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Anterior and Posterior Association Cortex Contributions to the Somatosensory P300

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A P300 (P3)-evoked response is generated in a variety of mammalian species upon detection of significant environmental events. The P3 component has been proposed to index a neural system involved in attention and memory capacity. We investigated the contribution of anterior and posterior association cortex to somatosensory P3 generation. Somatosensory event-related potentials (ERPs) were recorded in controls (n = 10) and patients with unilateral lesions in temporal–parietal junction (n = 8), lateral parietal cortex (n = 8), or dorsolateral frontal cortex (n = 10). Subjects pressed a button to mechanical taps of the fifth finger (targets; p = 0.12), randomly interposed in sequences of taps to the second (standards; p = 0.76) and the third or fourth finger (tactile novels; p = 0.06). Occasional shock stimuli were delivered to the wrist (shock novels; p = 0.06).

The scalp-recorded P3 was differentially affected by anterior and posterior association cortex lesions. Subjects with temporal–parietal lesions showed markedly reduced P3s to all types of stimuli at all scalp locations. The reductions were largest at the parietal electrode site over the lesioned hemisphere. Parietal patients had normal P3s for all stimulus types except for contralateral shock novels, which generated reduced P3s. Frontal lesions had reductions of the novelty P3 over frontal sites with minimal changes in the target P3.

The data support the existence of multiple intracranial P3 sources. The data further indicate that association cortex in the temporal–parietal junction is critical for generating the scalp-recorded target and novelty P3s, whereas dorsolateral frontal cortex contributes preferentially to novelty P3 generation. The N2 component was reduced by parietal and frontal lesions in patients who had intact target P3s, suggesting that different neural systems underlie N2 and P3 generation.

Endogenous event-related potentials (ERPs) are time-locked electric fields generated by synchronous neural regions engaged in cognitive processing. ERPs have clarified the timing and ordering of stages of information processing and have provided insights into the neural basis of cognition in humans. The P300 (P3) component, first described in 1965 (Desmedt et al., 1965; Sutton et al., 1965), is a reliable ERP recorded in a variety of experimental paradigms. The P3 has been widely studied because of its association with psychological constructs including orientation, attention, stimulus evaluation, and memory. However, a generally accepted theory of the functional significance and neural generators of the P3 is lacking (Desmedt et al., 1979; Donchin, 1979).

Data from several areas of investigation have proposed P3 sources in limbic (Halgren et al., 1980; Okada et al., 1983; McCarthy et al., 1989), diencephalic (Yingling and Hosobuchi, 1984; Katayama et al., 1985; Velasco et al., 1986), and neocortical (Vaughan et al., 1983; Wood and McCarthy, 1985; Knight et al., 1989; Smith et al., 1990) regions. Limbic structures have received considerable attention as candidate P3 generators because large-amplitude, phase-reversing ERPs with latencies in the range of the simultaneously scalp-recorded P3 can be recorded from the human medial temporal structures (Halgren et al., 1980; Wood et al., 1980; Stapleton et al., 1987; McCarthy et al., 1989). However, unilateral anterior temporal lobectomy does not significantly reduce the P3 at midline scalp sites in humans (Wood et al., 1982; Johnson, 1988), and bilateral amygdalo-hippocampectomy does not reduce a monkey P3-like potential (Paller et al., 1988). Thus, the hippocampal contribution to the scalp P3 is uncertain.

Some of the controversy regarding the neural origin of the P3 may be due to the fact that multiple brain regions contribute to the scalp-recorded P3. For instance, at least two types of P3 are recorded in normal subjects in the visual (Courchesne et al., 1975; Beck et al., 1980), auditory (Squires et al., 1975; Knight, 1984), and somatosensory modalities (Yamaguchi and Knight, 1991). Task-relevant, correctly detected stimuli generate a parietal maximal P3 (target P3), whereas nontarget, deviant stimuli requiring no behavioral response generate an earlier latency, frontocentral P3 (novelty P3).

Lesions in the temporal–parietal junction result in comparable decrements in the auditory target and novelty P3 (Knight et al., 1989). Patients with similar temporal–parietal lesions have marked reductions of the visual novelty P3 comparable to that observed in the auditory modality. However, these same patients have lesser reductions of the visual target P3 (Knight, 1990). Prefrontal lesions are reported to produce larger decrements in the novelty P3 than in the target P3 in both the auditory and the visual modality (Knight, 1984, 1990; Scabini et al., 1989).

These data indicate that intra- and intermodality association

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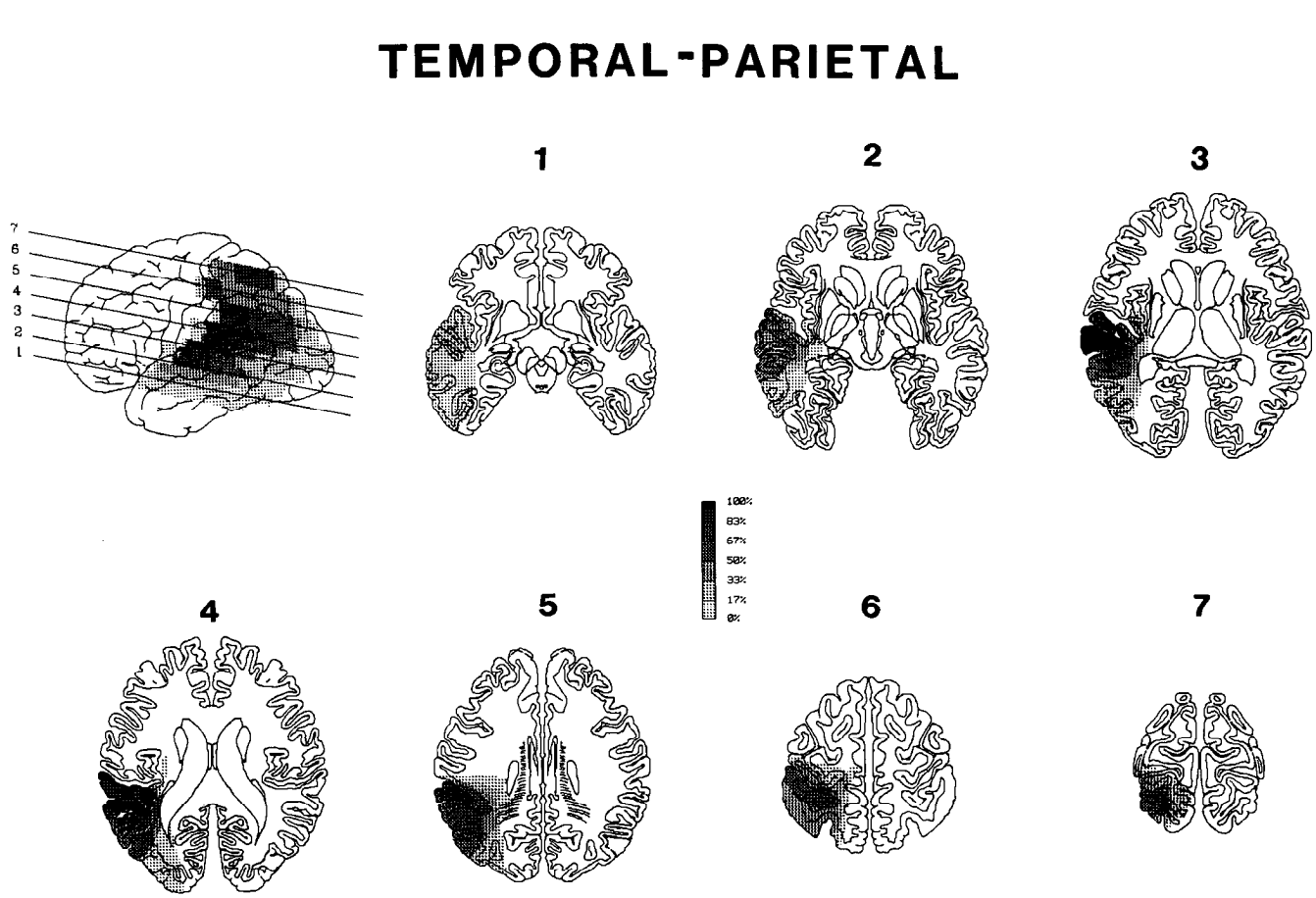


Figure 1. Lesion extent in patients with focal unilateral damage primarily in the temporal–parietal junction. The *numbered lines* on the lateral reconstruction (*upper left*) indicate the location of the axial sections (*1–7*) used in CT or magnetic resonance imaging (MRI) transcription. Lesions determined by CT scan from individual patients were transcribed onto templates 0° to canthomeatal line. A lateral view of the lesion extent was then projected from the axial sections by software reconstruction methods. The digitized lesion data from individual subjects were then averaged to generate the group lesion densities for both lateral and axial views. Unilateral right-hemisphere lesions have been reflected onto the left hemisphere. Lesions were averaged over eight patients (4 left, 4 right; mean lesion volume, 67 cc). The *shading scale* indicates the percentage of patients with damage in the corresponding area.

cortex circuits are engaged during target and novelty P3 generation. We assessed somatosensory target and novelty P3 in patients with a focal brain lesion in subregions of anterior and posterior association cortex to provide further information on the neural systems underlying scalp P3 generation.

Materials and Methods

Subjects. Controls and three patient groups were tested. The control group consisted of 10 right-handed subjects (mean age, 63 ± 9 yr), matched in age and sex to the patients. They were recruited from hospital staff personnel and were healthy and without history of neurological or psychiatric diseases. Patients were selected on the basis of a unilateral focal lesion in either anterior or posterior association cortex. Lesions evident on CT scan were transcribed onto corresponding CT templates by two independent raters. Software permitted reconstruction of the lateral perspective, determination of lesion volume and cytoarchitectonic areas affected, and extraction of group-averaged lesions. Figures 1–3 show the average axial reconstructions and lateral views of the three patient groups.

