Intracerebral potentials to rare target and distractor auditory and visual stimuli. II. Medial, lateral and posterior temporal lobe

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Abstract

Event-related potentials were recorded from 1221 sites in the medial, lateral and posterior aspects of the temporal lobe in 39 patients. Depth electrodes were implanted for about 4 days in order to localize seizure origin prior to surgical treatment. Subjects received an auditory discrimination task with target and non-target rare stimuli. In some cases, the target, distracting and frequent tones were completely balanced across blocks for pitch and volume. Some subjects also received an analogous visual discrimination task, or auditory tasks in which the rare target event was the omission of a tone, or the repetition of a tone within a series of alternating tones. In some subjects, the same auditory stimuli were delivered but the patient ignored them while reading.

A complex field was recorded, indicating multiple components with overlapping time-courses, task correlates and generators. Two general patterns could be distinguished on the basis of their waveforms, latencies and task correlates. In the temporal pole and some middle temporal, posterior parahippocampal and fusiform gyrus sites, a sharp triphasic negative-positive-negative waveform with peaks at about 220–320–420 msec was usually observed. This wave was of relatively small amplitude and diffuse, and seldom invert. I in polarity. It was multimodal but most prominent to auditory stimuli, appeared to remain when the stimuli were ignored, and w: s not apparent to repeated words and faces. A second broad, often monophasic, waveform peaking at about 380 msec was generated in the hippocampus, a limited region of the superior temporal sulcus, and (by inference) in the anterobasal temporal lobe (possible rhinal cortex). This waveform was of large amplitude, often highly focal, and could invert over short distances. It was equal to visual and auditory stimuli, was greatly diminished when the stimuli were ignored, and was also evoked by repeating words and faces. Preceding this waveform was a non-modality-specific negativity, possibly generated in rhinal cortex, and a visual-specific negativity in inferotemporal cortex.

The early triphasic pattern may embody a diffuse non-specific orienting response that is also reflected in the scalp P3a. The late monophasic pattern may embody the cognitive closure that is also reflected in the scalp P3b or late positive component.

Keywords: P3; N2; Orienting; Generators; Hippocampus; Superior temporal sulcus

1. Introduction

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Ubiquitous across a wide variety of cognitive tasks are 3 generic *components* of the human scalp-recorded evoked potential (EP): a negativity at around 200 msec (the "N2"), followed by a positivity ("P300" or "P3"), and then "slow wave" (SW) (Desmedt 1981; Pritchard et al. 1988; Halgren 1990). While the cognitive correlates of these EP components, as well as their changes with respect to disease and development, have been extensively investigated, their synaptic generators remain controversial.

The *N2b* is evoked by attended and processed stimuli. It has a modality-specific topography, and it has been proposed that it reflects activity in both sensory association and multimodal association cortices (Renault et al. 1982; Näätänen and Picton 1986). In contrast, the *P3* has a widespread scalp topography with no clear modality specificity, consistent with either widespread cortical generators, or a deep generator, or both (Vaughan et al. 1980). The P3 has been further subdivided into a fronto-central P3a relatively enhanced by non-target rare or novel stimuli, and a later parietal P3b enhanced by certainty of target detection (Squires et al. 1975; Snyder and Hillyard 1976). However, the task correlates and scalp topography of P3a and P3b overlap very substantially, posing the question of to what degree this overlap is due to similarities in the scalp projections of the generating structures versus similarities in their task correlates.

Extracerebral mapping of evoked magnetic fields correlated with the scalp P3 have yielded mixed results, indicating an apparent endogenous magnetic field generator in either the medial temporal lobe (MTL; Okada et al. 1983; Lewine et al. 1989), in the association cortex specific to the modality of stimulation (Richer et al. 1983), or in specific sensory association cortex and then the thalamus (Rogers et al. 1991). It must be appreciated that these MEG measurements cannot detect dipoles perpendicular to the scalp (Hari and Lounasmaa 1989). Furthermore, any given extracerebral magnetic field could theoretically have been generated by an infinite number of different brain dipole sets (Nunez 1981). The dipoles "localized" by the above studies were merely the brain locations that best fitted the data, given the assumptions of the model. All of the above studies assumed a single intracerebral dipole, whereas current data (reviewed briefly below) indicate that the P3 is generated in *multiple* regions, each one of which is actually an extensive convoluted dipole sheet.

Animal models of the P3 have also yielded seemingly conflicting results. In cats, lesions of the specific auditory cortex or of the entire association cortex did not significantly affect P3 amplitude, whereas lesions of cholinergic afferents to the cat hippocampus resulted in a long-term severe decrease of the skull "P3" (Buchwald 1990). Furthermore, recording from the cat hippocampus revealed locally generated potentials, polarity-inverting across the pyramidal cell layer (Kaga et al. 1992). Retrograde tracers established that the hippocampal P3 generating areas received cholinergic afferents from the medial septum. This is consistent with pharmacological studies implicating cholinergic synapses in the human P3 (Meador et al. 1988). However, in monkeys, noradrenergic synapses modulate the "P3" (Pineda et al. 1989), and bilateral removal of the hippocampus and surrounding structures fails to significantly reduce the skull "P3" (Paller et al. 1988).

Another method for localizing EP generating structures is to record directly from candidate structures using depth electrodes, implanted in order to define surgical treatment of intractable epilepsy. In contrast to the indirect inferences of generator localization from scalp topography, lesional and pharmacological studies and animal models, direct and definitive localization is possible using human intracranial recording from implanted electrodes. Using depth electrodes, a very large P3b generator has been localized to the hippocampal formation (Halgren et al. 1983, 1986; McCarthy et al. 1989). Across a wide range of tasks, the scalp P3 and the hippocampal P3b have similar cognitive correlates, and similar latency ranges (Stapleton and Halgren 1987; McCarthy et al. 1989). Indirect evidence for local P3 generation is a local decrease of the hippocampal P3b when the hippocampus is damaged (Squires et al. 1983; Wood et al. 1988; Meador et al. 1989; Puce et al. 1989). Local generation is directly implied by the greater P3 amplitude in the hippocampus than in surrounding structures, its steep local voltage gradients and polarity inversions, and the parallel changes observed in hippocampal unit activity (Halgren et al. 1980; McCarthy et al. 1989; Heit et al. 1990). An apparent homolog of the human P3 has been recorded in the hippocampus of monkeys (Paller et al. 1992) and cats (Başar-Eroglu et al. 1991; Kaga et al. 1992).

While depth electrodes thus clearly demonstrate that the hippocampus generates a large P3b, they do not reveal whether these fields passively propagate to the scalp to form a major component of the scalp-recorded P3. Indeed, most studies have failed to find any significant decrement of the P3b after either unilateral anterior temporal lobectomy (which includes most of the hippocampal formation; Wood et al. 1982; Stapleton et al. 1987; Johnson 1988), or even after bilateral hippocampal lesions (Onofrj et al. 1992; Polich and Squire 1993). Significant effects of brain lesions on the scalp N2, P3a and P3b *have* been demonstrated after lesions to the parietal lobe, frontal lobe or temporo-parietal junction, respectively (Knight 1990). However, these effects are predominantly bilateral even though the lesions are unilateral, suggesting that at least part of the decreases could be ascribed to the disruption of necessary neural calculations antecedent to the generator.

Few studies have recorded P3 generators outside of the MTL. Evidence for a diffuse non-specific N2a/P3a/SW generator in cingulate, frontal, lateral temporal and parietal cortices is found in the moderately large potentials and mild voltage gradients recorded in these areas (Alain et al. 1989; Wood and McCarthy 1985; Stapleton and Halgren 1987; Smith et al. 1990). A comparison of the P3 to the slow wave following interictal spikes revealed that within the MTL these potentials have very similar topographies, but that in the lateral temporal lobe the P3 is much larger, suggesting a contribution from a lateral generator (Altafullah et al. 1986). A focal P3 was recorded in one patient using subdural electrodes over the temporal lobe (Neshige and Lüders 1992).

