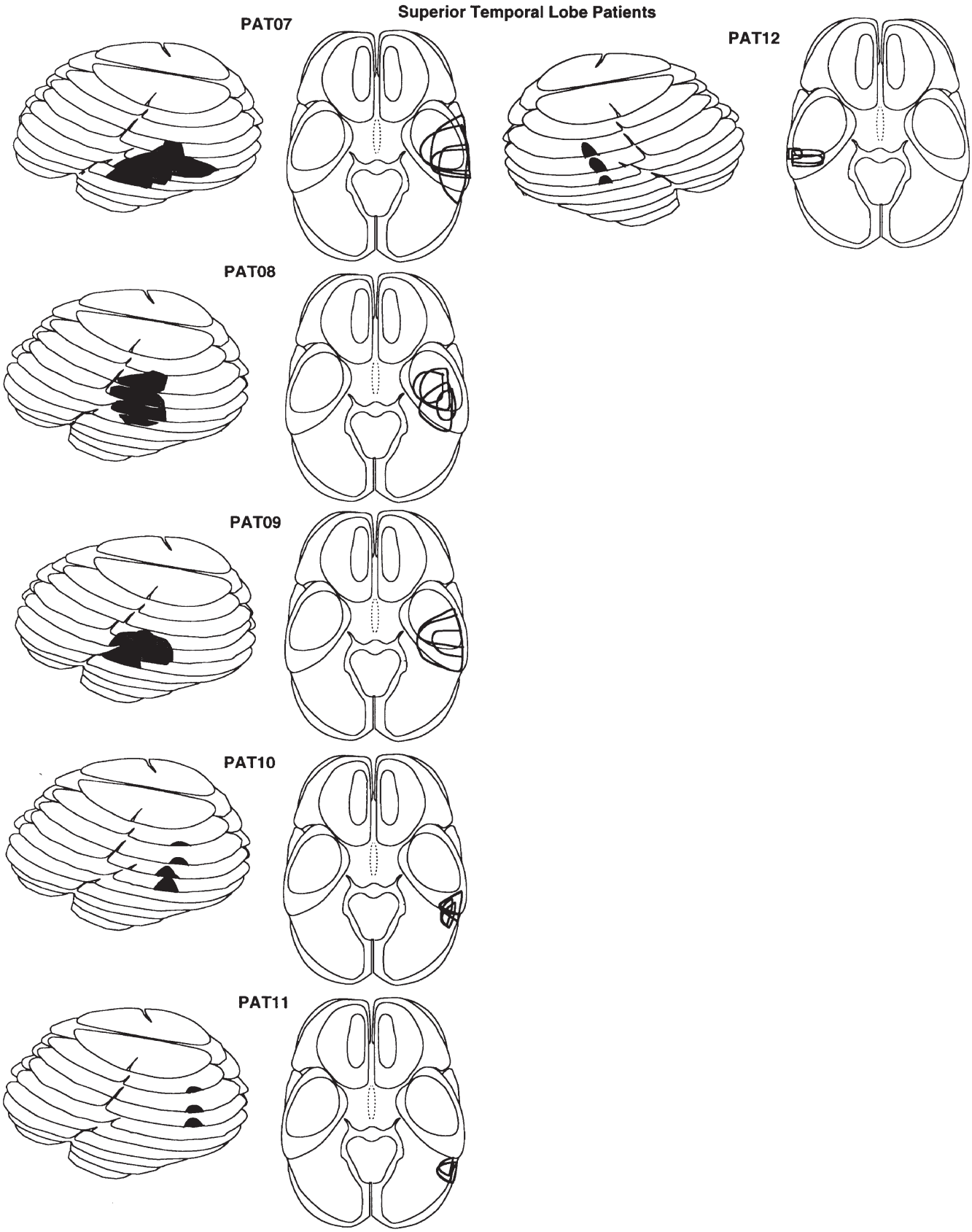

Superior Temporal Lobe Patients
PAT07
PAT12
PAT08
PAT09
PAT10
PAT11

Figure 1*B*

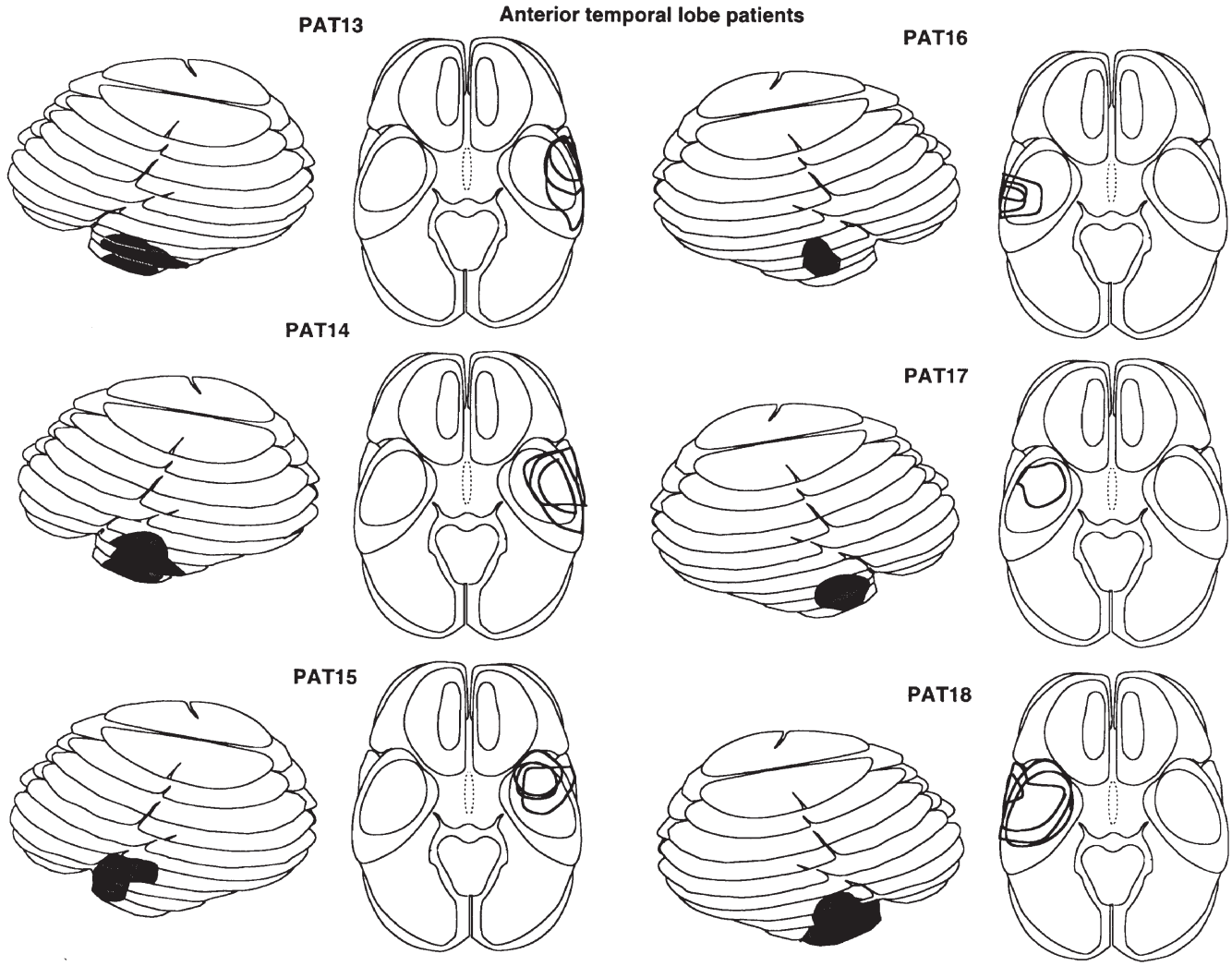


Figure 1*C*

randomly presented (centered on the display), in one of two time intervals (denoted by auditory tones). The observer was instructed to maintain fixation during the trial and judge in which time interval the pattern was presented. The instruction made clear to the subject that a judgment should be made on each trial. The subjects responded by pressing one of two levers on a response box (CB1, Cambridge Research Systems). The left lever was pressed with the left thumb to indicate that the stimulus was in the first interval and the right level was pressed by the right thumb to indicate that the stimulus was presented in the second interval. The subject had 2 s to respond. Reaction times were not recorded during the detection task. The best-PEST (Parametric Estimation by Sequential Testing) algorithm (Lieberman and Pentland, 1982) guided the trial-by-trial selection of pattern contrast. Psychometric functions estimated the contrast level at which the subject performed with 75% accuracy.

Discrimination performance was determined for two stimuli presented either simultaneously or with a delay. Each stimulus consisted of a 6 × 6 matrix of contiguous blocks, and both were presented on each trial. The patterns subtended 3° × 3° of visual angle, each block was $0.5°^2$. In each pattern, half of the blocks were dark and half were light, and their arrangement was randomly determined by the computer on each trial.

For the *simultaneous presentation* condition, on each trial two stimuli were presented simultaneously for 200 ms, followed 50 ms later by a mask of 240 ms duration (Fig. 2). The mask consisted of a series of random block patterns with a check size equal to $0.25°^2$. The mask appeared to be a brief sequence of flickering spatial noise. Any possible after-images resulting from the test presentation could thus be eliminated.