Eight patients had lesions primarily involving lateral superior temporal gyrus, posterior superior temporal plane, and inferior portions of the supramarginal gyrus (temporal–parietal group; mean age, 63 ± 8 yr; 4 right, 4 left; mean lesion volume, 67 ± 42 cm^3; Table 1, Fig. 1). The second patient group consisted of eight patients with lesions primarily involving superior parietal lobule and superior portions of the supramarginal and angular gyri (parietal group; mean age, 60 ± 11 yr; 4 right, 4 left; mean lesion volume, 27 ± 14 cm^3; Table 2, Fig. 2). Although temporal–parietal and parietal groups had substantial overlaps in lesions, these groups were anatomically differentiated on the basis of involvement of lateral superior temporal gyrus, posterior superior temporal plane, and inferior portions of the supramarginal gyrus. The third group consisted of 10 patients with dorsolateral frontal lesions (frontal group; mean age, 66 ± 8 yr; 5 right, 5 left; mean lesion volume, 37 ± 13 cm^3; Table 3, Fig. 3).

All lesions were due to cerebral infarctions and were at least 1 yr postonset. Craniotomy patients were excluded to avoid possible effects on ERP scalp voltages of current shunting through bone defects. Patients with medical complications, psychiatric disturbances, substance abuse, or dementia were also excluded. Neurological examinations showed neither marked hemiparesis nor peripheral neuropathy.

Primary somatosensory sensation (pain, touch, vibration, and proprioception) was assessed in all subjects prior to the experiment. Two subjects (both with right lesions) in the temporal–parietal group and one subject (with right lesion) in the parietal group showed moderate disturbances in primary somatosensory sensation and could not perform the detection task correctly in the limb contralateral to the lesion. These three subjects had reduced somatosensory evoked potentials (SEPs). For these three subjects, ERP data only from the unaffected hand were used for analysis. All other subjects in the temporal–parietal and parietal groups and all subjects in the control and frontal groups could make correct discriminations with more than 60% accuracy (see Tables 1–3 for details).

Experimental design. The somatosensory stimuli consisted of mechanical taps to the digits and electric shocks to the wrist. Mechanical taps were delivered separately to the second, third, fourth, and fifth fingertips with solenoids activated by a 50-msec-duration square-wave

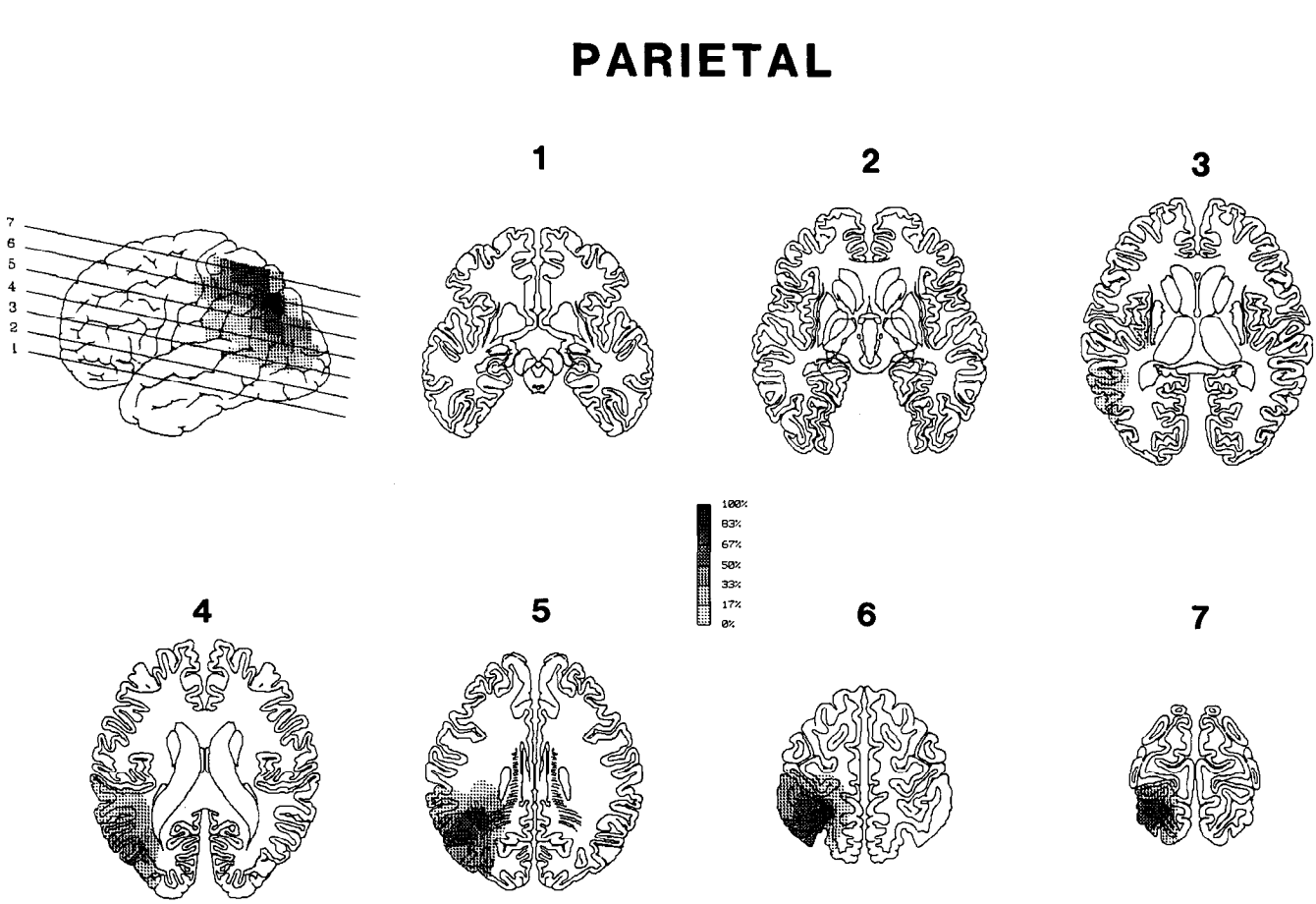


Figure 2. Averaged lesion extent in patients with lateral parietal lesions (n = 8; 4 left, 4 right; mean lesion volume, 27 cc; same format as Fig. 1).

electric pulse. All fingers were fixed in a hand brace, which limited finger movement. For the shock stimuli, electrical square pulses of 0.2 msec duration were delivered to the median nerve at the wrist by a stimulator (Grass Instrument Co.) through an isolating transformer. The intensity of the shock stimulation was in the range employed to produce an opponens pollicis twitch in conventional SEP recordings. The twitch threshold was determined by delivery of a few stimuli prior to ERP recording. There was no significant difference in intensity of delivered current to the right and left wrist among the four groups.

The experiment consisted of four blocks designed to produce replication of each wave form. Each block consisted of 500 stimuli delivered at a rate of 1/sec. Of these stimuli, 76% were mechanical tactile stimuli to the second finger (standards), 12% were mechanical tactile stimuli to the fifth finger (targets), 6% were mechanical tactile stimuli to the third or fourth finger (tactile novels), and 6% were electric shock stimuli to the median nerve (shock novels). Target and novel stimuli were interspersed at random in the sequence. A previous study showed that occasional shock stimuli interposed in trains of tactile stimuli generated a prominent novelty P3 that was similar in latency and scalp topography to the novelty P3 reported in the auditory and visual modalities (Yamaguchi and Knight, 1991). Stimulus randomization and delivery were controlled by a PC computer. Two blocks (first and fourth block) were assigned to the one hand, and another two blocks (second and third block) were given to the other hand. The order of hand stimulation was counterbalanced across subjects.

The subject was seated in a reclining chair in a sound-attenuated chamber and was instructed to press a button with the thumb of the nonstimulated hand only upon detection of tactile stimuli to the fifth finger. The subject was instructed to press as accurately and quickly as possible and not to respond to any other stimuli. Two- or three-minute rest periods intervened between blocks. During the experiment, white noise (70 dB SPL) was presented through headphones to mask the sound produced by the solenoid. The subject was encouraged to minimize eye movements and blinks throughout the periods of stimulation.

Brain electrical activity was recorded using Ag/AgCl electrodes placed at 15 scalp locations (Fpz, F3, Fz, F4, T3, C3, Cz, C4, T4, T5, P3, Pz, P4, T6, and Oz) based on the 10–20 system and below the left eye, all referenced to linked earlobes. Electrode impedances were kept below 5 KΩ. The EEG was amplified (band pass, 0.1–100 cycles/sec), digitized (250 Hz/channel), and stored on magnetic tape for off-line analysis by a PDP 11/73 computer. The averaging epoch was 1024 msec, including 200 msec of prestimulus baseline. Individual trials with excessive muscle activities (peak-to-peak amplitude, 80 μV) or eye blinks (peak-to-peak amplitude, 100 μV) were excluded from the average. Because lesions had effects on exogenous, stimulus-dependent ERPs to the standard stimuli (i.e., P200) as described later, difference waves were derived by subtracting the ERP to standard stimuli from the ERP to target, tactile, and shock novel stimuli. This permitted extraction of endogenous, cognitively related ERP components (i.e., N2, P3).

Data analysis. Peak amplitudes were measured relative to the 200-msec prestimulus baseline in the difference waves. Measurement windows were determined from inspection of individual subject averages and group superaverages. The P200 component was measured within a poststimulus window of 160–230 msec in the ERPs for standard stimuli. The P3 component was defined as the most positive peak occurring in a window of 270–650 msec for all infrequent target and novel stimuli. The N2 component was measured within a window of 180–270 msec for all infrequent stimuli. Peak latency of each component was also tabulated in these windows. Only data from correctly detected targets were included in the averages. Correct responses were defined as a reaction time (RT) between 150 and 1000 msec after stimulus delivery.