In summary, depth recording supported by other data

clearly demonstrates that a P3 is locally generated in the HC. Furthermore, scalp recording after hippocampal lesions clearly implies the existence of other P3 generators. The location of these generators has been suggested by depth recording outside the MTL, but such recordings have been limited in scope. Since depth electrodes are only implanted in order to localize the epileptogenic zone so as to define subsequent surgical therapy, and inasmuch as the most common form of partial epilepsy (as well as the one with the highest rate of surgical cures) is that arising in the MTL, the most complete investigations of P3 generators have concentrated on that region (Halgren et al. 1986). Since depth electrode recording is ineffective for localizing generators that are distant from the recording contacts, this has significantly limited previous studies. The current study attempts to partially redress this difficulty, by presenting the results of a relatively large number of recordings during a variety of tasks. This paper concentrates on the endogenous potentials evoked by simple stimuli in the temporal lobe, with particular emphasis on recording from multimodal cortex in the superior temporal sulcus, from the limbic and perilimbic structures in the MTL, from lateral and basal occipito-temporal cortices, and from the temporal pole (the results of similar recording in the parietal lobe, superior temporal plane, and frontal lobe are presented in parts I and III of this study: Baudena et al. 1995; Halgren et al. 1995). Evidence was obtained for two distributed systems of N2/P3 generation.

2. Methods

Patients

Adequate recordings were obtained from 39 patients with grossly normal personality and intelligence, suffering from epilepsy that had proved resistant to trials of all appropriate anticonvulsant medications (see Table 1 of Halgren et al. 1995). Electrodes were implanted for 4–14 days in order to localize the sites of seizure onset. While awaiting spontaneous seizure onset, recordings were obtained during cognitive tasks. Selection of patients and sites to implant, as well as the duration of implantation, were made entirely on clinical grounds without reference to the experimental protocol. Cognitive recordings were made only after fully informed consent monitored by the appropriate human subject protection committees.

Electrodes and localization

A total of 1221 posterior sites (284 left hemisphere, 937 right) were recorded, with 145 electrodes (see Fig. 1 of Halgren et al. 1995, for locations). Recording contacts were 2.0 mm in length, and successive contacts were separated by 1.5 mm. Electrodes were localized based upon statistical studies (Talairach et al. 1967), confirmed and refined by stereoscopic stereotaxic angiography (Szikla et al. 1977), as well as stereotaxic MRI in most patients

(Talairach and Tournoux 1988; Musolino et al. 1990). Estimated cytoarchitectonic locations are sometimes indicated (Brodmann 1909). The occipital pole and anterobasal temporal lobe were relatively poorly sampled because electrodes nearly always entered from the lateral surface and followed a trajectory that was perpendicular to the midline. Frequently sampled sites (and their approximate coordinates in the Talairach axes [4]) include: lingual gyrus (Lg: ±20, −58, −4); fusiform gyrus (Fg: ±30, −55, −5); lateral occipito-temporal cortex (OT: ±52, −62,+ 2); posterior parahippocampal gyrus (pHg: ±17, −31, −8); posterior hippocampus (pHC: ±28, −31, −8); anterior hippocampus (aHC: ±27, −16, −18); amygdala (Am: ±25, −5, −18); posterior middle temporal gyrus (±55, −25, −10); anterior middle temporal gyrus (±56, −5, −18); temporal pole (TP: ±35,+ 10, −30). For analysis, electrodes passing through the middle temporal gyrus (MT) were divided into the following 6 anterior-to-posterior groups: TP, 5–15 mm (mean 8.7 mm) anterior to the anterior commissure line (CA: 7 electrodes); MTa, 1–9 mm (mean 5.4 mm) posterior to CA (37 electrodes); MTb, 1–17 mm (mean 7.4 mm) anterior to the posterior commissure line (CP: 36 electrodes); MTc, 1–14 mm (mean 7.4 mm) posterior to CP (39 electrodes); MTd, 17–35 mm (mean 25.4 mm) behind CP (15 electrodes); and OT, 36–53 mm (mean 40.9 mm) behind CP (8 electrodes).

Recording, averaging and analysis

Bandpass was 0.1–35 Hz. Simultaneous recordings were made from 29 to 105 depth contacts, 0–5 EEG electrodes including one placed approximately at CPz, and a vertical EOG derivation. All recordings were referenced to the tip of the nose. In some patients, additional contacts were recorded in a subsequent session. Waveforms were digitized every 6 msec at 12-bit accuracy for 1200 msec beginning 100 msec before stimulus onset. Trials were rejected if they were contaminated by eye movements, by epileptiform EEG spikes, or by other large transients (detected on amplitude criteria set individually for each patient's data). Qualitative analysis consisted of identifying regions with steep voltage gradients that changed over short distances, indicative of local generation. Quantitative analysis was based on peak measurements in those sites that displayed clearly identifiable components. If there were multiple contacts within a single structure in a given patient, then the contact with the largest amplitude EPs was chosen for measurement.

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[4] Throughout the text, electrode contact location is indicated in relation to the axes defined by the Talairach system using the format "(x, y, z)" where: (x) lateral, mm to midline, positive right hemisphere; (y) antero-posterior, mm to the CA line, positive anterior; (z) vertical, mm to the CA-CP line, positive dorsal (up).

Behavioral tasks

In all tasks, the patient responded to rare target stimuli by incrementing a silent count and by pressing a microswitch in the dominant hand. Frequent and in some tasks non-target (but rare) distracting stimuli were also presented, but required no response. In all auditory tasks, a 48 msec sound was presented at a comfortable level (about 65 dB SPL) binaurally through a speaker located 2 m behind the patient's head. All stimuli except distractors in AD were sine wave tones and were enveloped with a 12 msec rise and 12 msec fall. Amplitude was constant for all stimuli.

The basic task (performed by 28 patients) was a typical *auditory oddball task with distractors* (AD). The sounds, occurring every 1600 msec, were either *target* (11% of trials), *frequent* (78%) or *distractor* (11%), presented in random order except that at least two frequents occurred after each target or distractor. The target stimuli were tones ascending from 700 to 1000 Hz. The frequent stimuli were tones at a constant pitch of 670 Hz. Each distracting stimulus was unique, with varying waveshape, pitch and envelope.

In *auditory oddball task with distractors – cyclic* (AC 17 patients), *target* (13% of trials), *frequent* (74%), or *distractor* (13%) tones were presented every 1450 msec in psuedo-random order, with the pitch of the stimuli rotating between blocks so that the number of tones of each pitch was equal for each of the 3 behavioral categories (target, frequent or distract). In *high-low* (HL), the same high, medium and low pitched tones were presented as in AC, but every 800 msec and in an alternating order (13 patients). Rare target tones were those which were a repeat of the immediately preceding tone (and thus constituted rare breaks in the regular alternation). Again, the number of tones of each pitch was equal for each of the two behavioral categories (target and frequent). In *omitted* (OM), only 1000 Hz tones were presented, every 800 msec (15 patients). Rare targets were occasional omissions of tones from the series. In *visual oddball with distractors* (VD), single letters or symbols subtending 0.43° of visual angle were presented in white on a video monitor for 200 msec every 1600 msec (14 patients). Target stimuli were the symbol " ∗," frequents were an "O" (or an "x" in patients after patient no. 12), and distractors were capital letters. Between stimuli, fixation was maintained on a central " +." Finally, 6 patients were presented with the same stimulus train as was presented in one of the auditory paradigms (2 AC and 3 HL), but while reading a book and instructed to ignore the tones. The distribution of tasks across patients is shown in Table 1 of Halgren et al. (1995).