The observer was warned at the beginning of each trial (~500 ms before stimulus presentation) by a change in color of the fixation cross (black during the trial, white during the intertrial interval). This change was subtle and could best be perceived by foveal fixation. The subjects were instructed to fixate the central cross and to respond as quickly as possible whether the two stimuli were identical (left button response) or different (right button response). Trials containing two identical stimuli occurred in 50% of all trials. In the other trials, the stimuli differed, and this difference was made by randomly inverting 12 of the 36 blocks in the test stimulus from light to dark or vice versa. The program was designed in a way such that half of the blocks that changed were inverted from light to dark and half from dark to light, so as to avoid any differences in the overall luminance of the patterns. With these limitations the information in each stimulus was equal to: $\{\ln(n!) - \ln[(n/2)!]\}/\ln(2.0) = 34$ bit, where n is the number of dark (luminance contrast) or red (color contrast, see below) checks.

The patterns were defined either by luminance contrast or by near isoluminant, color contrast. The latter were produced by color contrast along the long–middle wavelength axis. Variations along this axis lead to a differential stimulation of the long and medium wavelength sensitive cone photoreceptors with a constant short-wavelength stimulation (Vos and Walraven, 1971). The patterns were equated for visibility by

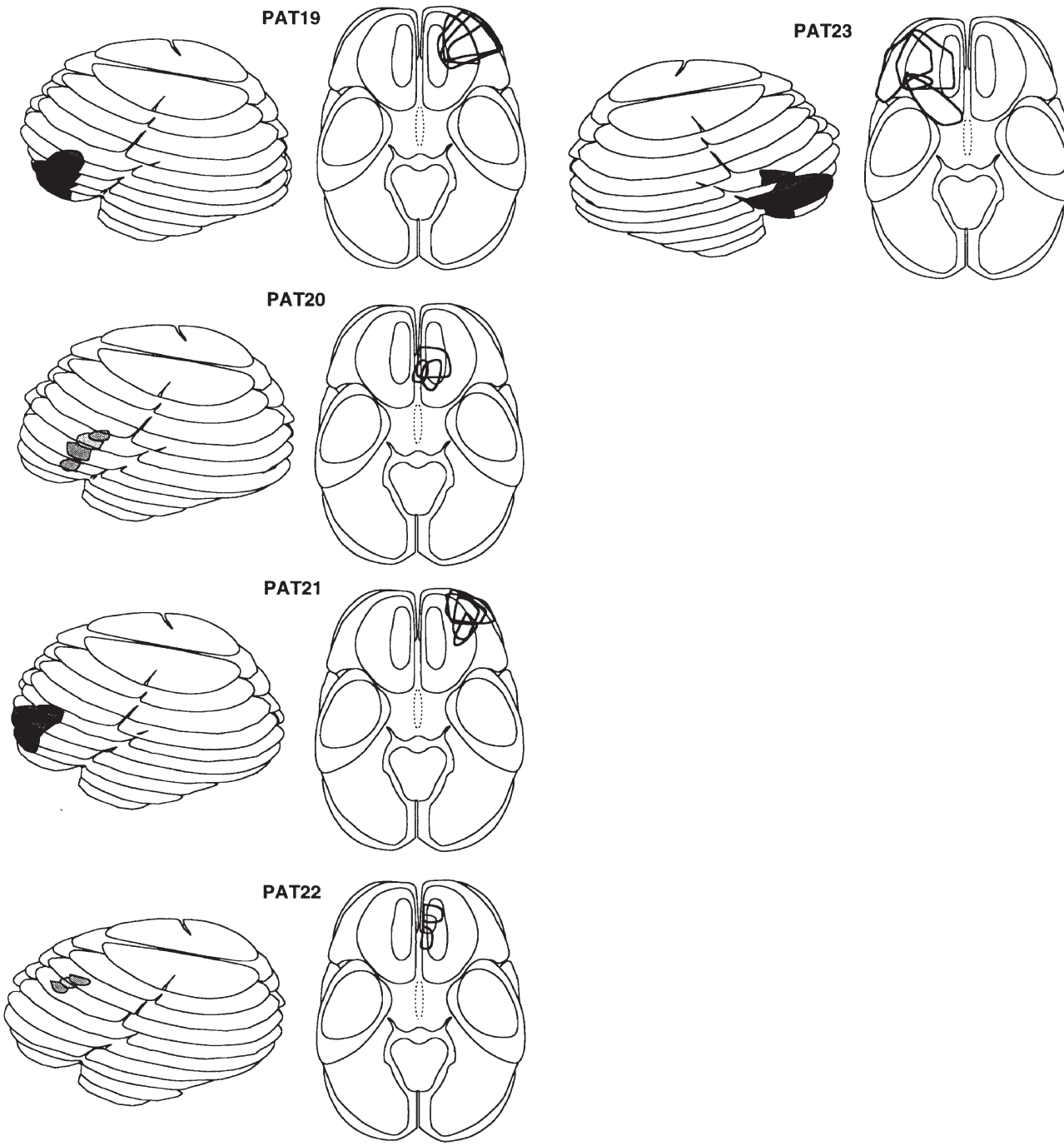


Figure 1*D*

multiplying the patient/control's threshold contrast level by a factor of 10. This assured that the patterns were equally visible for all participants.