The data were organized as a function of the stimulated hand contralateral or ipsilateral to lesion and as a function of electrode site over lesioned (i.e., Pi, Fi, Ti, Ci, pTi) or nonlesioned (i.e., Pc, Fc, Tc, Cc, pTc) hemisphere. The scalp voltages were then subjected to repeated-measures analysis of variance. Because scalp recordings do not provide independent measures, amplitude changes were considered significant only if seen at single electrode sites. In the control group, there was no

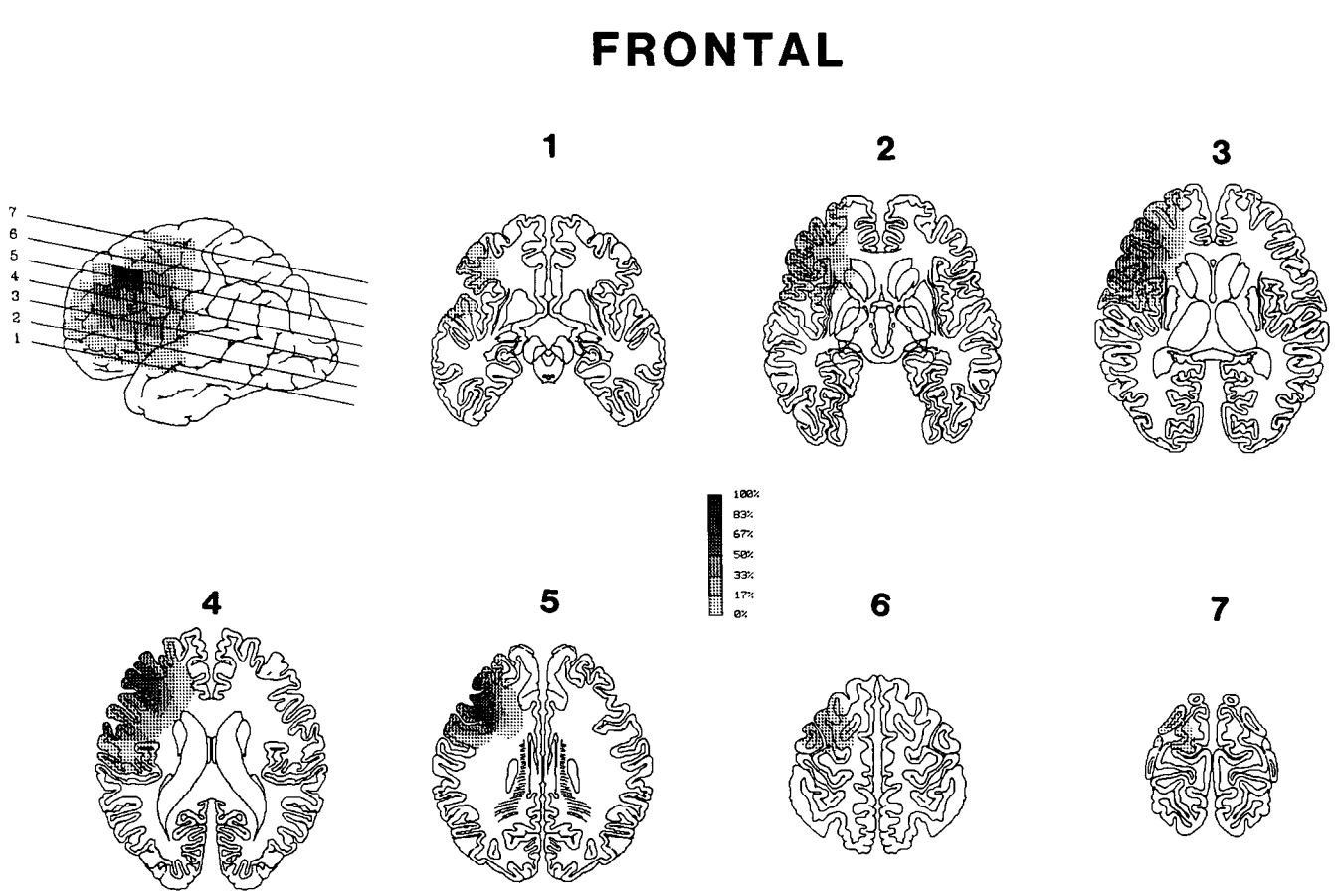


Figure 3. Averaged lesion extent in patients with frontal lesions (n = 10; 5 left, 5 right; mean lesion volume, 37 cc; same format as Fig. 1).

difference in ERP wave shapes between right- and left-hand stimulation, and ERPs were averaged across four blocks. The control data are shown with the stimulated hand on the same side as the side of stimulation in the patient group.

SEPs. After ERP recording, conventional SEPs were recorded to assess the intactness of primary somatosensory cortex. Three-hertz electric stimulation sufficient to induce a thumb twitch was applied to the median nerve at the wrist. Electrodes and references were the same as for the ERP study. Amplifier band pass was set at 10–1000 Hz, and a 331-msec epoch was digitized on line to magnetic tape at a sampling rate of 769 points/sec. Trials with excess EMG interference were automatically excluded from the average. A total of 500 responses were averaged with replications of an additional 500 responses for each hand of stimulation in a counterbalanced design.

Two components (N20 and P27) were measured at the parietal electrode contralateral to the hand of stimulation. These components represent the neural activity at the primary somatosensory cortex (N20 from area 3b and P27 from area 1 or 2; Sutherling et al., 1988; Allison et al., 1989; Yamaguchi and Knight, 1990). Peak amplitudes were measured relative to the 20-msec prestimulus baseline activity with a window of 17–23 msec for the N20 and 24–33 msec for the P27. Peak latency was tabulated relative to stimulus delivery in these windows.

Results

Behavioral

Temporal–parietal and frontal groups showed decreased detection accuracies for targets delivered contralateral to the lesion (percent correct detection; controls: 98.0 ± 1.5%; temporal–parietal: 83.2 ± 11.4%, $p < 0.001$; frontal: 87.8 ± 9.8%, $p < 0.01$). The parietal group performed comparably to controls (parietal, 95.0 ± 7.2%, p = NS). For stimulation ipsilateral to the lesion, detection accuracy was reduced only in the frontal group (frontal, 86.9 ± 15.4%, $p < 0.05$). Controls and the temporal–parietal and parietal groups performed comparably for ipsilateral stimuli (temporal–parietal, 91.9 ± 10.3%; parietal, 96.2 ± 4.3%; p = NS). False alarm rates were not significantly different among the four groups (control: 2.6 ± 1.9%; temporal–parietal: contralateral, 15.1 ± 19.4%; ipsilateral, 11.7 ± 17.0%; parietal: contralateral, 2.8 ± 3.8%; ipsilateral, 3.7 ± 4.6%; frontal: contralateral, 6.2 ± 6.5%; ipsilateral, 8.5 ± 9.2%).

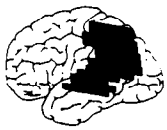
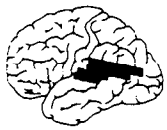
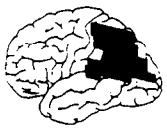
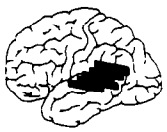
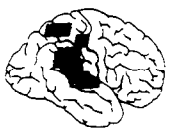
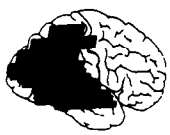
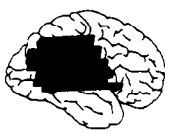
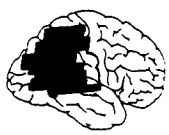
RTs were prolonged in all patient groups compared with controls for stimulation contralateral to the lesion (controls: 437 ± 57 msec; temporal–parietal: 557 ± 42 msec, $p < 0.001$; parietal: 535 ± 78 msec, $p < 0.01$; frontal: 523 ± 47 msec, $p < 0.01$). There was no difference in RTs between the patient groups. For stimulation ipsilateral to the lesion, all patient groups again had significantly delayed RTs compared with controls (controls: 437 ± 57 msec; temporal–parietal: 556 ± 81 msec, $p < 0.005$; parietal: 524 ± 92 msec, $p < 0.05$; frontal: 505 ± 49 msec, $p < 0.001$). However, RTs again did not differ between the patient groups. RTs for contralateral stimulation were prolonged relative to ipsilateral stimulation, but the differences did not reach significance in any patient group.

RTs were inversely correlated with correct detection rate in the temporal–parietal and parietal groups (temporal–parietal: $r = -0.63$, $p < 0.05$; parietal: $r = -0.77$, $p < 0.01$) and showed a trend of inverse correlation in the control and frontal groups (control: $r = -0.59$, $p < 0.1$; frontal: $r = -0.38$, $p < 0.1$).