Results

Behavioral performance

Subjects detected correctly 93 ± 9% of the target tones in AD with a reaction time of 508 ± 98 msec, and 91 ±

10% of the target tones in AC with a reaction time of 513 ± 93 msec. False detections were less than 5% in all cases.

General patterns of responses

Behavioral identification of endogenous potentials. Operationally, endogenous potentials were identified as those that were evoked by rare target and/or distractor stimuli, but not by the frequent stimuli. In AD, target, distractor and frequent stimuli were approximately matched on sensory variables, thus differential responses would probably reflect non-sensory effects. This inference could be confirmed in most patients by observing the same components evoked either by auditory stimuli when the 3 types of stimuli were exactly matched on all sensory characteristics (AC and HL tasks), by visual stimuli (VD task), and/or by the absence of an expected stimulus (OM task). In all these cases, the frequent stimuli were attended and processed; thus the differential responses to rare stimuli must reflect an additional process evoked by these distinctive stimuli. Since no overt or covert response was required to the non-target distractors, any potential occurring to non-target as well as to target rare stimuli could not be due to a process that is motor in any simple sense.

N2a / P3a / SW. Visual inspection revealed two distinct waveforms. The most common was triphasic (usually negative-positive-negative) and sharply peaked. This was observed both medially and laterally in the temporal lobe, for example in: MT (Fig. 5-C58; Fig. 9-left 58, right 49) [5], posterior inferior temporal gyrus (Fig. 7-X57), and pHg (Fig. 10-0). Across 6 temporal structures (TP, MTc, MTd, OT, pHg and Fg), the average latency of the 3 peaks was 221–324–465 msec to targets, and 204–300–425 msec to distractor stimuli. Simultaneous recording from the scalp at CPz also revealed a negative-positive-negative waveform commonly labeled N2-P3-SW, with average latencies of 244–359–493 msec to targets, and 214–313–462 msec to distractor stimuli. Given its relatively short latency, as well as its task correlates (see below), the triphasic depth waveform was labeled the depth N2a/P3a/SW [6].

The latency of the CPz-P3 was found to be significantly longer than that of the P3a recorded in MTc, MTd and pHg (Fg and OT had too few measures to allow statistical testing: see Tables 1 and 2). An early N2a/P3a was observed also in MTa and MTb, and the P3a in MTb had a

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[5] Note that in the text, figure numbers are followed by the electrode letter (omitted if only one electrode is displayed in the figure), followed by a prime if the electrode is in the left hemisphere, and then the distance in mm from the center of the contact to the interhemispheric plane.

[6] It must be emphasized that we do not wish to imply that the scalp N2a/P3a/SW or the scalp P3b is generated entirely or in part by the depth potentials with the corresponding appellations. Yet the "familial" or "generic" resemblance of the scalp and depth components are undeniable, and so they merit similar names, without asserting an absolute identity.

Table 1
Average latency and amplitude of lateral temporal potentials to target and distractor tones

		TP		MTa		MTb			MTc		MT2		OT	
		T	D	T	D	T	D		T	D	T	D	T	D
N2	Lat	226	218	223	212	213	204	N2	212	204	220	194	220	202
	Amp	-42	-41	-14	-18	-18	-13		-15	-34	-21	-31	-21	-38
	N	8	8	14	13	10	9		15	12	15	16	5	5
P3a [a,b]	Lat	336	328	300	294	+++308	+287	"P3+"	+++295	+++264***	+++296	+282 ns	364	291
	Amp	33	24	52	41	68	60		52	36	43	25	48	53
	N	6	6	6	6	10	7		13	11	13	14	4	4
P3b [a,b]	Lat			ns 380	++ 352*	ns 375	+ 356***	"P3−"	380	330	301	271		
	Amp			48	38	49	46		-55	-69	-90	-96		
	N			12	10	9	7		3	3	2	2		
SW	Lat	463	417	521	488	513	487	SW	414	397	438	405	567	467
	Amp	-42	-52	-16	-15	-29	-37		-34	-40	-20	-27	-36	-25
	N	7	7	8	8	9	8		13	12	14	15	3	3

Please see list of abbreviations for anatomical sites. P3+ = positive potential measured at P3 latency; P3− = negative potential measured at P3 latency; Lat = latency; Amp = amplitude; N = number of observations; T = target stimuli; D = distractor stimuli.

[a] Plusses before the numbers indicate a significantly different latency in the depth site as compared to CPz (2-tailed group t test, performed if N > 6).
+ $P < 0.05$; ++ $P < 0.01$; +++ $P < 0.001$; ns = not significant.
[b] Stars after the numbers indicate a significantly shorter P3a latency to rare distractors (D) as compared to rare targets (T) (1-tailed paired t test, performed if N > 6).
* $P < 0.025$; *** $P < 0.001$; ns = not significant.

Table 2
Medial temporal potentials to tones

		Lg		Fg		pHg			pHC		aHC			Am	
		T	D	T	D	T	D		T	D	T	D		T	D
N2	Lat	217	211	227	203	221	203	N2	251	234	263	239	N2	236	212
	Amp	-18	-9	-35	-30	-24	-29		-38	-44	-67	-68		-45	-65
	N	4	4	5	6	12	12		11	11	9	9		20	20
P3 [a,b]	Lat	294	271	335	341	++316	+293 *	P3	ns386	ns357 ns	+394	++367 ns	P3+	++401	++361 ***
	Amp	16	20	35	40	20	8		-97	-75	-151	-106		60	29
	N	4	3	5	6	13	13		8	8	9	9		13	12
SW	Lat	401	377	432	455	478	410	SW1	532	481	509	487	P3-	382	330
	Amp	-11	-7	-16	-21	-30	-25		-77	42	-109	-78		-37	-74
	N	3	3	4	5	10	10		6	6	7	7		7	7
	Lat							SW2			742	689	SW	558	480
	Amp										61	61		-34	-53
	N										3	3		9	9

Please see list of abbreviations for anatomical sites. P3 + = positive potential measured at P3 latency; P3 − = negative potential measured at P3 latency; Lat = latency; Amp = amplitude; N = number of observations; T = targets; D = distractors.

[a] Plusses before the numbers indicate a significantly different latency in the depth site as compared to CPz (2-tailed group t test, performed if N > 6).
+ $P < 0.05$; ++ $P < 0.01$; ns = not significant.

[b] Stars after the numbers indicate a significantly shorter P3a latency to rare distractors (D) as compared to rare targets (T) (1-tailed paired t test, performed if N > 6).
* $P < 0.05$; *** $P < 0.001$; ns = not significant.

shorter latency than at the scalp, but the following SW occurred much later, possibly because of another positivity following the P3a.

In most trajectories, no polarity inversions were observed (see below for exceptions). However, in many cases, the N2a/P3a/SW was larger both medially and laterally than in intermediate sites. Generally, the N2a/P3a/SW was less clear in the temporal lobe than has been observed in the parietal or frontal lobes, presumably due to overlap with the N2/P3b pattern described below.