The patterns were presented 4° eccentric to the centrally located fixation cross, randomly in two of the four visual quadrants. Performance was determined separately for stimuli presented in the upper and lower, as well as the left and right visual hemifields. Stimuli were also presented in crossed visual quadrants (i.e. upper left–lower right and lower left–upper right). The order in which the six conditions were performed was determined randomly for each participant.

The subject's performance was recorded along with the reaction time (the time between the stimulus onset and the button press). Reaction times were measured using the frame counter of the stimulus-generating board (VSG system), which allows a high precision of time recording (microsecond range) and synchronizes the onset of the time period to the frame sync of the display. Owing to the expected skewed distribution of reaction times, all statistical analyses were performed on the logarithm of reaction time.

The experimental paradigm is schematically presented in Figure 2. In

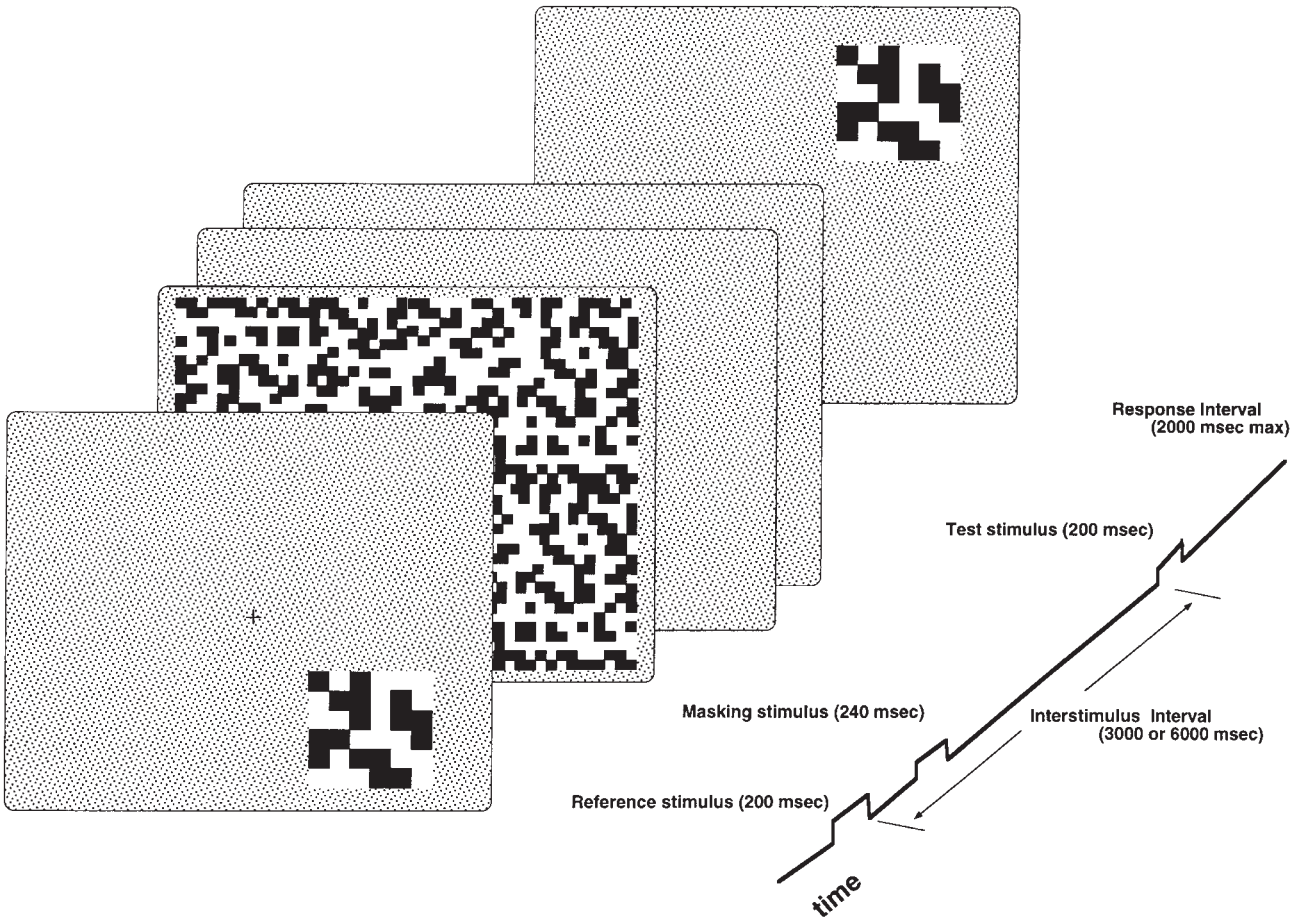


Figure 2. Schematic illustration of the stimulus configuration and the experimental paradigm used in the pattern discrimination task.

the *delayed discrimination* condition, the first stimulus was followed by a mask, and then a blank screen with the same mean luminance (containing only the fixation cross) was shown. The duration of this interstimulus interval (ISI) was either 3 or 6 s (including mask presentation time). Afterwards the test stimulus was presented and subjects indicated whether the two stimuli were the same or different.

We applied signal detection theory (assuming the equal variance Gaussian model) to derive d' as a measure of discriminability and the natural logarithm of beta as an estimate of the response bias (Green and Swets, 1966). The index of discriminability d' reflects the distance between the statistical distributions of neural activity caused by the two types of trials (trials in which both stimuli were the same and those in which they were different). Typically d' = 1.0 is designated as the threshold performance level. Log beta indicates the discrimination strategy applied by the observer: significant positive deviations from zero indicate a conservative strategy, in which the observer makes few false alarms, a significant negative deviation from zero depicts a liberal response bias with frequent false alarms. In the discrimination task, a false alarm is defined as a 'different' response on a trial in which the stimuli were the same.

Subjects were instructed to respond as accurately and quickly as possible and were told that their reaction times would be measured. Trials in which the subject did not respond within 2 s were classified as a having no response (i.e. lapses), and were recorded as such. An audible tone was presented for 100 ms after an incorrect response to provide the participants with feedback regarding their performance. Informed consent was acquired from all participants. They were given a standard instruction protocol which briefly explained the basis of the study. The experimenter read aloud the instructions while the participant was asked to read along. Separate instructions were given for detection and discrimination tasks. A trial run was performed for each type of task until both the participant and the experimenter were assured that the instructions had been understood and the participant could perform the task. For the condition with a 6 s ISI and color contrast only 13 patients and 17 controls participated. Patients and controls alike reported that the tasks were demanding, but within their performance abilities. With only a few exceptions, all patients performed clearly above chance levels (i.e. $d' >> 0$).

Eye position was not explicitly monitored during the experiments. Inaccuracies in fixation could have led to the stimuli falling in different parts of the visual field. The instructions made explicit that central fixation of the fixation cross was required. It was also made clear to the participants that the best strategy was to center their gaze in the center of the display and to attend to the central $8°^2$ of visual field. Randomization of test and reference presentation as well as the short presentation durations were used to encourage central fixation.