Electrophysiological P200 component

The standard stimuli generated little or no P3 and thus allow examination of P200 uncontaminated by P3 (Fig. 4). The control

Table 1. Summary of patient information in the temporal-parietal group

Pt/Age/ Sex/Side	CT Scan	Duration	Clinical deficits at time of testing	Behavior Correct response	False alarm	Reaction time
RJ/55/ M/L		5 yrs	Moderate Wernicke aphasia, mild hemianesthesia, mild finger agnosia	C: 69.2 I: 100	7.1 0	583 474
DL/56/ M/L		4 yrs	Conduction aphasia, finger agnosia	C: 74.3 I: 98.7	43.6 26.4	577 453
MV/65/ M/L		20 yrs	Anomia, moderate Wernicke aphasia	C: 98.1 I: 97.1	2.3 2.9	550 540
EB/67/ M/L		5 yrs	Moderate Wernicke aphasia	C: 95.2 I: 95.2	0 1.0	483 499
JC/53/ M/R		30 yrs	Decreased proprioception, finger agnosia, agraphesthesia	C: 81.7 I: 96.2	35.7 4.8	546 623
RM/69/ M/R		10 yrs	Moderate hemianesthesia, finger agnosia, astereognosis, pseudoathetosis	C: -- I: 75.0	-- 9.3	-- 696
HS/74/ M/R		15 yrs	Moderate hemianesthesia, finger agnosia, astereognosis	C: -- I: 75.7	-- 47.9	-- 595
HH/67/ M/R		4 yrs	Mild hemianesthesia, finger agnosia, agraphesthesia	C: 80.8 I: 97.0	1.1 1.1	601 563

group generated a frontocentral maximal P200 component to standard stimuli (latency, 202 ± 32 msec). The temporal–parietal group had a reduced P200 amplitude (contralateral stimuli: 65% reduction at Cz, $F_{1,14} = 15.6$, $p < 0.01$; ipsilateral stimuli: 47% reduction at Cz, $F_{1,16} = 10.1$, $p < 0.01$). Parietal lesions did not affect the P200. Frontal lesions also had reduced P200 amplitudes in comparison to the control group (contralateral stimuli: 58% reduction at Cz, $F_{1,18} = 18.7$, $p < 0.001$; ipsilateral stimuli: 42% reduction at Cz, $F_{1,18} = 10.4$, $p < 0.01$). Latency was unaffected in any lesion groups (at Cz: temporal–parietal, 191 ± 25 msec; parietal, 197 ± 27 msec; frontal, 182 ± 22 msec; all p = NS vs controls).

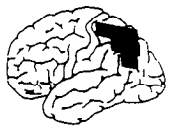
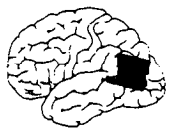
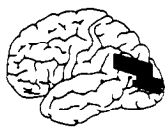
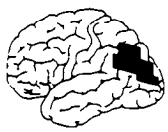
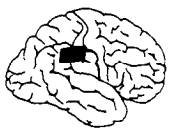
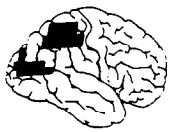
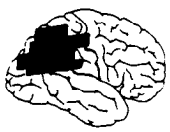
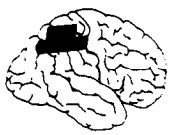
N2 and P3 components

Control group

Controls generated a parietal maximal target P3 (latency, 396 msec) and a frontocentral maximal novelty P3 (latency for tactile novels, 417 msec; for shock novels, 352 msec; see Fig. 5). The target P3 had an asymmetrical scalp distribution at frontocentral scalp site. The novelty P3 had a symmetrical scalp distribution.

An N2 was observed prior to the P3. This component was maximal at central sites and symmetrical over both hemispheres for all infrequent stimuli (latency for targets, 205 msec; for tactile

Table 2. Summary of patient information in the parietal group

Pt/Age/ Sex/Side	CT Scan	Duration	Clinical deficits at time of testing	Behavior Correct response	False alarm	Reaction time
MK/43/ M/L		22 yrs	Mild L/R difficulty, mild finger agnosia	C: 95.2%	0%	597msec
				I: 96.4	1.2	555
FO/60/ M/L		7 yrs	Conduction aphasia, stuttering	C: 98.8	0.9	414
				I: 100	0.9	419
JP/67/ M/L		2 yrs	Mild finger agnosia, mild agraphesthesia	C: 98.1	10.5	549
				I: 96.1	2.9	483
BC/71/ M/L		3 yrs	Mild finger agnosia	C: 97.9	2.0	484
				I: 99.0	2.8	488
JR/42/ M/R		20 yrs	Mild agraphesthesia, mild finger agnosia	C: 78.8	4.8	657
				I: 87.5	11.2	635
RR/61/ M/R		4 yrs	Decreased proprioception, mild pseudoathetosis, astereognosis, agraphesthesia	C: 99.0	1.0	523
				I: 100	0	463
JM/65/ M/R		11 yrs	Moderate hemianesthesia, decreased 2 point discrimination	C: --	--	--
				I: 92.3	10.6	682
WP/66/ M/R		1 yr	Normal	C: 97.1	0	522
				I: 98.1	0	464

novels, 216 msec; for shock novels, 207 msec). Shock novel stimuli generated additional symmetrical frontocentral P100 and N145 components prior to the N2.

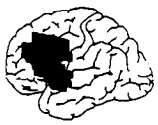
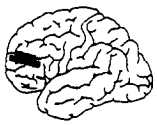
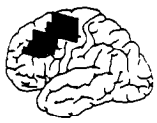
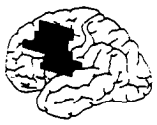
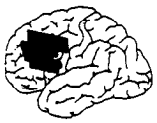
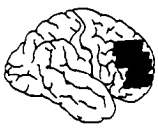
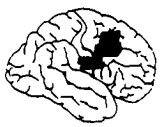
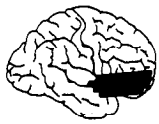
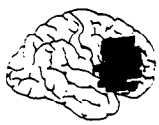
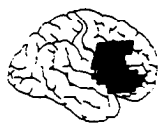
N2 and P3 latencies were correlated with RTs (N2 latency vs RT: $r = 0.45$, $p < 0.05$; P3 latency vs RT: $r = 0.65$, $p < 0.01$). Amplitude was not correlated with RTs. Correct response rates were not related to N2 and P3 measures.

Temporal–parietal group

Temporal–parietal lesions markedly reduced the P3 over the lesioned hemisphere to both target and novel stimuli delivered to the hand contralateral to the lesion (targets: 88% reduction at Pi, $F_{1,14} = 54.3$, $p < 0.001$; tactile novels: 99% reduction at Pi, $F_{1,14} = 30.5$, $p < 0.001$; shock novels: 91% reduction at Pi, $F_{1,14} = 80.5$, $p < 0.001$; see Fig. 5). P3s were also reduced over the nonlesioned hemisphere (targets: 79% reduction at Pc, $F_{1,14} = 26.1$, $p < 0.001$; tactile novels: 78% reduction at Pc, $F_{1,14} = 14.4$, $p < 0.01$; shock novels: 85% reduction at Pc, $F_{1,14} = 60.8$, $p < 0.001$).

For ipsilateral stimulation, temporal–parietal lesions also resulted in P3 amplitude reductions for all types of infrequent stimuli (targets: 67% reduction at Pz, $F_{1,16} = 22.3$, $p < 0.005$; tactile novel: 86% reduction at Cz, $F_{1,16} = 16.0$, $p < 0.001$; shock novels: 74% reduction at Cz, $F_{1,16} = 17.3$, $p < 0.001$). The P3

Table 3. Summary of patient information in the frontal group

Pt/Age/ Sex/Side	CT Scan	Duration	Clinical deficits at time of testing	Behavior		
				Correct response	False alarm	Reaction time
TJ/63/ M/L		2 yrs	Moderate Wernicke aphasia	C: 79.6 I: 74.3	8.9 23.4	480 515
RS/66/ M/L		5 yrs	Normal	C: 82.6 I: 76.0	7.0 11.2	539 534
FR/67/ M/L		5 yrs	Anomia, transcortical motor aphasia	C: 91.3 I: 96.2	6.3 2.0	511 464
HF/69/ M/L		8 yrs	Anomia, mild finger agnosia	C: 67.9 I: 60.9	21.9 22.9	464 573
RT/73/ M/L		6 yrs	Anomia, transcortical motor aphasia	C: 81.5 I: 92.3	2.9 1.9	569 536
WV/46/ M/R		4 yrs	Normal	C: 98.1 I: 99.0	0 0	437 403
RM/64/ M/R		4 yrs	Flat affect	C: 94.2 I: 98.1	2.0 1.9	576 547
RF/65/ M/R		30 yrs	Normal	C: 99.0 I: 92.3	3.7 15.7	480 499
MH/69/ M/R		6 yrs	Normal	C: 88.0 I: 93.1	9.3 5.0	536 496
MM/73/ M/R		3 yrs	Normal	C: 95.2 I: 97.1	0 1.0	554 479

was reduced in each subject with a temporal–parietal lesion (see Fig. 6). P3 reductions were greater at the parietal site over the lesioned hemisphere in comparison with the nonlesioned hemisphere (Pi vs Pc; targets: $F_{1,7} = 7.15$, $p < 0.05$; tactile novels: $F_{1,7} = 6.71$, $p < 0.05$; shock novels: $F_{1,7} = 10.9$, $p < 0.05$; Figs. 5, 6). The P3 to ipsilateral shock stimuli was partially preserved at anterior scalp sites (Fig. 5).