N2b/P3b. The second pattern recorded was a large, primarily monophasic waveform. This potential tended to be very focal, with steep voltage gradients and common inversions. Consistent with previous studies, this pattern was prominent in the hippocampus (Fig. 8-28; Fig. 9-left 26, right 35; Fig. 10-14; Fig. 11-B32). However, it also occurred in recordings from MT near the superior temporal sulcus (sTs: Fig. 1-B64, T60; Fig. 2-65; Fig. 3-44). In addition, it occurred in Am and TP with characteristics suggesting a basal temporal generator. The average latency of this potential was 394 msec to targets and 367 msec to distractor stimuli in aHC, significantly later than that measured at CPz (Table 2). This potential was termed P3b[6]. The amplitudes of the P3 to targets versus distractors were
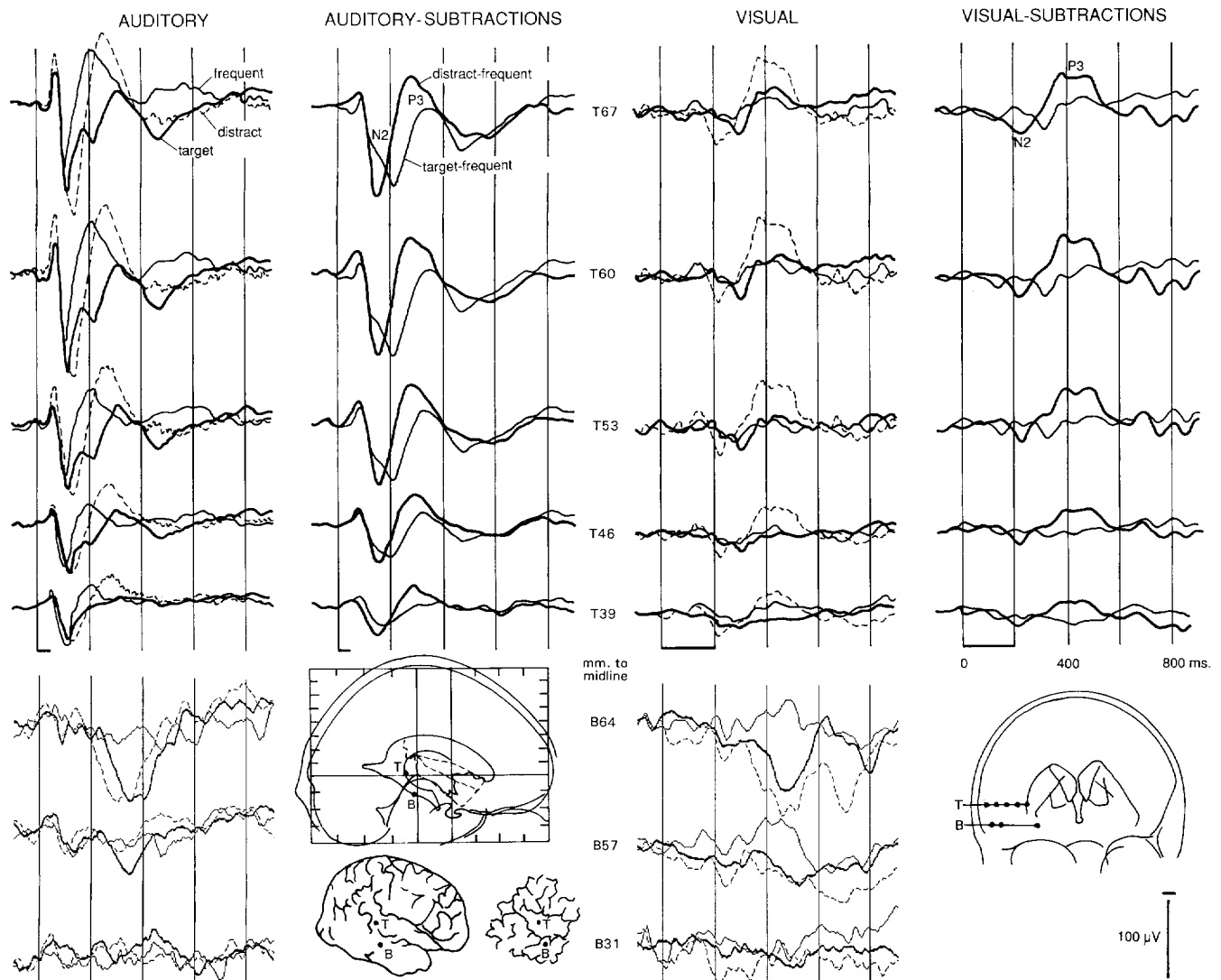
Fig. 1. Large inverted N2/P3 in the superior temporal sulcus to rare target and non-target stimuli in both the auditory and visual modalities. The activity from two electrodes is illustrated: T (upper traces) in the upper bank of the sulcus, and B about 10 mm inferior and anterior to T, in the lower bank of the sTs (see the sagittal MRI tracings at two lateral distances from the midline below). Due to the position of electrode T beneath Heschl's gyrus, the inverted N2/P3 is superimposed on large exogenous potentials in the auditory oddball task, where subtractions (second column) are needed to reveal large potentials in the latency range of the scalp N2/P3 to rare stimuli, but with inverted polarity. A similar P3 but smaller N2 is evoked by distractor visual stimuli (third column), where subtractions (fourth column) are not necessary because the exogenous potentials are much smaller. The N2/P3 in T and B do not polarity invert but grow smaller as the sulcus is penetrated (see the lower sites – the mm from the recording site to the midline is indicated by the numbers between columns 3 and 4). However, an inversion of polarity is observed for both the auditory and visual P3s between electrodes T and B, i.e., across the sTs. Pt. no. 6.
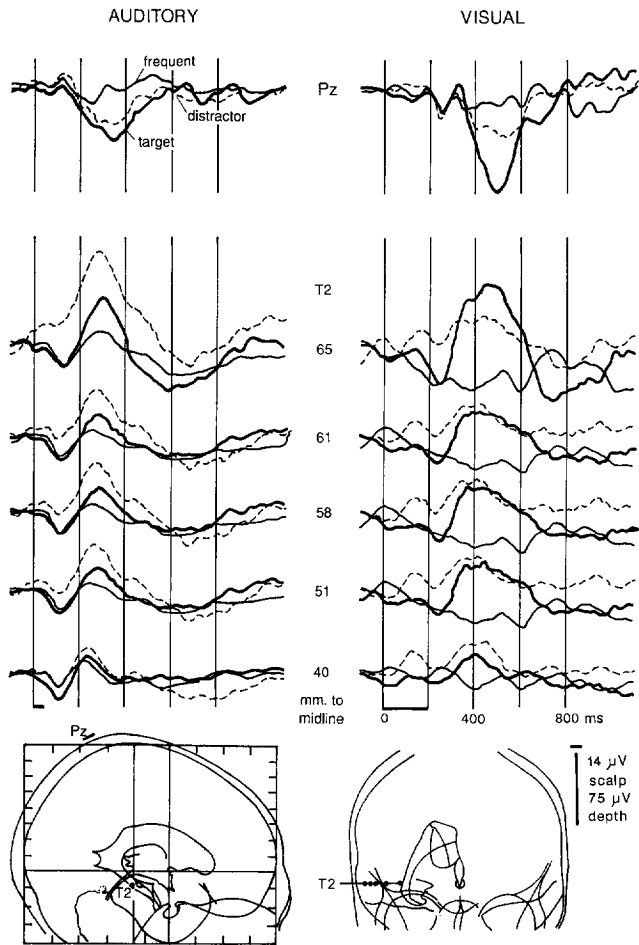
AUDITORY   VISUAL

Fig. 2. Possible large inverted P3 near the superior temporal sulcus. A large (− 90 μV) somewhat focal inverted P3-like potential recorded from the middle temporal gyrus (MT) just inferior to the sTs during auditory and visual oddball tasks. This potential is largest at the most lateral lead (65 mm to midline) and has about the same latency as the simultaneously recorded P3 at the scalp (Pz). Pt. no. 22.

compared using a paired t test, but were not found to be significantly different at any site (P (2-tailed) > 0.05).