Results

Corsi Block Tapping and Digit Span

There was no significant difference between the patients and the controls with respect to performance on the block tapping test. The mean score on the Corsi test for the patients was 5.74 ± 0.54 and that for the controls was 5.73 ± 0.63 (maximum score = 9, which indicates the number of blocks tapped in correct order). Patients with IT_{ant} lesions scored highest on the Corsi test (6.17 ± 0.17) followed by patients with ST lesions (6.00 ± 0.0), patients with OT lesions (5.6 ± 0.25) and patients with frontal lesions (5.2 ± 0.2). These group differences were significant [$F(3,19) = 5.9$; P

Figure 3. Discrimination performance for simultaneous presentation (measured in units of d') as a function of the location of the test stimuli in the visual field (icons along the abscissa). Filled symbols denote the values for the condition with luminance-contrast stimuli and open symbols present the results for the condition with isoluminant color-contrast stimuli. The upper row presents the results for the delayed presentation condition with ISI = 6 s, the middle row shows the results for the delayed condition with ISI = 3 s, and the lower row depicts the findings for the simultaneous presentation condition. The findings for patients with damage in the left cerebral hemisphere (n = 16) are shown in (*a*), those for patients with damage in the right hemisphere (n = 7) in (*b*) and the results of the controls (n = 23) are given in (*c*). The dashed horizontal line depicts the d' value of unity, which signifies the standard threshold performance level.

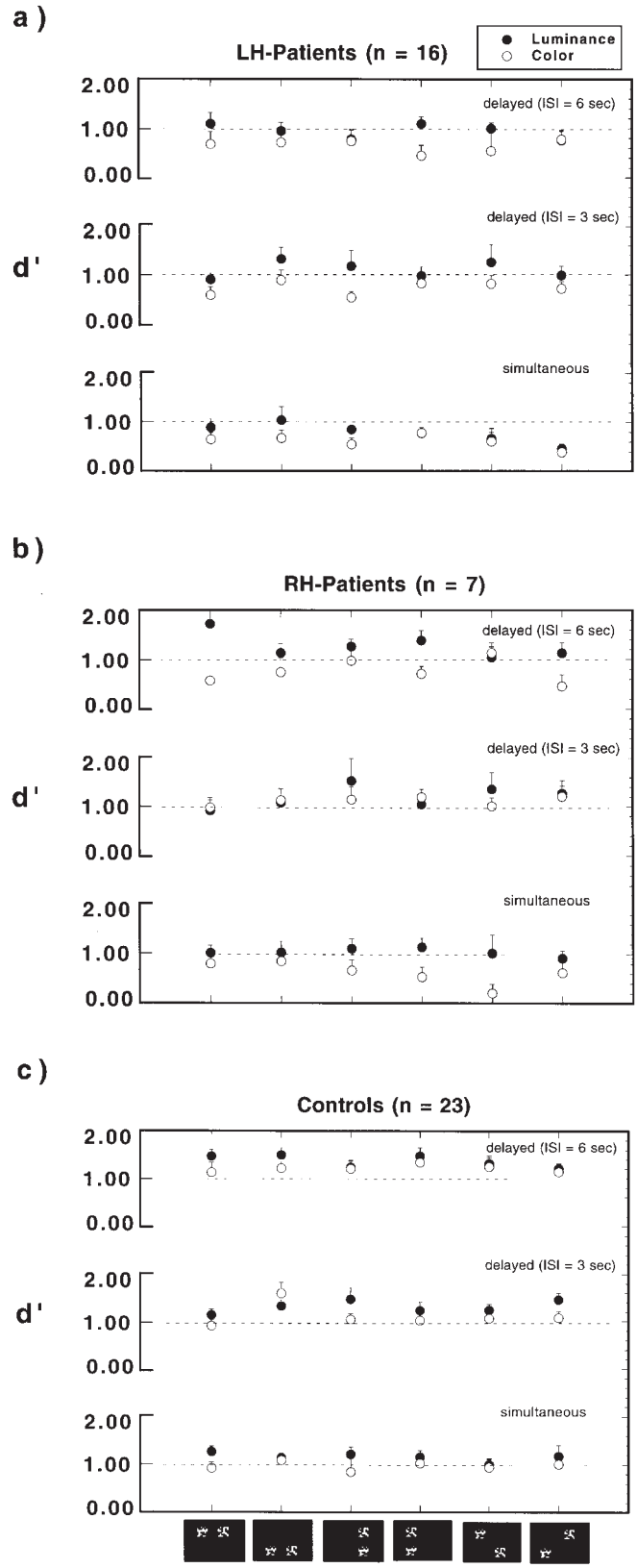
< 0.005]. The mean performance on digit span was significantly lower in the patients [$F(1,44)$ = 12.7; P = 0.001], where the patients had a mean score of 6.22 ± 2.99 and the controls 8.91 ± 1.93 (maximum score = 12; total of 12 trials, each digit length performed twice, starting with three and ending with eight digits). There was no significant difference, however, between the different patient groups [$F(3,17)$ = 0.85; NS].

Detection Thresholds

To control for the possible effects of visual sensitivity on performance in the pattern discrimination tasks, we first measured the patients' and control subjects' ability to detect the block patterns. We determined individual patients' thresholds for luminance and color contrast stimuli (see Materials and Methods). An analysis of variance was computed on the log of contrast thresholds, which indicated that there was no difference between the patients and control subjects with respect to their ability to detect the centrally presented block patterns [$F(1,44)$ = 0.8, P = 0.38, NS]. The mean threshold for luminance contrast patterns was 0.96 ± 0.34% for the patients and 0.88 ± 0.26% for the controls. The mean thresholds for the patterns defined by color contrast was 0.26 ± 0.18% for the patients and 0.20 ± 0.07% for the controls. These values for luminance and chromatic contrast detection thresholds are in close agreement with reported values for this range of spatial frequencies (Noorlander, *et al.*, 1983; De Valois and De Valois, 1988). There was also no effect of lesion location among the patients on the log sensitivity for luminance [F(3,19) = 0.32; P = 0.8, NS] and color defined patterns [$F(3,19)$ = 0.49; P = 0.7, NS]. These findings indicate that, on average, the patients were able to detect the random block patterns at low contrast with an efficiency similar to that shown by the control group. Three exceptions should be mentioned: PAT03 demonstrated thresholds that were normal for luminance contrast but high for color contrast, whereas PAT10 and PAT22 had significantly elevated thresholds for both luminance and color contrast.

Simultaneous Discrimination

The results for the condition in which the stimuli to be compared were presented simultaneously are shown in Figure 3: d' is plotted as a function of the visual field condition (denoted by the icons along the lower abscissa). Overall the patients performed worse than the controls on the simultaneous task, with d' ranging between 1.1 and 0.2. An analysis of variance was performed on these results which indicated that the main effect of experimental group (patients versus controls) was highly significant [$F(1,44)$ = 9.18; P = 0.004]. Both patients and controls show higher d' values for patterns defined by luminance contrast compared to those defined by color contrast [$F(1,44)$ = 9.54; P = 0.0035]. There is no systematic effect of the visual field condition, with the exception that the patients tended to exhibit lower d' values for the condition in which the stimuli to be compared were presented in diagonal quadrants. Overall, however, the effect of visual field was not significant [$F(5,220)$ = 1.64; P = 0.15], nor was the interaction between visual field and experimental group significant [$F(5,220)$ = 0.86; P = 0.51].