Reliable P3 latencies were not obtainable for contralateral stimuli. P3 latencies were significantly prolonged for ipsilateral target and tactile novel stimuli compared with the control group

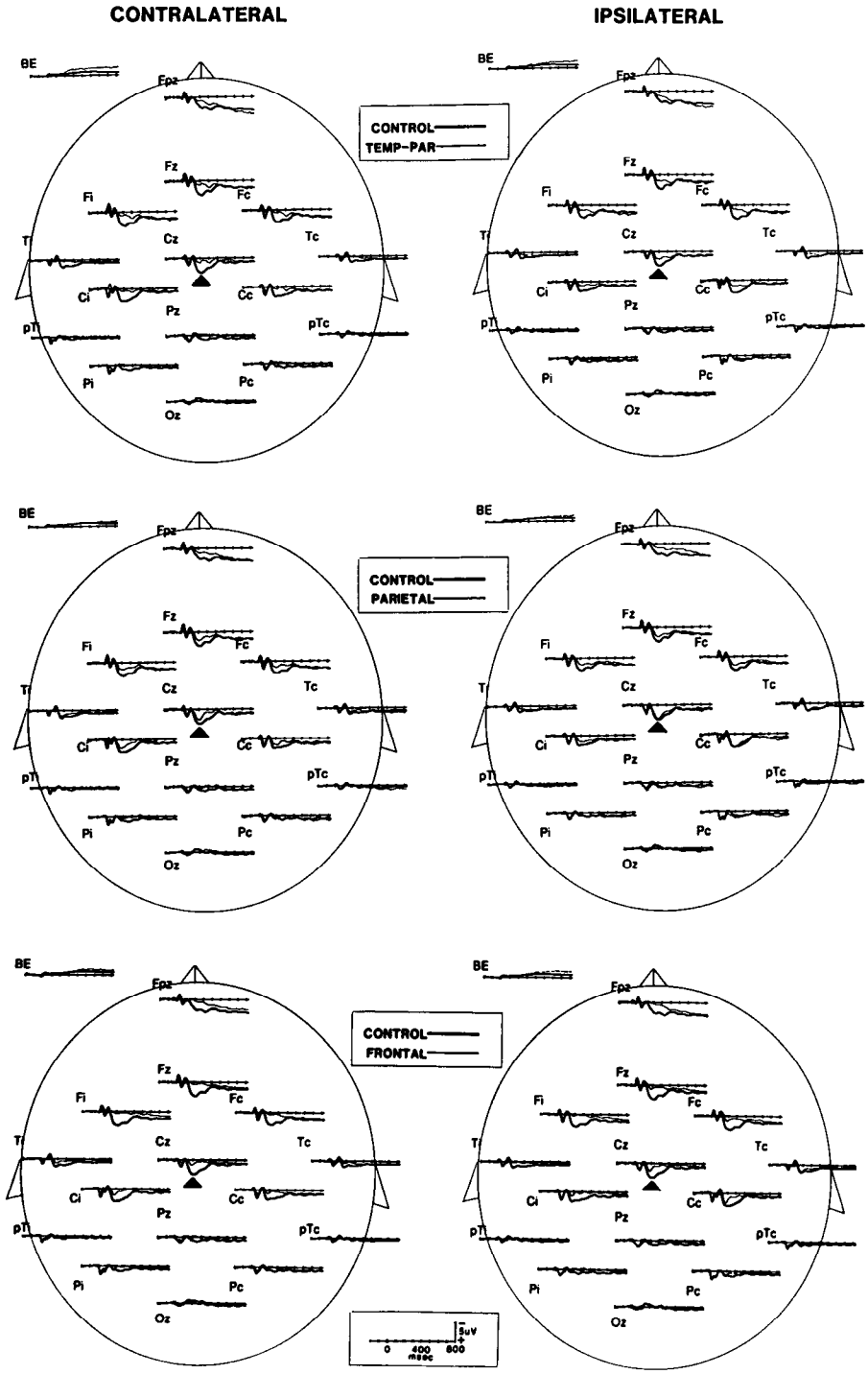


Figure 4. Grand average ERPs generated by standard stimuli to the hand contralateral (*left column*) or ipsilateral (*right column*) to the lesion for each patient group. The patient data are compared with the control group and are presented as a function of scalp sites ipsilateral (i.e., *Pi, Fi, Ti, Ci, pTi*) or contralateral (i.e., *Pc, Fc, Tc, Cc, pTc*) to the lesioned hemisphere. In the *left column*, data are shown as if the right hand were stimulated, and all lesions were in the left hemisphere. *Solid triangles* indicate the P200 component. *BE*, below eye; *TEMP-PAR*, temporal–parietal.

(targets, at Pz: $F_{1,16} = 9.23$, $p < 0.01$; tactile novels, at Cz: $F_{1,16} = 22.6$, $p < 0.001$) but not for shock novel stimuli.

The N2 amplitude was not different from the control group for target and tactile novel stimuli. The N2 component to contralateral shock stimuli was not decreased, though the N145 component was not clearly seen. The N2 component to ipsilateral shock novel stimuli was significantly reduced in amplitude (46% reduction at Cz; $F_{1,16} = 6.74$; $p < 0.05$), though latency was normal.

Correct response rates and RTs were not correlated with N2 and P3 measures.

Parietal group

The parietal group generated P3 components to target and tactile novel stimuli comparable to controls for stimulation both contralateral and ipsilateral to the lesion (Fig. 7). A nonsignificant reduction in target P3 amplitude was observed at the parietal electrode over the lesioned hemisphere. Shock novel stimuli delivered to the hand ipsilateral to the lesion also generated a normal P3. By contrast, the P3 evoked by shock novel stimuli delivered contralateral to the lesion was significantly reduced in amplitude over scalp sites in both hemispheres (vs. control:

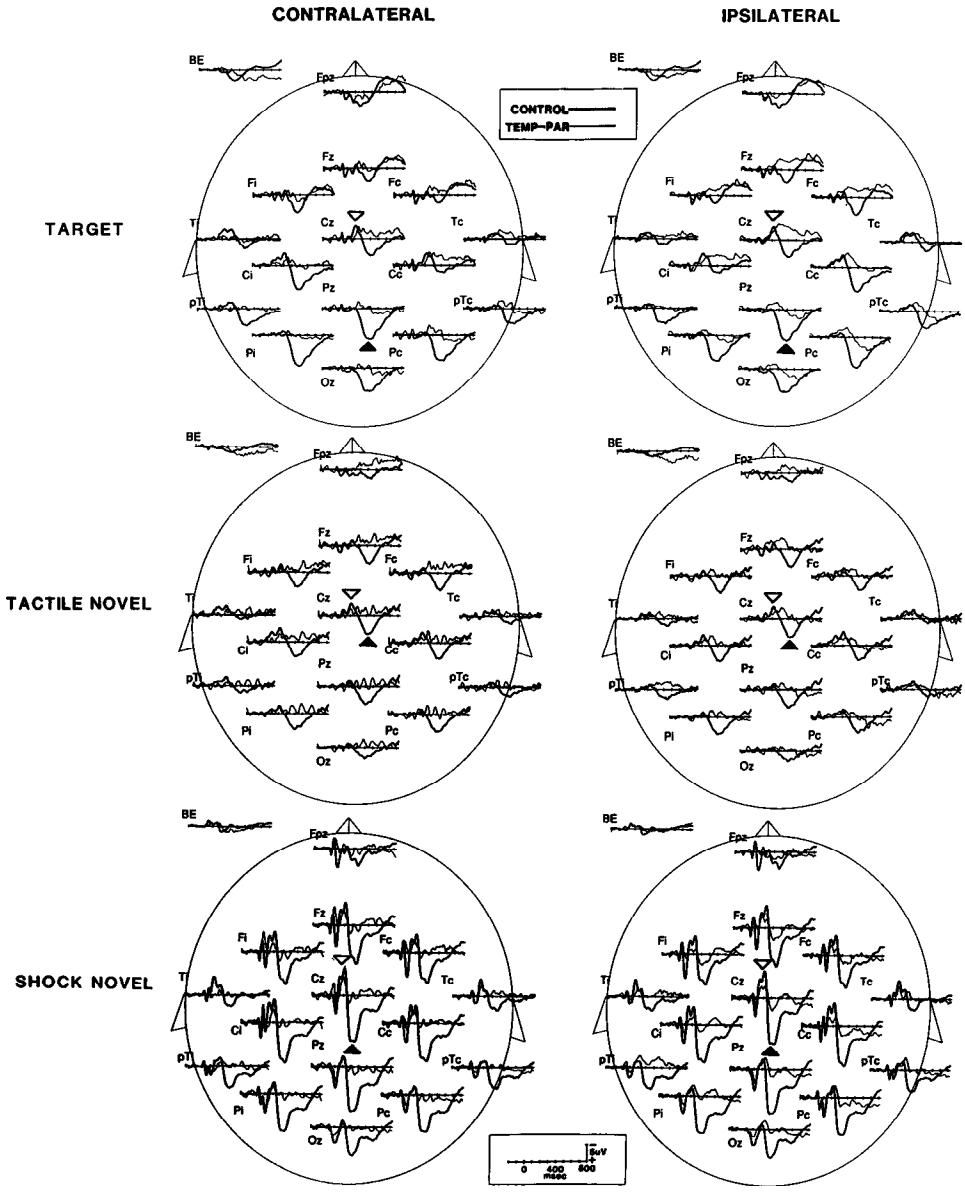


Figure 5. Grand average ERPs for temporal–parietal patients generated by target, tactile novel, and shock novel stimuli delivered to the hand contralateral or ipsilateral to the lesion (*thin line*). Data are compared with the control group (*thick line*). See *Experimental design* for stimulus parameters. *Open* and *solid triangles* indicate the N2 and P3 components, respectively. The patient data are organized as a function of electrodes ipsilateral or contralateral to the lesion. *Abbreviations* are as in Figure 4.

33% reduction at Cz, $F_{1,15} = 5.52$, $p < 0.05$). P3 latencies for all stimulus types were not affected by parietal lesions.

N2 amplitudes were significantly reduced for all types of contralateral infrequent stimuli in comparison with controls (at Cz; targets: 64% reduction, $F_{1,15} = 4.84$, $p < 0.05$; tactile novels: 75% reduction, $F_{1,15} = 6.15$, $p < 0.05$; shock novels: 89% reduction, $F_{1,15} = 24.0$, $p < 0.001$). N2 amplitude for ipsilateral shock novel stimuli was also reduced (64% reduction at Cz; $F_{1,16} = 15.0$; $p < 0.005$). N2 amplitude to ipsilateral target and tactile novel stimuli was not affected. N2 latencies were not affected by parietal lesions.

N2 and P3 latencies for contralateral target stimuli were correlated with RTs (N2 latency vs RT: $r = 0.75$, $p < 0.01$; P3 latency vs RT: $r = 0.68$, $p < 0.05$), whereas those for ipsilateral stimuli showed no correlations (N2, $r = 0.09$; P3, $r = 0.10$). Correct response rates did not correlate with N2 and P3 measures.