Lateral temporal neocortex: superior temporal sulcus, middle and inferior temporal gyri

EPs in this region were sampled mainly by electrodes that entered different antero-posterior levels of MT from the lateral surface and were perpendicular to the interhemispheric plane, thus passing in the white matter just inferior
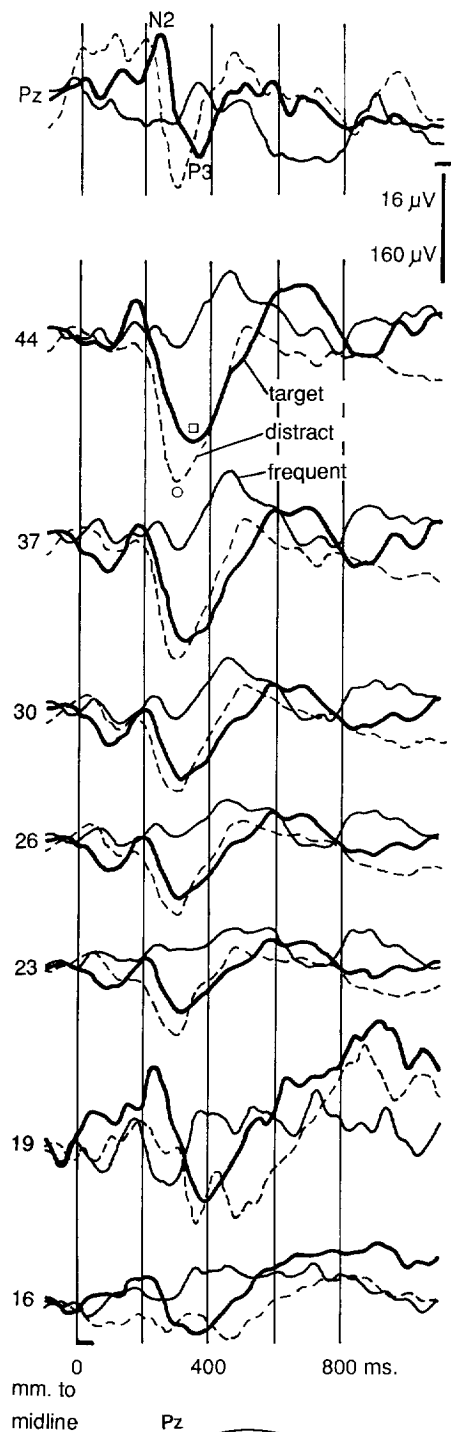
Fig. 3. Large lateral temporal P3. A large (+ 150 μV) somewhat focal P3 is evoked by rare auditory stimuli (□ to targets, ○ to distractors) in the most superficial leads (44 and 37 mm to midline) of an electrode penetrating the middle temporal gyrus just below the sTs. A small (+ 60 μV) P3 is evoked in a medial lead (19 mm) located beneath the HC, where a focal (− 85 μV) N2 is also observed. The P3 is smallest in the white matter between lateral and medial recording contacts. AD task. Pt. no. 23.
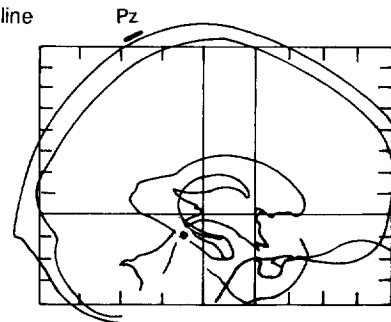
to sTs. Occasionally, the electrode passed through the gray matter of the sulcus or one of its branches, or superior to the sulcus in the white matter of the superior temporal gyrus (passage through the fundus itself is not possible because of the presence of a blood vessel). The sites are labeled, from anterior to posterior, TP, MTa, MTb, MTc, MTd, and OT (see Methods for anatomical localizations).

Large (up to 150 μV) P3b-like potentials were recorded from a minority of the electrodes in zones MTa, MTb, MTc and MTd. The critical region appeared to be in the vicinity of the sTs centered about 6 cm posterior to the tip of the temporal lobe. These potentials could be of either negative polarity, especially in MTc or MTd (Fig. 1-T60; Fig. 2-65; Fig. 4-50) or positive polarity, especially in MTa or MTb (Fig. 1-B64; Fig. 3-44; Fig. 4-40 and Table 1). In one patient the sTs-P3 appeared to polarity invert with increasing depth in an electrode as it passed through the lower bank of sTs, near its fundus (Fig. 4). In another patient, a clear polarity inversion was observed between two electrodes separated by 10 mm and on opposite sides of the sulcus (Fig. 1). The latency of the sTs-P3 was generally somewhat longer than that observed for the scalp P3 at CPz (Table 1) and thus could be similar to the P3b-like activity recorded simultaneously from the hippocampus. The sTs-P3 could be distinguished from endogenous potentials simultaneously recorded in the superior temporal plane by latency as well as task correlates: the sTs-P3 was evoked by rare stimuli in both the visual and auditory modalities (Figs. 1 and 2). In addition, the sTs-P3 was evoked by both target and distractor stimuli (Figs. 1, 2, 3 and 4), as well as by repeated words and faces (Halgren et al. 1994). In two cases, P3b-like activity recorded near sTs was found to be abolished when the subject was ignoring the stimuli.

In addition to this large focal response, a smaller triphasic negative-positive-negative waveform was recorded at multiple antero-posterior levels of the sTs (Fig. 5-C58 and

Fig. 7-X54). In some recordings, this was a typical N2/P3a/SW sequence, as is seen in parietal and frontal sites, but in others, the waveform was atypical, presumably reflecting superimposed P3b activity. This potential could
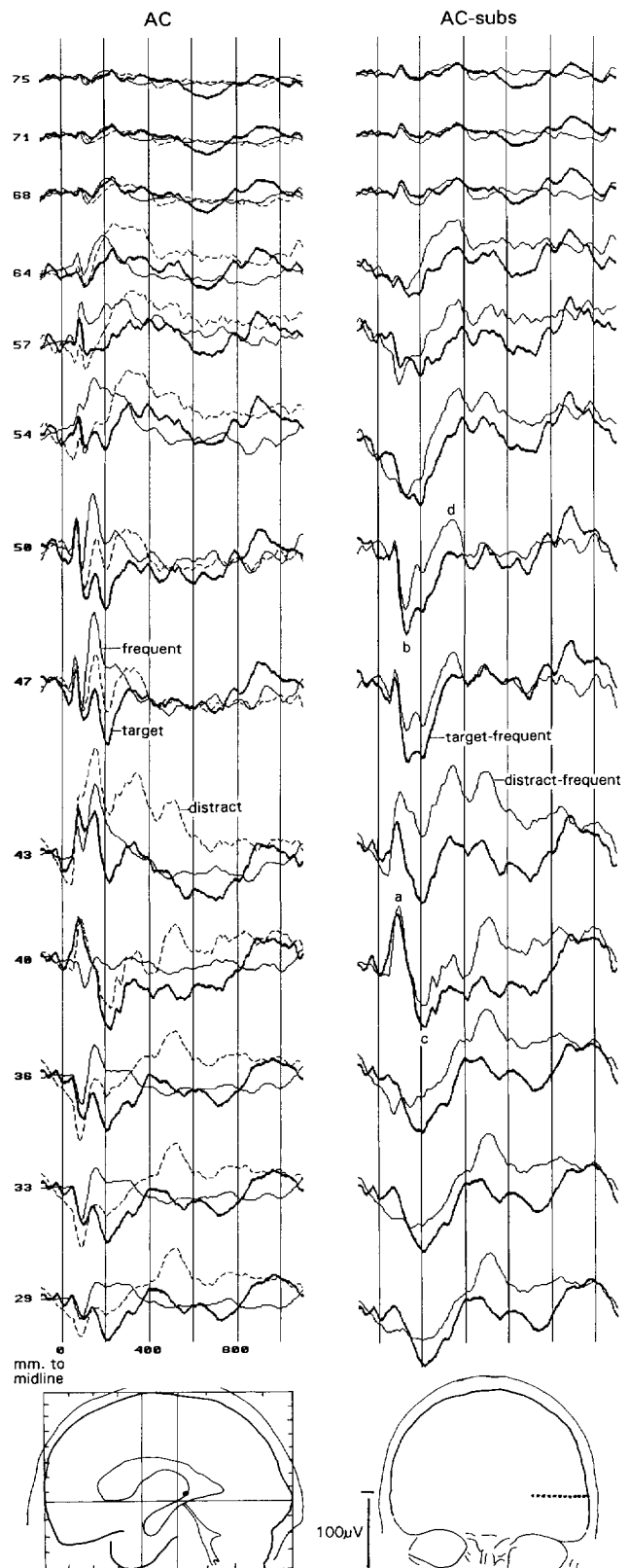