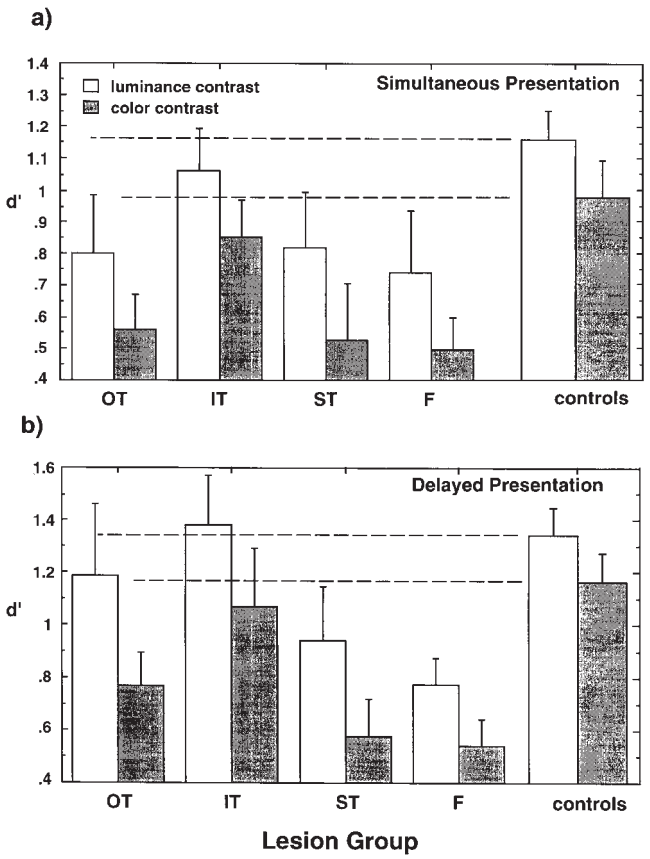


Figure 4. Mean *d′* values for the simultaneous (*a*) and delayed (*b*) presentation conditions for the four patient groups. Values for the delayed condition are averaged over both short and long delays. Open columns present the results for luminance-contrast stimuli and filled columns give the results for color-contrast stimuli. The mean values for the control subjects are shown on the right and dashed horizontal lines are given to facilitate comparison. Error bars present 1 SE of the mean.

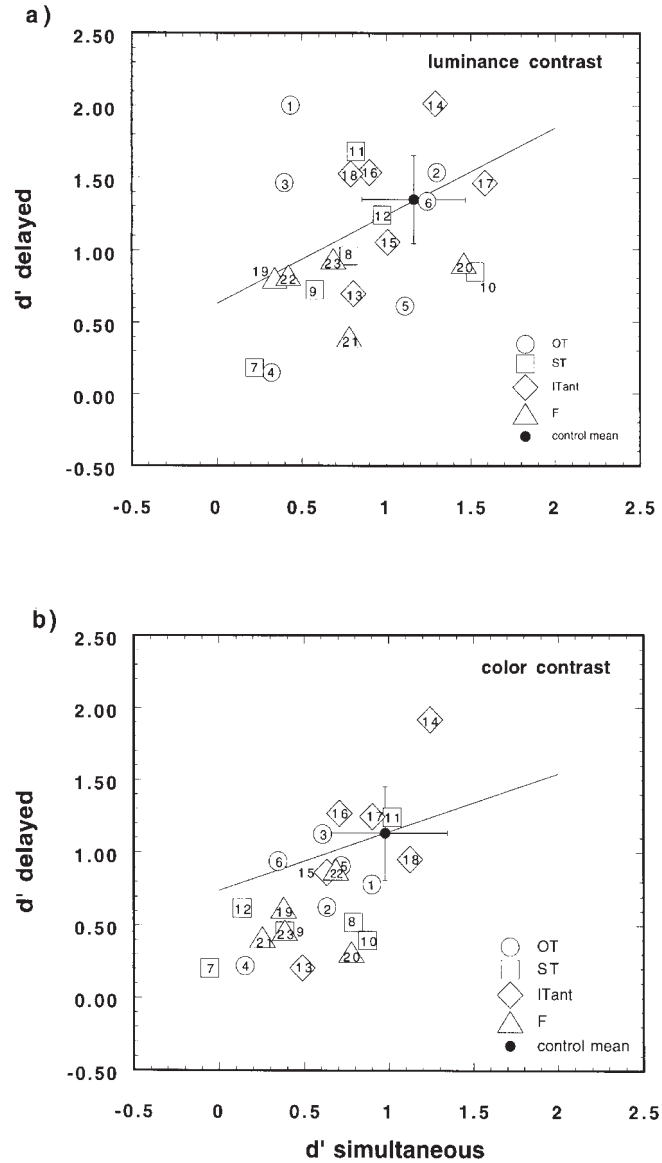


Figure 5. A scatter diagram depicting individual patient's mean *d′* score in the delayed conditions as a function of their score in the simultaneous condition. The different symbols denote the different patient and control groups and patient identifiers are as in Figure 1. Control mean *d′* value ± 2 SE and the best-fitting regression line (control data only) are presented for sake of comparison. The results for conditions with stimuli defined by luminance contrast are presented in (*a*), and those for stimuli defined by red–green color contrast in (*b*).

Delayed Discrimination

The results for the conditions in which the two stimuli were presented with a delay are shown in the upper two rows of Figure 3 for the conditions with an ISI of 3 s (middle row) and 6 s (upper row). Overall, most patients and controls are able to perform the delayed discrimination task for both short and long delays without a great reduction in *d′*. The controls show very consistent *d′* values which vary around 1.4 for patterns defined by luminance contrast and 1.2 for color-contrast patterns. Performance for the patients is overall more variable, with *d′* falling below 0.5 in some cases. An analysis of variance was also performed on these results, which indicated that the main effect of experimental group (patients versus controls) was significant [$F(1,44) = 5.588$; $P = 0.023$]. Performance with stimuli defined by luminance contrast was significantly better than that with color contrast patterns [$F(1,44) = 22.4$; $P = 0.0001$]. The overall effects of ISI [$F(1,44) = 0.29$; $P = 0.59$] and visual field [$F(5,220) = 2.15$; $P = 0.06$] were not significant. Although the patients tended to exhibit lower *d′* values for the longer delay, the statistical interaction between experimental group and ISI was only marginally significant [$F(1,44) = 3.27$; $P = 0.077$].

Effect of Lesion Location

Figure 4 presents the results with respect to the effect of lesion location on performance in simultaneous and delayed presentation conditions. The different patient groups were formed according to the division shown in Figure 1. In addition, Figure 5 illustrates the variability in performance found among the patients in the different lesion groups, where each patient's mean *d′* value in the simultaneous presentation condition is plotted against the same patient's mean value in the delayed presentation condition (averaged over short and long delays).