Because there was substantial lesion overlap between the parietal and temporal–parietal group and the mean lesion volume was significantly larger in the temporal–parietal group ($F_{1,14} = 6.86$; $p < 0.05$), the relation between lesion volume and P3 amplitude was examined. No significant correlation was observed between lesion volume and P3 amplitude for any infrequent stimuli (targets, $r = 0.04$; tactile novels, $r = 0.14$; shock novels, $r = 0.05$). Furthermore, in subjects with the smallest temporal–parietal lesions (DL and EB; see Table 1), P3 was abolished for all types of infrequent stimuli (Fig. 8). Thus, the lesion effects on the P3 do not appear to be due to differences in lesion volume, but are related to damage in the lateral superior temporal gyrus, posterior superior temporal plane, and inferior portions of the supramarginal gyrus.

Frontal group

Frontal lesions had differential effects on target and novelty P3 (Fig. 9). Tactile and shock novelty P3 amplitudes were bilaterally reduced over frontal scalp sites for both contralateral and

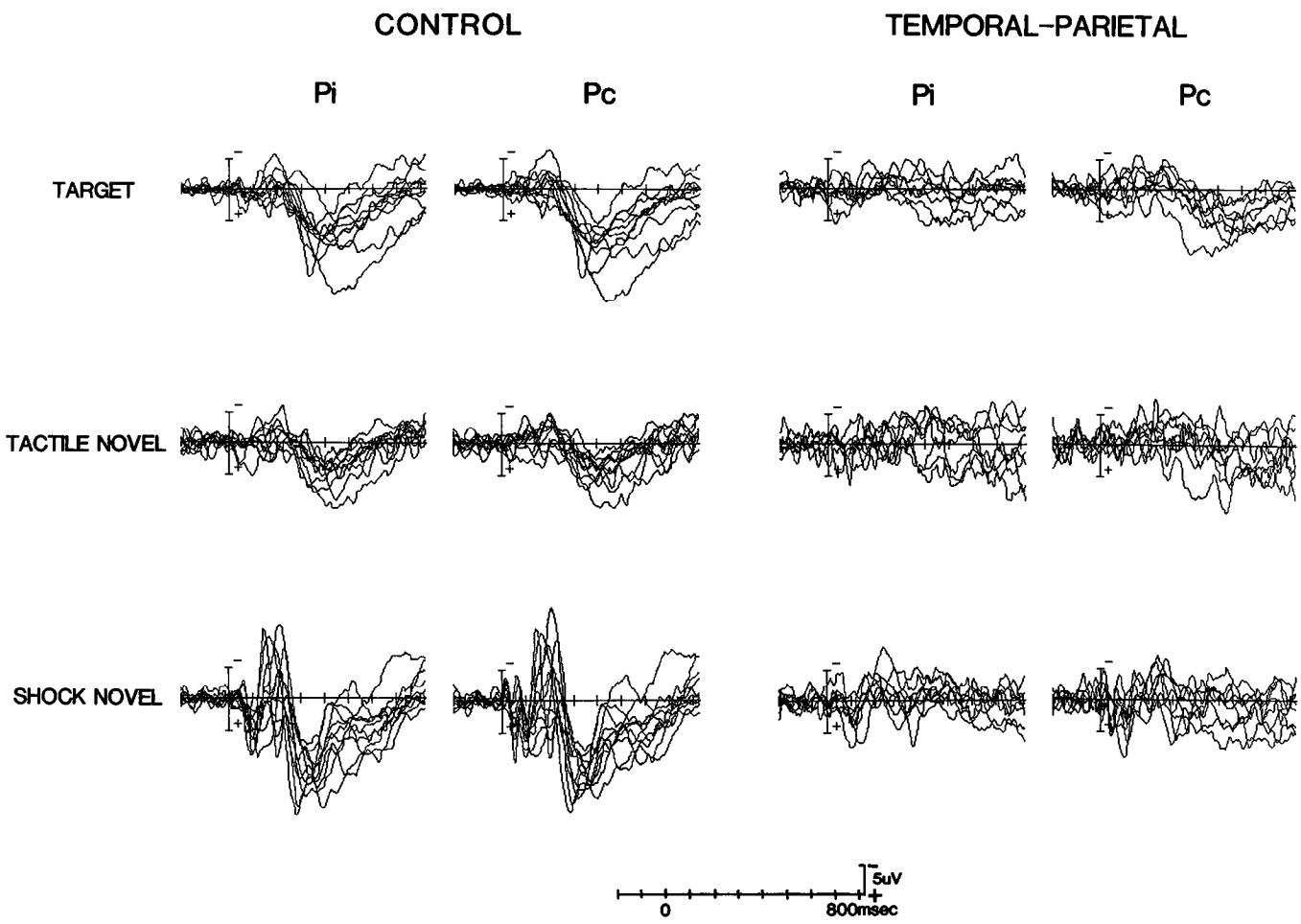


Figure 6. Superimposition of ERPs from individual subjects recorded at lateral parietal scalp sites in the control and temporal–parietal groups. In the temporal–parietal group, ERPs are shown for stimuli delivered to the hand ipsilateral to the lesion.

ipsilateral stimulation (at Fz; contralateral tactile novels: 65% reduction, $F_{1,18} = 14.5$, $p < 0.01$; contralateral shock novels: 58% reduction, $F_{1,18} = 13.2$, $p < 0.01$; ipsilateral tactile novels: 53% reduction, $F_{1,18} = 8.35$, $p < 0.05$; ipsilateral shock novels: 49% reduction, $F_{1,18} = 7.51$, $p < 0.05$). There was no significant difference in novelty P3 reduction between lateral frontal electrode sites (Fi vs Fc for contralateral shock novels, $F_{1,9} = 1.56$, NS). The frontal reduction in the novelty P3 amplitude was significantly larger than that seen at parietal sites (Fz/Pz ratio; tactile novels: control, 1.32; frontal, 0.73; $F_{1,18} = 6.22$; $p < 0.05$; shock novels: control, 1.10; frontal, 0.72; $F_{1,18} = 4.91$; $p < 0.05$). Novelty P3 reductions were greater than target P3 reductions at frontal sites (target P3 reduction of 37% vs tactile novels reduction of 67%: $F_{1,9} = 9.00$, $p < 0.05$; vs shock novels reduction of 60%: $F_{1,9} = 6.10$, $p < 0.05$). Novelty P3 amplitude for contralateral shock stimuli was more reduced than ipsilateral stimuli, but the difference did not reach significance. The target P3 was reduced over the lesioned hemisphere only for contralateral stimulation (47% reduction at Fi: $F_{1,18} = 6.05$; $p < 0.05$). There was no significant P3 latency delay for any types of infrequent stimuli.

Frontal lesions reduced N2 amplitude for all types of infrequent stimuli delivered to the contralateral hand (at Cz; targets: 64% reduction, $F_{1,18} = 6.06$, $p < 0.05$; tactile novels: 67% reduction, $F_{1,18} = 7.96$, $p < 0.05$; shock novels: 75% reduction, $F_{1,18} = 15.5$, $p < 0.001$). N2 amplitude was also reduced for ipsilateral shock novel stimuli (82% reduction at Cz: $F_{1,18} = 28.5$; $p < 0.001$) and showed a trend toward reduction for ipsilateral target and tactile novel stimuli (at Cz; targets: 49% reduction, $F_{1,18} = 3.57$, $p < 0.1$; tactile novels: 59% reduction, $F_{1,18} = 3.88$, $p < 0.1$).

The target P3 latency and amplitude for contralateral stimuli were correlated with RTs (P3 latency vs RT: $r = 0.47$, $p < 0.05$; P3 amplitude vs RT: $r = -0.46$, $p < 0.05$), whereas those for ipsilateral stimuli showed no correlations. N2 latency and amplitude did not correlate with RTs. Correct response rates were also not correlated with N2 and P3 measures.

SEPs

After exclusion of three patients with primary somatosensory loss, all patient groups had N20 components comparable to the control group recorded over both lesioned and nonlesioned hemisphere (Fig. 10). The P27 amplitude was not affected by temporal–parietal and parietal lesion. However, the frontal group had an enhanced amplitude of the P27 component with delayed latency for stimulation contralateral to the lesion (amplitude: 64% increase, $F_{1,18} = 4.70$, $p < 0.05$; latency: $F_{1,18} = 8.61$, $p <$