Fig. 4. Focal early endogenous potential in the superior temporal sulcus. Recordings made during AC from an electrode that passed through the middle temporal gyrus just inferior to the sTs. According to MRI, the contact at 47 mm to midline was located in the cortex of the lower bank of the sTs, about 5 mm lateral to its fundus. In the subtraction waveforms (right column), at least 4 components with clearly different latencies and topographies can be observed (a, b, c, d). At about the level where the electrode passes the fundus, the early potentials at 95 (a) and 110 msec (b) evoked by rare target and distractor stimuli change rapidly in amplitude over a short distance. It is possible to interpret this change as an inversion in polarity from positive medially (29, 33 and 36 mm to midline), to negative (a: 40 and 43), and again to positive (b: 47, 50, 57, and 64) in the most lateral leads. Note that the potentials evoked by frequent tones in the same latency range invert polarity at entirely different mediolateral levels. Note also that the later potentials to rare tones (c at 205 msec, and d at 350 msec) show substantial voltage gradients, and the later potential (d) may even change polarity over this trajectory. Pt. no. 31.
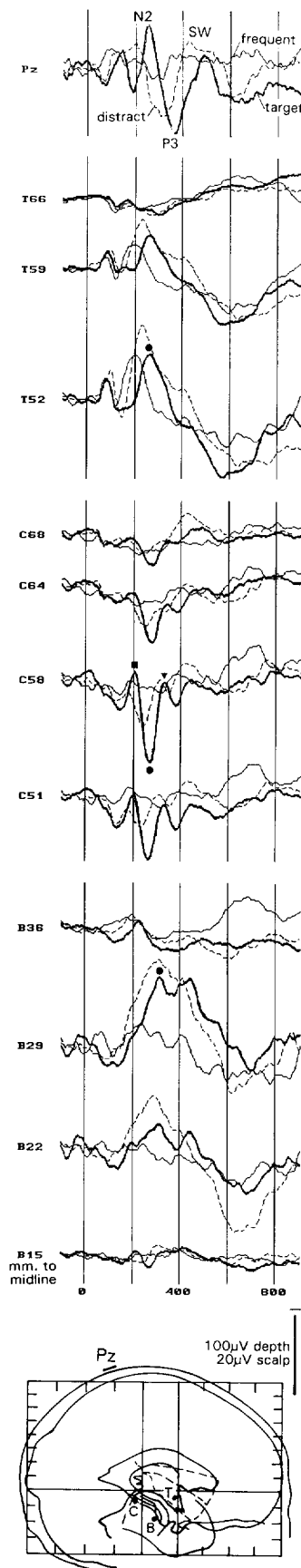
be up to 100 μV in amplitude and often showed steep voltage gradients. It was evoked by rare target and distractor visual and especially by rare auditory stimuli, but little or not at all by repeated words or faces (Halgren et al. 1994). These peaks resembled the scalp N2a/P3a/SW, but often occurred about 60 msec earlier than the peaks at the scalp (CPz). This pattern could be observed even in more posterior middle and inferior temporal gyrus sites, at the lateral occipito-temporal junction (Fig. 6-42 and Fig. 7-X54). At these sites, the N2a/P3a/SW sequence may be preceded by a positivity at about 100 msec, similar to that recorded by electrodes penetrating the superior temporal gyrus at the same antero-posterior level (Fig. 6-42 and Fig. 7-X54; see also Halgren et al. 1995). In one subject, the P3a underwent a double polarity inversion in the vicinity of the sulcus separating the inferior temporal and fusiform gyri (Fig. 7-D'36). Focal large (about 100 μV) N2s may occur in this region, either specific to the visual modality (Fig. 6-42), or non-specific, being also evoked by auditory stimuli (Fig. 7-X36, D'40).

Medial temporal lobe

Hippocampal formation. As previously reported, very large (up to 300 μV in amplitude) polarity inverted P3bs were commonly observed in the hippocampus (Table 2, Figs. 5, 8, 10 and 11). In contrast to the sharp depth P3a, which was 50–70 msec in duration, the HC-P3b was very broad, 300–500 msec in duration. It was approximately equal in amplitude but clearly longer in latency to visual stimuli (Figs. 8 and 9).

The HC-P3b was greatly decreased or abolished when the stimuli were ignored (Fig. 11-B32; see also Fig. 12 of Halgren et al. 1995), as reported previously (Stapleton and Halgren 1987). This observation was replicated in all 5 subjects in which large hippocampal P3bs were recorded in the attend condition: in all cases the HC-P3b was not detectable in the ignore condition (3 subjects received the HL paradigm, and 2 subjects AC).

The peak latency of the HC-P3b (Table 2: 394 msec to targets; 367 msec to distractors in aHC) was significantly

Fig. 5. Distinct potentials recorded during the scalp N2/P3, near the superior temporal sulcus (electrode C), in the superior temporal plane (T), and anterior hippocampus (B). The potential overlapping in latency with the scalp N2/P3 is negative, large, of long duration, monophasic and late in the HC (●, lead B29, 29 mm to midline). Just inferior to the sTs (maximum in C58), a triphasic sharp negative-positive-negative waveform (■ – ● – ▼, termed N2a/P3a/SW) is recorded. The principal potential in the superior temporal plane (●, T52) is negative at the latency slightly later than that of the scalp N2. Small polarity inversions are seen in the superior temporal plane (to lead T66) and HC (to lead B36), but not in the sTs. Note that although these recordings are simultaneous, the waveforms as well as the relative responsiveness to targets versus distractors vary substantially between different sites. In all sites, the response is earlier to distractors than to targets. Pt. no. 9, AD task.
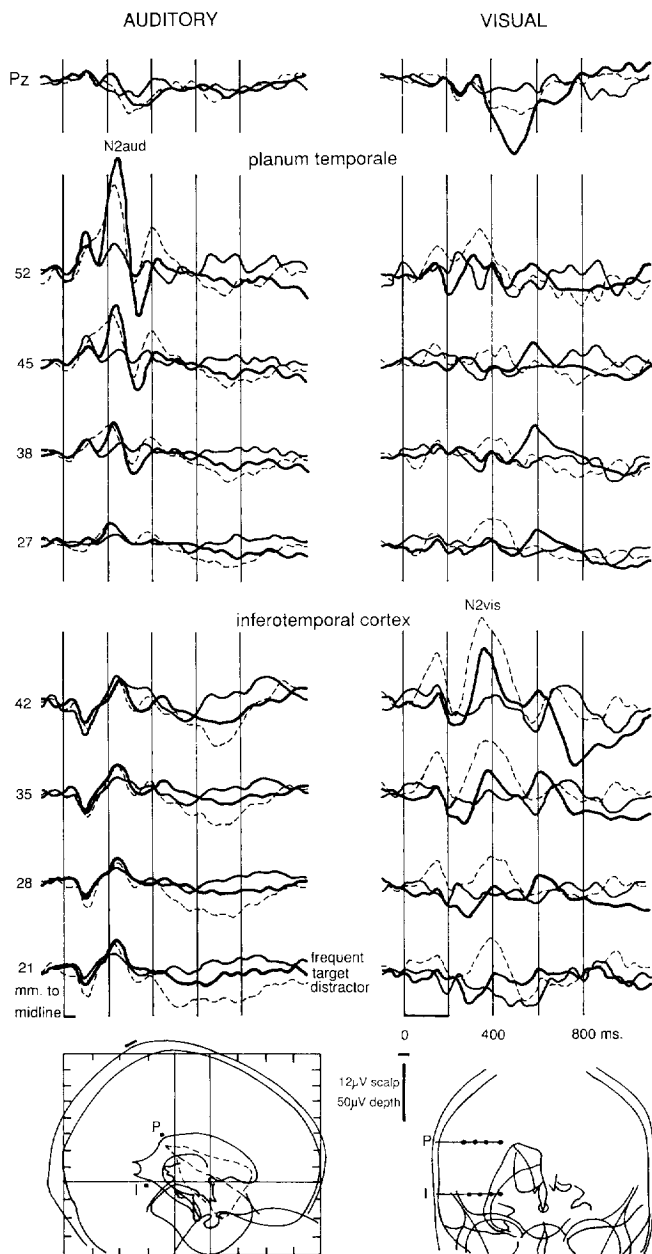
Fig. 6. Modality-specific N2s generated in the supramarginal gyrus to rare auditory targets and distractors, and in the infero-temporal cortex to rare visual stimuli. Simultaneous recordings from the sMg in the posterior bank of the ascending ramus of the Sylvian fissure (planum temporale, upper trace) and from the infero-temporal cortex (lower traces) during the AD tasks show a large N2$_{aud}$ localized to the sMg. Conversely, recordings from the same leads during VD show a large N2$_{vis}$ in the lateral infero-temporal cortex but not sMg, at about the same latency as the scalp N2. Note also that the potential at about 100 msec to auditory stimuli is negative in the sMg (upper) and positive in the infero-temporal cortex (lower), whereas the potential at about 140 msec to visual stimuli appears to be negative in both places. Pt. no. 22.