Overall, the patients performed worse than the controls, with the exception of those with damage in the anterior part of IT cortex (PAT13–18). None of these latter patients performed worse than the controls for luminance contrast and only PAT13 performed significantly worse for color patterns. One patient in the IT_{ant} group (PAT14) actually exceeded the mean + 2 SE performance level of the control group for both types of stimuli.

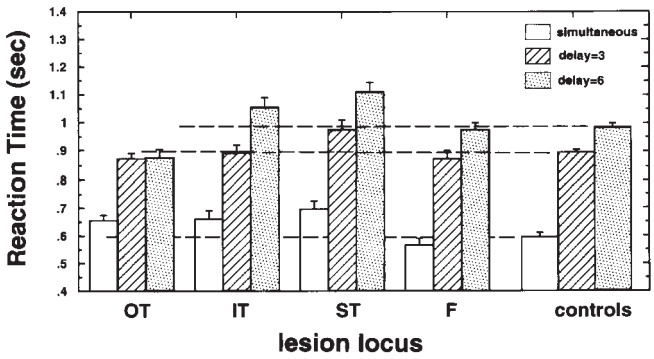


Figure 6. Mean reaction times (s) are shown separately for the four patient groups for the three conditions of delay. The results are averaged over luminance- and color-contrast conditions. The results of the controls are presented on the right and dashed lines are shown to facilitate comparison. Error bars give + 1 SE of the mean.

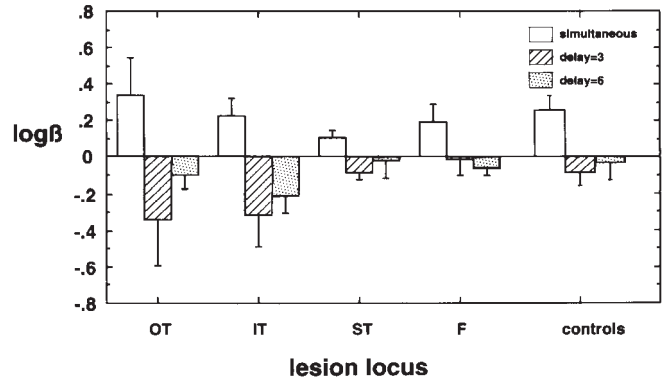


Figure 7. Response bias (as measured in terms of log beta) is shown for the four patient groups and the three delay conditions. Values for the controls are shown for comparison on the right. Error bars give 1 SE of the mean.

Patients with damage in OT cortex performed, on average, worse than the controls for both types of patterns. The difference in d' for the luminance and color patterns was also more pronounced in this patient group (mean d' luminance contrast: 1.03 ± 0.08; color contrast: 0.7 ± 0.05, averaged over all delay conditions). PAT04, with medial occipitotemporal damage, scored poorly on all conditions, performing just above chance levels on simultaneous and delayed conditions. PAT01 and PAT03 performed well in the delayed condition, but poorly in the simultaneous condition. PAT02 and PAT05 performed fairly well with luminance contrast stimuli but less well on color-contrast stimuli. In a similar fashion, patients with damage in ST cortex also exhibited overall significantly lower d' values. PAT07 has a large lesion that encorporates most of the left superior temporal gyrus. Although her ability to detect the stimuli was unimpaired, she was completely unable to discriminate the stimuli. Of the remaining ST patients, only PAT11 exhibited d' values comparable to the mean values of the controls. All frontal lobe patients performed worse than controls on both types of stimulus contrast, with a more pronounced defect for color contrast stimuli.

The poor performance shown by ST and F patients (Figs 4 and 5) suggests that the impairment in function is not restricted to damage in OT cortex, but is also evident in dorsal and frontal lesions. The overall effect of lesion location on the mean d' was only marginally significant [$F(3,19) = 2.3$; $P = 0.1$]. *Post-hoc* (Bonferroni/Dunn) comparisons revealed a significant difference ($P = 0.025$) between the F and IT_{ant} lesion groups and a marginally significant ($P = 0.06$) difference between the ST and IT_{ant} lesion groups. The side of cortical damage (left or right hemisphere) did not have a significant effect on d' [$F(1,22) = 1.08$; $P = 0.32$, NS], nor was the interaction between hemisphere and visual field condition significant [$F(5,110) = 1.03$; $P = 0.4$, NS].

Effect of Lesion Size

As can be seen in Figure 1, the size of the cortical lesion varied to a considerable extent among the patients. Since it seems reasonable to consider that the larger the cortical lesion the larger its effect would be on performance in a visual discrimination task, we analyzed the relationship between the size of the lesions and the patient's performance level. To estimate lesion size we calculated the total area of lesioned tissue from the postoperative CT and MR images. The patients were ranked according to the size of their lesion: the smallest lesion was assigned the rank of 1 and the largest the rank of 23. These ranks were then correlated with the ranks given to the average performance values for the luminance and color-contrast stimuli separately, whereby low d' values were associated with a low rank and high d' values with a high rank. The degree of association between the lesion size and test performance was calculated using the Spearman rank correlation coefficient, r_S (Siegel, 1956). Although the correlation between the ranks for mean d' in the luminance and color-contrast conditions was highly significant ($r_S = 0.77$, $P < 0.01$), the correlation between the rank for the mean d' for the luminance contrast condition ($r_S = -0.19$; NS) and the color-contrast condition ($r_S = -0.32$; NS) with lesion size, though in the expected direction (i.e. larger lesions associated with lower performance scores), did not reach significant levels. There was no significant differences between the four lesion groups and the size of the cortical lesion [$F(3,19) = 0.73$; NS].

Reaction Times

Figure 6 presents a summary of the results with respect to the reaction times for the patients and the control subjects. Reaction time increased significantly with increasing ISI for both luminance and color contrast conditions [$F(2,88) = 91.38$; $P = 0.0001$]. The mean RTs increased from 621 ± 231 ms in the simultaneous presentation condition to 901 ± 203 ms in the 3 s delay condition to 996 ± 209 ms for the 6 s delayed conditions. This effect has been reported for other types of visual discriminations (Phillips and Baddeley, 1971; Magnussen *et al.*, 1996). On average, the patients require only 24 ms longer to respond than do the controls (mean RT; 851 ± 272 versus 827 ± 262 ms), an effect which was not significant [$F(1,44) = 0.26$; $P = 0.6$], nor was the interaction between ISI and experimental group (patients versus controls) significant [$F(2,88) = 0.4$; $P = 0.7$]. The overall effect of visual field was significant [$F(5,220) = 4.2$; $P = 0.001$]. Reaction times for stimuli presented in the right visual field were slightly lower than for stimuli presented in the left visual field (840 versus 854 ms). The effect of damaged hemisphere (left or right) was not significant [$F(1,22) = 0.6$; $P = 0.5$, NS], nor did the side of cortical damage interact with the visual field position of the stimuli [$F(5,105) = 0.42$, NS]. The

overall effect of lesion location on log RT was not significant [$F(3,19) = 0.48$; NS].