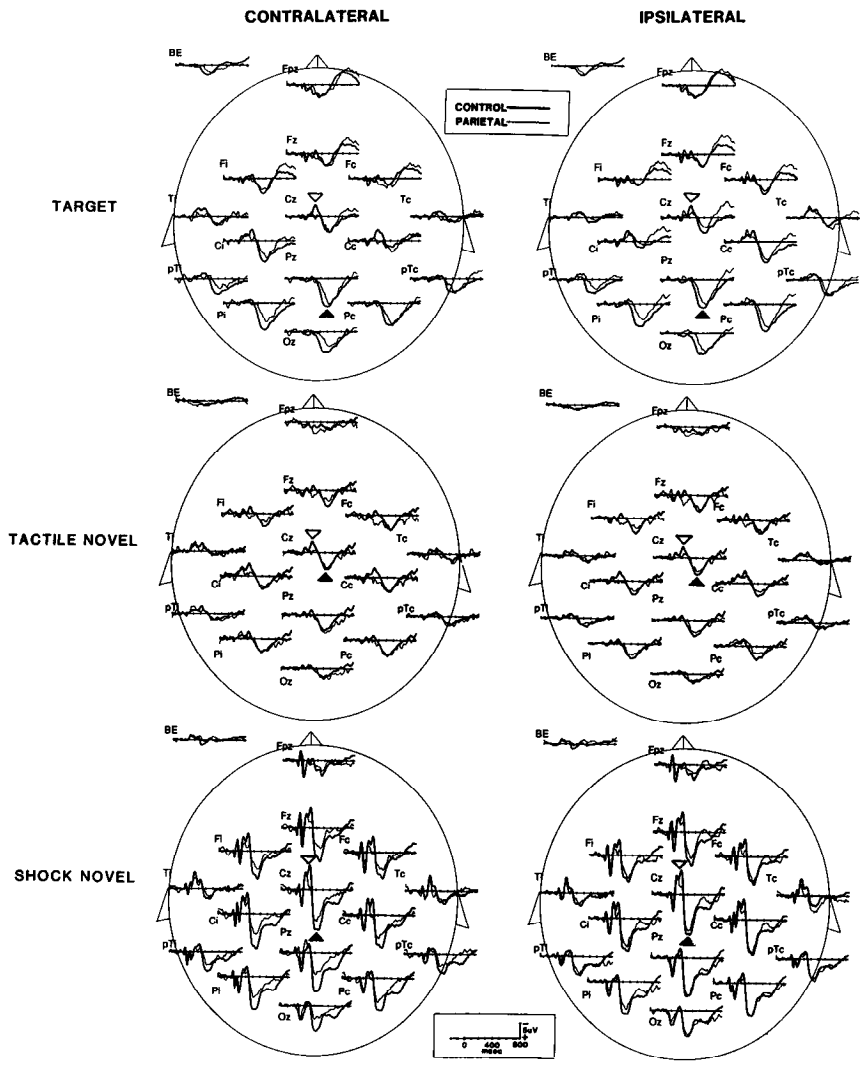


Figure 7. Grand average ERPs for parietal patients generated by target, tactile novel, and shock novel stimuli delivered ipsilateral and contralateral to the lesion (same format as Fig. 5).

0.01; Fig. 10). P27 amplitude was normal for stimulation ipsilateral to the frontal lesion.

Discussion

Temporal–parietal lesions

Unilateral temporal–parietal junction lesions markedly reduced P3 responses to all types of infrequent stimuli delivered either ipsilateral or contralateral to damage, supporting the notion that this region plays a critical role in scalp P3 generation. It is unlikely that the P3 reductions are due solely to deficits in stimulus discriminability because the averaged ERP for target stimuli was obtained from correctly detected events, group mean detection accuracy was above 80%, and P3 was reduced for stimuli delivered to the limb ipsilateral to the lesion with normal detection capacity. RTs also did not vary between patient groups with and without P3. These results indicate that the neural systems involved in somatosensory discrimination may be distinct from those necessary for P3 generation.

Several possibilities arise regarding the bilateral reduction of the P3 by unilateral lesions. In a previous auditory study, five of six temporal–parietal patients studied had lesions in the dominant (left) hemisphere. Thus, a hemispheric asymmetry for P3 generation could not be ruled out (Knight et al., 1989). The present somatosensory study found equivalent P3 reductions in left ($n = 4$) and right ($n = 4$) temporal–parietal patients. Thus, an asymmetrically organized neural system for P3 generation is unlikely. Second, scalp-recorded P3 may be generated by subcortical midline structures dependent on bilateral hemispheric input. Diencephalic structures including thalamus, septal basal forebrain, and locus coeruleus have been proposed as candidate P3 generators or modulators (Yingling and Hosobuchi, 1984; Velasco et al., 1986; Harrison et al., 1988; Pineda et al., 1989). Although a subcortical midline generator does not easily explain the asymmetrical amplitude reduction of the P3 observed in some conditions in the temporal–parietal and frontal patients, abnormal cortical input to the structures off the midline, such as the amygdala and hippocampus, or to midline structures with laterally oriented dipoles could contribute to the asymmetric amplitude reductions recorded on the scalp. Third, interhemispheric integration of environmental information in the temporal–parietal junction may be necessary for P3 generation. In either of these explanations, it should be noted that an isolated temporal–parietal junction cannot function as the sole generator of the P3, but must also provide modulatory input to generators in either distant subcortical or cortical sites.

The data from the brain-damaged subjects provide some sup-

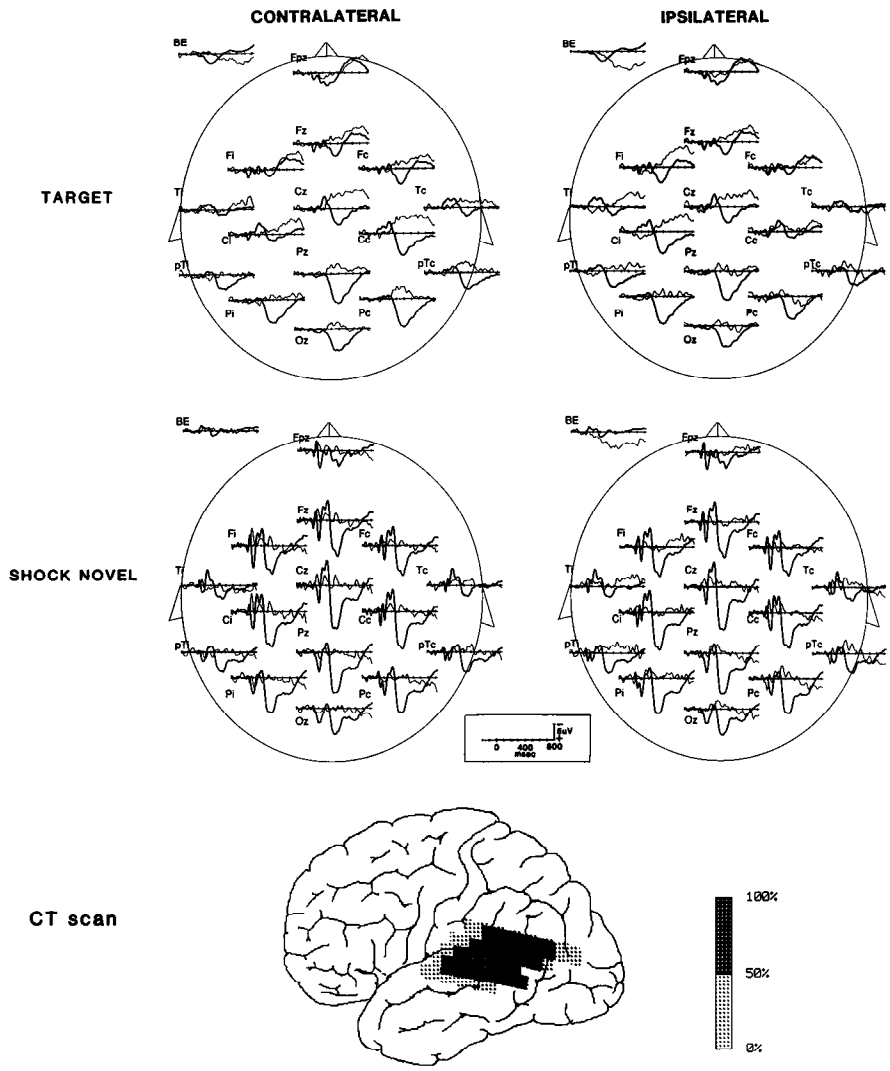


Figure 8. Grand average ERPs in two temporal–parietal patients with the smallest lesion centered in the posterior superior temporal gyrus (same format as Fig. 5). The drawing at bottom shows lesion extent in two patients.

port for the third hypothesis. Stimuli delivered contralateral to the lesion resulted in bilateral P3 reduction. This could be explained by loss of a generator in the lesioned temporal–parietal junction and dysfunction of the unlesioned temporal–parietal generator due to loss of facilitatory input from the lesioned side. The P3 was reduced over the lesioned hemisphere when stimuli were delivered ipsilateral to the lesion, though some P3 activities could be recorded over the intact hemisphere in some conditions. This could be modeled by P3 generation in the intact temporal–parietal junction receiving the lateralized sensory information and loss of activity in the contralateral lesioned temporal–parietal junction (Scherg and Von Cramon, 1986). A report of intact P3 responses in callosotomy patients indicates that this putative interhemispheric effect may not be dependent on callosal pathways (Kutas et al., 1990).

Primate studies have documented that the inferior parietal lobule and superior temporal sulcus (STS) have reciprocal connections with frontal cortex, limbic structures, and reticular structures. Interaction between these regions and posterior association cortex may be necessary for sustaining a sensory template of the extrapersonal world and for directing attention towards behaviorally relevant sensory events (Mesulam, 1983). These regions appear to function both inter- and intrahemispherically and have substantial anatomical connections with ipsilateral and contralateral structures (Mesulam et al., 1977; Goldman-Rakic and Schwartz, 1982; Andersen et al., 1985; Seltzer and Murphy, 1989).

Studies using single-unit recording have revealed specific neurons in area cSTP of the caudal STS whose neurons respond to polymodal sensory stimuli and have large receptive fields. These units have been proposed to index global attention to the external world (Hikosaka et al., 1988). Neuropsychological studies in humans have also described profound hemi-inattention or hemi-neglect syndromes from acute lesions in the temporal–parietal junction, particularly evident after right hemisphere damage (Heilman et al., 1987).

The temporal–parietal junction in humans may correspond to multimodal area cSTP and auditory association area Tpt in the monkey. These regions have bidirectional connections to area TH in the parahippocampal gyrus. A network involving area Tpt and medial temporal structures has been proposed to be necessary for learning and memory in animals and humans (Amaral et al., 1983).