longer than that of the scalp CPz-P3. However, this latency difference (35 msec for targets, 54 msec for distractors) was very small compared to the long duration of the

HC-P3b, and thus the scalp and depth potentials overlapped nearly completely.

The inverted HC-P3b occurred in both pHC (Fig. 8-28 and Fig. 10-14) and aHC (Fig. 5-B29; Fig. 9-L26, R35; Fig. 11-B32). Consistent with the much greater size of the anterior as compared with the posterior hippocampus (Talairach et al. 1967; Duvernoy 1988; Amaral and Insausti 1990), the inverted P3 was present over a greater mediolateral distance in anterior placements (commonly 14–17 mm: Fig. 9). Immediately medial and lateral to the hippocampus, the P3 was much smaller and often positive (Figs. 5, 8, 9 and 11).

In one patient, vertical recording electrodes also demonstrated that the P3 is small and positive above and below the hippocampus (Fig. 10). The recordings illustrated in Fig. 10 were obtained from depth electrodes that had been implanted after surgical removal of the posterior part of the right inferior parietal lobule and the most posterior parts of the superior temporal gyrus. Thus, these recordings demonstrate that the HC-P3 is not dependent on the integrity of these temporo-parietal structures. In another patient, an electrode passing inferior to the middle hippocampus recorded a moderately large $(-85/+60\ \mu V)$ and focal N2/P3 sequence, where the P3 was polarity inverted from that habitually found in the hippocampus (Fig. 3-19). Small negative-positive-negative sequences resembling the N2a/P3a/SW were not only seen underneath the posterior hippocampus (Fig. 10-0, 7), but also medial to the hippocampus, in the anterior parahippocampal gyrus (Fig. 5-B15). The average latency of the P3a in the pHg (Table 2) was significantly shorter than that recorded at the scalp and was comparable to that observed in sMg and pCg. Similar potentials were observed in the lingual gyrus (which is the posterior extension of the pHg), as well as in the adjacent Fg (Table 2). These potentials were usually small and without significant voltage gradients (Fig. 6).

In addition to the P3b, other components were measured in the hippocampus, including an earlier negativity at about 250 msec latency ("HC-N2"), a following negativity at about 500 msec ("HC-SW1"), and finally, a positivity at about 700 msec ("HC-SW2"; Table 2). While the HC-N2, P3b and SW1 tended to merge into each other in most recordings, they could sometimes be distinguished as inflections in the broad negativity (mainly HC-SW1; Fig. 5-B22), or even as differential inversions (HC-N2; Fig. 11-B32). In addition, the HC-SW1 was often relatively smaller to distractors as compared to targets (Table 2, Fig. 5-B29 and Fig. 10-14).

Amygdala. Multiple components were also observed in Am, beginning with a rather large negativity at a latency of 236 msec to targets and 216 msec to distracts (termed "Am-N2") followed by a usually positive peak at 401 msec to targets and 361 msec to distracts termed "Am-P3" (Table 2). This potential had about the same latency as the large negativity in the adjacent aHC and was thus about 45
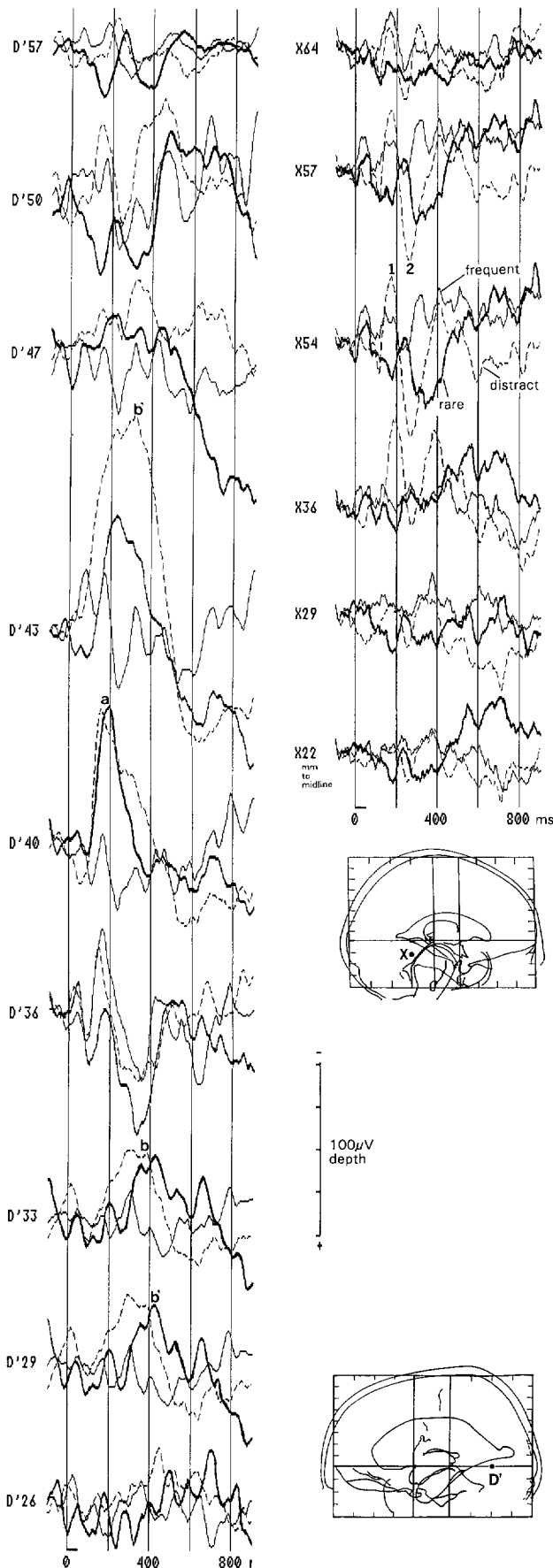
msec later than at CPz. In several patients, the potential in Am remained negative in this time period ("P3 – " in Table 2). Again, following the Am-P3, a negative slow wave peaking at about 520 msec was recorded. None of these components was observed to definitely polarity invert over a given electrode track. Nonetheless, the large size, steep voltage gradients and much smaller potentials recorded both medially and laterally all imply local generation in an immediately adjacent structure.