Although the patients were instructed to respond as quickly as possible, they occasionally made a response after the end of the response interval or did not respond at all. Fortunately, these occasions were rare, but could have affected the results in a systematic way. We recorded the number of lapses per experimental measurement and explored the possible effect of lesion location on the frequency of lapses. Overall, there was no significant difference between the mean number of lapses and the location of the cortical lesion. There was a slight tendency for patients with ST and F lesions to make more lapses (mean lapses ST, 1.04 ± 0.42; F, 0.8 ± 0.27) than either the OT (0.29 ± 0.06) or IT_{ant} patients (0.3 ±0.14), but this difference was not significant [$F(3,19) = 2.23$; NS]. There was also no correlation between the size of the cortical lesion and the mean number of lapses (r = 0.25, NS).

Response Bias

Figure 7 presents the results with respect to the subject's response bias and how this is affected by the ISI. The ideal response strategy yields a log beta = 0: negative values indicate a tendency to make too many false alarms, positive values point to a conservative strategy and thus to fewer false alarms. Although there is a tendency for patients with temporal lobe damage to show log beta values that deviated more from zero, overall there was no significant difference in the response bias between patients and controls [$F(1,44) = 1.77$; $P = 0.2$]. Both groups tended to be less conservative (i.e. more often responded with 'different' and thus made more false alarms) for conditions with longer ISIs [$F(2,88) = 7.58$; $P = 0.0001$]. The type of stimulus contrast (luminance versus color contrast) had no effect on log beta [$F(1,44) = 0.22$; $P = 0.64$, NS]. Neither lesion location [$F(3,19) = 1.05$; $P = 0.4$, NS] nor damaged hemisphere [$F(1,21) = 2.3$; $P = 0.14$, NS] had a significant effect on response bias.

Discussion

The present results support the idea of a distributed representation of visual encoding and storage in the human brain. Patients with focal lesions in disparate areas of the neocortex perform worse than the age-matched control subjects on the pattern-discrimination tests implemented here. With a few noted exceptions, the same patients had little difficulty detecting the presence of a low-contrast stimulus — defined either by luminance or color contrast — suggesting that primary visual processing was intact. By scaling the stimuli used in the pattern-discrimination task to be a constant factor above each individual's contrast detection threshold, we could further control for the possible effects of any loss in contrast sensitivity. Despite these precautions, the patients performed overall worse than the controls on the pattern-discrimination task.

Patterns defined by isoluminant color contrast are more difficult to discriminate than patterns defined by luminance contrast. Despite the contrast normalization we employed (pattern contrast 10 times higher than detection threshold), the isoluminant color-contrast patterns appeared to have less edge contrast than patterns defined by luminance contrast, an effect which has been reported earlier (Gregory and Heard, 1977). Overall d' values for color-contrast patterns were 30% lower in the patients and 15% lower in the controls compared to the values for luminance-contrast patterns. These differences were highly significant and suggest that the mechanisms underlying pattern discrimination operate less efficiently for patterns defined by isoluminant color contrast. A lesion in visual associational cortex leads to more pronounced effects on performance for patterns with near isoluminant color contrast compared with luminance contrast patterns (Figs 3–5).

The differences in performance between the patients and controls were already evident for stimuli presented simultaneously (Fig. 3), suggesting that the neural mechanisms underlying pattern discrimination were affected in these patients. Surprisingly, d' values for both patients and controls were lower for the simultaneous presentation condition than for the condition in which the patterns were presented with a short delay. Owing to our experimental design, the position of the patterns on any given trial was uncertain. Spatial uncertainty has been shown to decrease detection and discrimination performance (Cohn and Lasley, 1974; Graham *et al.*, 1978; Pelli, 1985). This aspect of our experimental design most likely led to relatively low d' values in both patients and controls. Furthermore, our use of a dynamic mask following presentation of the test stimuli could have led to a greater effect on the simultaneous discrimination condition, since both test and reference stimuli were followed by the mask in this condition.

The position of the stimuli in the visual field (ipsi- and contralesional, upper and lower, diagonal) had only a minor effect on the patients' performance level (Fig. 3). In an earlier study with a comparable patient sample (Greenlee *et al.*, 1993), simple pattern-discrimination thresholds (requiring the discrimination of the spatial frequency of sinewave gratings) were more affected in the contralesional visual field. The visual discriminations required in the present study did not show any systematic visual field effects, suggesting that the cortical lesions affected mechanisms whose actions are not tied to retinotopic coordinates. It could be argued that our present use of randomized location, along with simultaneous versus sequential stimulus presentation, confounds processes underlying attention, discrimination and short-term memory. Although we have sought to determine the effects of these factors by comparing performance on detection and discrimination tasks, none of the tasks employed has isolated these individual processing components. However, the finding that the patients had little difficulty in detecting stimuli presented randomly in one of two time intervals suggests that their ability to attend to single stimuli was unaltered by their cortical damage. It should be emphasized that the introduction of a delay between the standard and comparison cannot alone isolate the processes underlying memory storage and retrieval. Further studies are necessary to tease out the effects owing to these different factors.

No attempt was made to measure eye movements. Thus the extent to which gaze position and eye movements could have entered into the results is left unknown. However, in a subsequent study in patients with similar brain lesions, we have measured eye movements while the patients performed visual discrimination tasks comparable to those used in the present study (Greenlee *et al.*, 1995b). Although the saccadic eye movements of some of these patients were characterized by longer latencies and lower accuracy, their ability to fixate a clearly visible fixation mark remained unaltered. Based on this evidence, it seems unlikely that the patients should differ considerably from controls with respect to their ability to maintain fixation.

Our screening procedures were such that patients having a poor prognosis and/or postsurgical complications were not included in the study. Despite these precautions, 10 out of 23

patients were receiving anticonvulsant medication (Table 1) at the time of study, so that this alone could have affected memory performance to some unknown extent. Although we could observe a moderate effect of the drugs on performance on the discrimination tasks, this effect was not significant [$F(1,22) = 3.4$; $P = 0.08$]. Performance on digit span and the Corsi test was also unaffected by anticonvulsant therapy. It should be empha -sized here that the patients studied were recruited, on average, 34 months after surgery. As such, the effects documented in this study represent chronic, long-lasting impairments, which cannot alone be attributed to the use of anticonvulsant medication.

The use of signal detection theory allowed us to differentiate between changes in performance owing to a loss in discriminative sensitivity from changes resulting from response bias. Both patients and controls responded less conservatively and tended to make more false alarms with increasing delays (Fig. 7). There was, however, no significant difference between the patients and controls in their overall response bias, indicating that, on average, both patients and controls applied a similar strategy. Nor was there a significant trend for response bias to differ over the different lesion groups. Therefore the differences we have observed are related to changes in the patients' ability to discriminate patterns and not to a general difference in their strategy applied to a difficult psychophysical task.

Effect of Lesion Location

Patients with damage in the OT cortex exhibited d' values that were significantly lower than those of the controls and also somewhat lower (but not significantly) than those of patients with damage in the anterior section of IT cortex (Fig. 4). Two of the OT patients (PAT04 and PAT05), with small lesions in ventro-medial OT cortex, performed significantly worse than controls on both luminance and color-contrast tasks (Fig. 5). Such significant impairments with focal lesions suggest a role of this cortical area in visual discrimination.