Studies in normals suggest that P3 amplitude predicts subsequent memory performance (Fabiani et al., 1986; Neville et al., 1986; Paller et al., 1987). A subset of the frontal and tem-

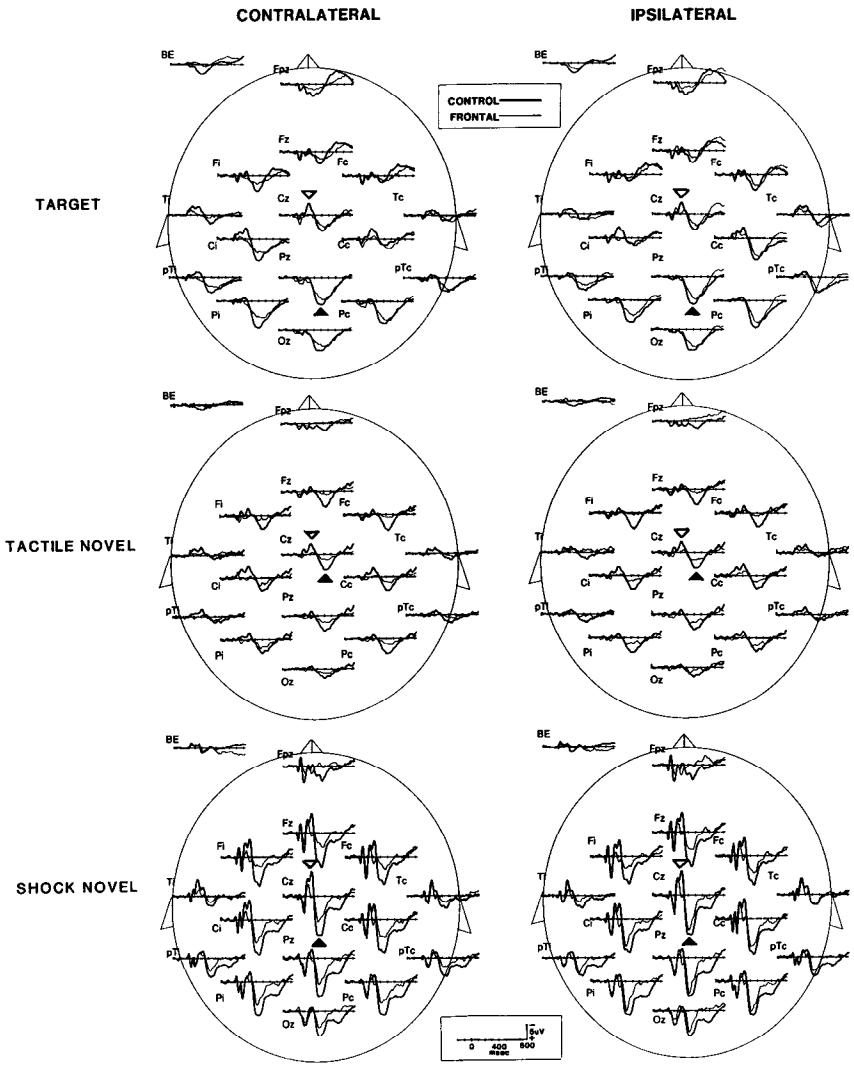


Figure 9. Grand average ERPs for frontal patients generated by target, tactile novel, and shock novel stimuli (same format as Fig. 5).

poral–parietal subjects from the present study were found to have memory deficits manifested by differential problems in short- and long-term priming (Kersteen-Tucker and Knight, 1989). Taken together, these results suggest that the P3 response is dependent on an association cortex and limbic system involved in sustaining and updating a model of the external environment (Donchin, 1979; Fabiani et al., 1986; Tulving and Schacter, 1990).

Parietal lesions

Parietal lesions had restricted effects on the P3. Ipsilateral shock P3, ipsilateral and contralateral target P3, and tactile novelty P3 amplitudes were normal. Thus, substantial portions of lateral parietal cortex do not appear to be necessary for P3 generation. Parietal patients showed P3 amplitude reduction only to contralateral shock stimuli. Dissociation between tactile and shock novelty P3 may be attributed to difference in the stimulus submodality (i.e., tactile and electric shock) because both stimuli had no primary task relevance. It is known that both tactile and electric stimulation excite the same type of peripheral nerve fibers, but that electric stimulation elicits larger primary cortical response in comparison with tactile stimuli (Pratt and Starr, 1981). However, the neural responses to various types of stimuli in the secondary or higher somatosensory cortex have not been examined in humans. The present results suggest that tactile and shock stimulation may be differentially processed in the lateral parietal cortex before being output to the temporal–parietal junction.

Behaviorally, the parietal group had minimal deficits in target detection, with delayed RTs in the order of 100 msec. These changes were not different from those seen in the other patient groups. Thus, the tactile target detection task employed in the present study does not seem to be selectively affected by unilateral parietal lesions. In monkeys, tactile discrimination was severely impaired by bilateral ablation of SII or area 7b but unilateral ablation did not result in consistent impairment (Garcha and Ettlinger, 1978; LaMotte and Mountcastle, 1979; Murray and Mishkin, 1984). Primary sensation was also preserved in the parietal patients. This result is consistent with Corkin's and Pause and co-workers' clinical observation that somatosensory functions such as pressure sensitivity, two-point discrimination, point localization, and position sense were preserved in the patients with extended unilateral parietal cortical removals sparing postcentral gyrus (Corkin and Milner, 1970; Pause et al., 1989). This contrasts with the severe deficits observed in postcentral gyrus–lesioned patients.

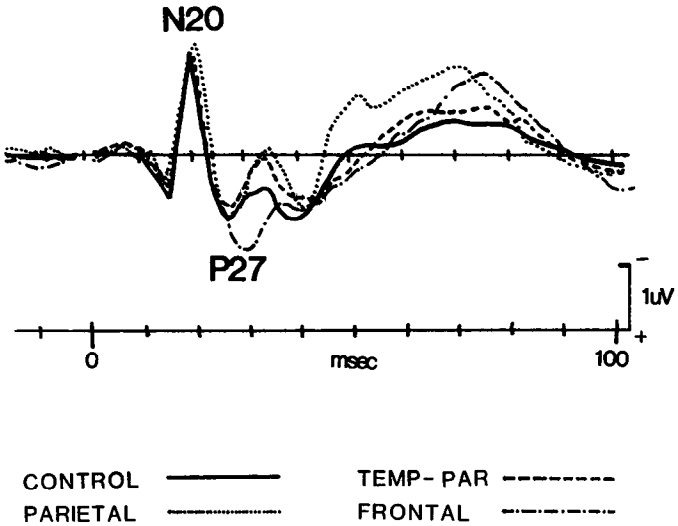


Figure 10. Grand average SEPs for the three patient groups and controls (sum of 500 stimuli; 3-Hz stimulation; wrist shock). *TEMP-PAR,* temporal–parietal groups.

Conversely, several higher-order symptoms have been described in posterior parietal lesions (e.g., Brodmann's areas 7, 39, and 40; Critchley, 1953; Denny-Brown and Chambers, 1958). Similar deficits in the analysis of the spatial relationships of somesthetic and visual stimuli, and difficulty in manual construction and somesthetic recognition of objects, were observed in 71% of our parietal patients.

Frontal lesions

Frontal patients had reduced tactile and shock novelty P3 amplitude for both contralateral and ipsilateral stimulation, while target P3 amplitude was mildly reduced only for contralateral stimulation. None of these reductions were as severe as those observed in the temporal–parietal junction group. The dissociative effects of dorsolateral frontal cortical lesion on target and novelty P3 suggest that the frontal cortex provides differential contribution to these two types of P3. Similar effects were observed in auditory and visual P3 studies of frontal patients (Knight, 1984, in press; Scabini et al., 1989).

The novelty P3 is related to the momentary shift of attention toward an unexpected perturbation in the environment (Ford et al., 1976; Näätänen and Gaillard, 1983). Thus, the novelty P3 deficits in frontal patients support a relative abnormality in automatic attention capacity in this group. Similar deficits in frontal patients have been demonstrated by other electrophysiological measures (Kimble et al., 1965; Luria and Homskaya, 1970).

Frontal patients had decreased target detection accuracy and prolonged RTs for both contralateral and ipsilateral stimuli in the present study. This result contrasts with studies reporting that frontal patients perform normally on simple discrimination tasks (Teuber, 1964, Benson and Stuss, 1982). No such impairments were observed in auditory or visual P3 studies in similar patients (Scabini et al., 1989; Knight, in press).

The somatosensory task employed in the present study requires a precise internal representation of the body schema. Subregions of frontal cortex are proposed to be involved in the processing of representational information about object location in the personal or extrapersonal space (Semmes et al., 1963; Rizzolati et al., 1983; Goldman-Rakic, 1987). Failure to manipulate accurately the representation of the body schema may lead to difficulty in accurate and quick discrimination of stimuli delivered to a part of one's own body and could contribute to the behavioral effects in the present study.

P3 amplitude was more reduced over frontal electrode sites in frontal patients, supporting the hypothesis that part of the scalp P3 may be generated in dorsolateral frontal cortex (Knight, 1984; Wood and McCarthy, 1985). The symmetrical reduction of the novelty P3 by unilateral lesion may be related to the dense transcallosal connections between prefrontal regions (Schwartz and Goldman-Rakic, 1984). Alternatively, dorsolateral frontal cortex could modulate remote P3 generators, resulting in a change of dipole orientation producing alterations in scalp topography.

N2 component

Double dissociations between the N2 and P3 components were observed. The N2 was reduced and the P3 was preserved in some conditions in the parietal group. Conversely, the P3 was abolished and the N2 was preserved for certain conditions in the temporal–parietal group. Because most of the lesioned area in the parietal group was also damaged in the temporal–parietal group, the reason for these dissociations is not apparent. It is conceivable that the "normal N2" in the temporal–parietal group might in part be due to a loss of the P3 component whose onset normally overlaps the N2 component.

The reduction of the N2 response in the frontal and parietal groups with the intact posterior P3 response to correctly detected targets argues against the notion that the discriminative processing reflected in the N2 is critical for P3 generation (Hillyard and Picton, 1987) and indicates that the N2 and P3 are generated by different neural processes.

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