Patients with damage in ST and F cortex also exhibit reductions in d' (Figs 4 and 5). In an earlier study, Greenlee *et al.* (1995a) reported that patients with lesions in ST cortex have difficulty discriminating and remembering the speed of moving stimuli, implying a role of this area in the short-term storage of motion information. These patients also have difficulty with smooth pursuit (Kimmich *et al.*, 1995), which most likely is a consequence of faulty speed perception. Interestingly, the patients with frontal lobe damage also showed significantly lower d' values, while their reaction times were even lower than those of the controls. It has been shown elsewhere that patients with lesions in the frontal lobe frequently tend to exhibit short latency (express) saccades to visual targets (Braun *et al.*, 1992; Rivaud *et al.*, 1994), which is indicative of response disinhibition. The shorter RTs shown by the frontal lobe patients in the present study could reflect their impaired ability to control motor responses in visually guided tasks. Taken together, these findings and our present ones suggest that areas in the ST gyrus, the inferoparietal lobulus and prefrontal cortex are involved in the information processing required in simultaneous and sequential visual discrimination.

Relation to Earlier Studies

The receptive fields of IT neurones in macaque cortex tend to be much larger and less confined to one visual field compared to those operating at earlier levels in the visual system (Gross *et al.*, 1972). Cells in IT cortex respond well to complex stimuli (Desimone *et al.*, 1984). It has been suggested that cells in posterior IT respond better to simple stimuli (oriented, colored bars and gratings), whereas anterior IT cells 'prefer' more elaborated stimuli including faces (Tanaka *et al.*, 1991). Some of these neurones have been shown to respond during the delay period in the delayed-match to sample (DMS) paradigm (Fuster and Jervey, 1982; Miyashita, 1988; Miyashita and Chang, 1988; Miller *et al.*, 1991; Puce *et al.*, 1991; Eskandar *et al.*, 1992; Quintana and Fuster, 1992; Nakamura and Kubota, 1995), suggesting a possible role for them in the mnemonic process. Experimentally induced lesions in this area lead to an impairment in visual memory in trained monkeys (Dean, 1976; Gaffan and Weiskrantz, 1980; Fuster *et al.*, 1981; Mishkin, 1982; Sahgal *et al.*, 1983; Britten *et al.*, 1992). In the study by Iwai and Mishkin (1969), small dorso-ventrally oriented strip lesions along the inferotemporal gyrus yielded a more pronounced effect when the lesions were in the posterior segment of IT cortex (OT region). This latter finding is compatible with our finding that patients with OT lesions exhibit significant impairments, whereas those with anterior temporal lobe lesions show little or no impairment in the discrimination tasks employed here.

Other studies in alert monkeys suggest a possible role of anterior IT cortex in visual memory. Reversible cooling lesions of anterior IT in macaques lead to an impairment in visual memory (Fuster *et al.*, 1981; Horel *et al.*, 1987). A recent study has suggested a role of IT cortex, anterior to area V4, in color detection and discrimination (Heywood *et al.*, 1995). In that study, lesions in OT cortex (including V4) had little effect on performance in luminance and hue discrimination tasks, whereas anterior IT lesions caused a severe impairment in color discrimination with only a mild effect on luminance discrimination. The present findings in patients with focal lesions suggest that anterior IT cortex is not directly involved in the visual processing required to perform simultaneous and sequential pattern discriminations (Figs 3 and 4). Although there are a number of differences in the requirements placed on the subjects by these different studies, this difference implies that anterior IT in humans is not directly involved in pattern and chromatic discrimination.

It has been shown that neurons in inferior and dorsolateral prefrontal cortex respond during the delay period of a delayed-response visual discrimination task (Goldman-Rakic, 1988; Fuster, 1995). These studies suggest that different prefrontal areas underly the working memory required for the monkey to remember the pattern versus the spatial location of the target stimulus: the dorsolateral prefrontal area mediates spatial representations and the inferior convexity codes object information (Wilson *et al.*, 1993). Indeed, evidence for coactivation of prefrontal cortex and inferior parietal cortex in monkeys performing working memory tasks has been found in a 2-deoxyglucose study, which showed an increase in cerebral glucose ulitization in an area in the principal sulcus (Friedman and Goldman-Rakic, 1994). Simultaneous single-unit recording in IT cortex and reversible cooling in prefrontal cortex (and vice versa) indicate the co-influence of these areas in monkeys performing color discrimination tasks (Fuster *et al.*, 1985). Interestingly, the lesions in some of the frontal lobe patients tested here could have involved an area homologous to the object memory area proposed by Wilson *et al.* (1993). These patients all had considerable difficulty on simultaneous and delayed presentation conditions. Compared to patients with OT damage, the frontal lobe patients studied here showed no benefit from

sequential presentation of the stimuli, suggesting that both visual encoding and working memory processes were impaired in frontal lobe patients (Fig. 5*a*,*b*).

Investigations using fMRI and positron emission tomography (PET) to map changes in regional blood flow and/or blood oxygenation in human brain support the idea of a distributed representation of visual processing and memory in the neocortex. In a PET study requiring subjects to retrieve information out of long-term visual memory, Roland and Friberg (1985) found significantly enhanced regional blood flow in ventral and dorsal prefrontal areas, inferoparietal areas and posterior inferotemporal cortex. In a spatial working memory task, McCarthy *et al.* (1994) found a significant increase in the blood oxygenation level dependent (BOLD) fMRI signal in Brodmann's area 46 in prefrontal cortex. By comparing the results from discrimination tasks with and without a delay, Swartz *et al.* (1995) reported that a significant activation in the angular gyrus, the supramarginal gyrus and dorsolateral prefrontal cortex was associated with memory processes. The areas identified in these studies appear to be involved in the storage and retrieval of visual information. The extent and diversity of cortical areas activated during task performance will clearly be related to the processing demands posed on the subject by the task in question. The present study suggests that an unilateral lesion in one of these areas can lead to an impairment in higher visual processing.

Patients with bilateral damage in the ventromedial OT cortex (lingual and fusiform gyri) often exhibit cerebral achromatopsia (Damasio, *et al.*, 1980; Zeki, 1990). Although acquired achromatopsia is often associated with field defects and prosopagnosia (Meadows, 1974), there have been case-study reports which suggesting that luminance-contrast detection can be spared (Heywood *et al.*, 1987), as well as the 'forced-choice' detection of chromatic boundaries (Heywood *et al.*, 1994; Troscianko *et al.*, 1996). All of the patients participating in the present study could detect the numbers embedded in the pseudo-isochromatic Ishihara plates, suggesting that their color vision was not significantly impaired. Despite this, a number of them had considerable difficulty discriminating patterns formed by isoluminant color contrast (Fig. 5*b*). It would be interesting to apply the present test to patients with established cerebral achromatopsia to explore residual pattern vision with luminance and chromatic contrast.

In summary, the presents results indicate that unilateral damage to the visual areas in the temporal or prefrontal cortex leads to an impairment in the encoding and retrieval of pattern information derived from luminance and/or color contrast. The anterior portion of the inferotemporal cortex does not appear to be directly involved in these processes, as patients with damage in this area showed little or no impairment. Taken together, our findings suggest that several areas of the human cortex subserve the processing required for the discrimination and storage of complex visual information.

Notes

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