4. Discussion

Multiple systems activated

The waveforms recorded in the current study could generally be classified into two broad anatomo-physiological patterns of activity evoked by rare target and distractor stimuli. The first was a sharp triphasic short-latency sequence that resembles the scalp N2/P3a/SW. This waveform was observed in all recorded neocortical areas and was most often focal or large in the anterior or posterior middle temporal gyrus, posterior parahippocampal gyrus and fusiform gyrus. The second pattern was a broad, usually monophasic, relatively long-latency, waveform that resembled the scalp P3b. It was localized to the hippocampus, to a part of the superior temporal sulcus, and by inference to rhinal cortex underlying the amygdala.

N2a / P3a / SW

Charcteristics. A characteristic sharp negative-positive-negative waveform was evoked by rare stimuli in several cortical areas distinct from the well-established MTL limbic P3 generators. Although polarity inversions were only very rarely observed, local generation was strongly suggested in many locations by the locally steep voltage gradients. In this study, the triphasic waveform was found in TP, as well as some pHg, Fg and MT sites (with polarity inversion in one subject in Fg). In companion studies, similar potentials were found to be generated in supramarginal and posterior cingulate gyri (Halgren et al. 1995), as well as in multiple frontal sites, including the anterior cingulate gyrus, gyrus rectus and dorsolateral prefrontal cortex (area 46, near the junction of the inferior and

Fig. 7. N2/P3a/SW in posterior infero-temporal cortex. In the left column (pt. no. 25), a large N200-P320 (a, b) to rare target and distractor tones (AD task) is recorded in the left basal occipito-temporal cortex (D'40), near the sulcus between the inferior temporal and fusiform gyri. The P320 potential polarity inverts to negative at the immediately lateral (D'43) and medial (D'33, D'29) contacts. In the right column (pt. no. 4), a large, somewhat focal N180-P280-N400 (1–2) is evoked by rare distractors in posterior lateral infero-temporal cortex (X54, X57), and a triphasic sequence is evoked at a longer latency (250–300–480 msec) by rare target tones in the same sites (AD task).
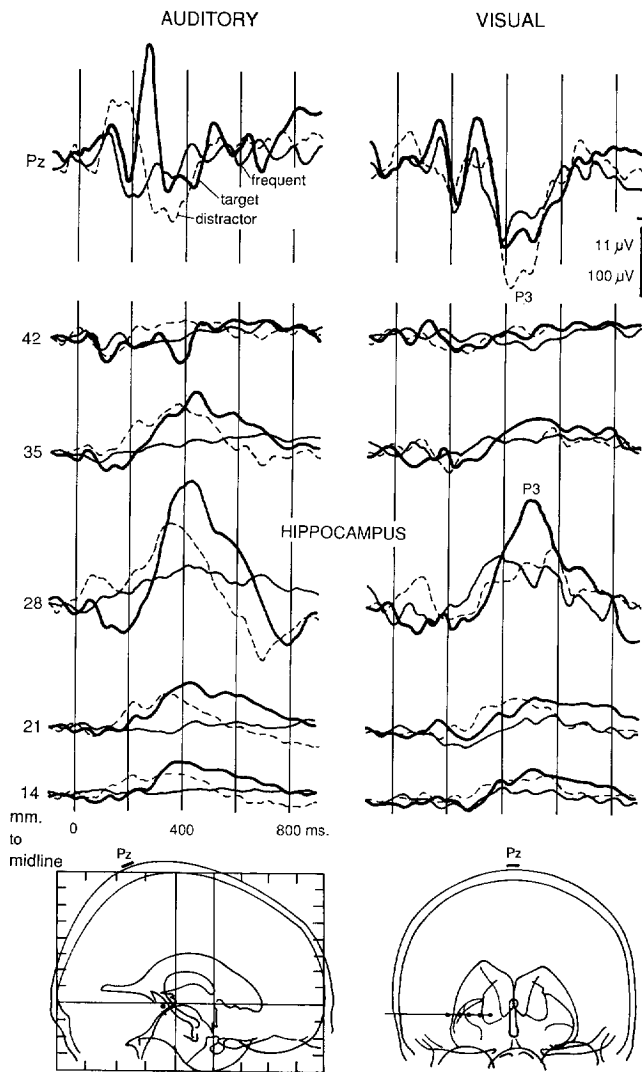
Fig. 8. Mediolateral topography of the P3b in the posterior hippocampus. A large (−160 μV) P3 is recorded in the posterior HC (28 mm from midline), but not in more medial (21 or 14) or lateral (35 or 42) leads. The HC-P3b is later to rare visual as compared to rare auditory stimuli, and in both cases is later than the scalp P3. AD and VD tasks. Pt. no. 10.

component of the orienting complex (for complete discussion see Halgren and Marinkovic 1993; Halgren et al. 1995). This interpretation is consistent with the autonomic correlates of the scalp P3a in the same task (Marinkovic and Halgren, in preparation), as well as the fact that the parietal-cingulate-frontal structures where the N2a/P3a/SW is most prominent are the same areas that have been hypothesized to constitute the cerebral network for the orientation of attention (Mesulam 1990).

Generators. The temporal lobe sites where the N2a/P3a/SW was recorded in the current study may be related to 3 parieto-frontal circuits concerned with the orientation of attention. The subicular complex in the pHg has strong bidirectional connections with the posterior cingulate gyrus (Rosene and Van Hoesen 1977) and contains cells that (at least in rats) fire in relation to head orientation (Taube et al. 1990). TP is also a complex region anatomically, including paralimbic cortex that is interrelated with the postero-medial frontal cortex (gyrus rectus) via the uncinate fasciculus (Amaral et al. 1992). Thus, the pHg and TP may complete a juxtalimbic cortical circuit with the anterior and posterior cingulate cortices.

The pHg also includes cortical area TF/TH (Amaral and Insausti 1990), a multimodal area bidirectionally connected to virtually all association cortex regions (Van Hoesen 1982). As discussed below, the MT recordings probably represent activity generated in the sTs. In primates, cells deep in the sTs are connected with auditory, visual and somesthetic association areas (Seltzer and Pandya 1978) and have multimodal responsiveness (Bruce et al. 1981). Areas TF/TH and sTs are also interconnected with the other neocortical areas with comparably widespread intercortical connections: the inferior parietal lobule (supramarginal gyrus) and area 46 of the dorsolateral prefrontal cortex,

Fg in the basal temporo-occipital cortex appears to be homologous to primate area V4 of the ventral visual system, where cells show strong effects of attention after a latency of about 90 msec (Wise and Desimone 1988). In addition, the inferior bank of the sTs contains visual association areas which are related both to the ventral "object-processing" stream (e.g., Fg), as well as to the dorsal "orientation" stream (e.g., sMg) (Ungerleider and Mishkin 1982; Felleman and Van Essen 1991). For example, sTs face cells are generally responsive to the orientation of gaze in the faces, rather than to the identity of the face (Perrett et al. 1992). Finally, area TF/TH is closely related to area V4 (Felleman and Van Essen 1991), while the cingulate and dorsolateral prefrontal cortices are not part of the visual orientation system as originally defined (Ungerleider and Mishkin 1982), subsequent work (Selemon and Goldman-Rakic 1988; Mesulam 1990; Morecraft et al. 1993) has shown that they are related to it both anatomically and functionally. For example, inferolateral parietal, posterior cingulate, and dorsolateral prefrontal cortices all have eye movement control functions, accord-

middle frontal gyri) (Baudena et al. 1995). Similar potentials have been reported in several posterior sites (Alain et al. 1989; Smith et al. 1990), and possibly also in basal temporal areas (Velasco and Velasco 1986). As elaborated in part I of this study (Halgren et al. 1995), the positive peak of this complex is termed "depth P3a" because it matches the scalp P3a in that it is evoked by non-attended rare auditory stimuli, at a significantly shorter latency than that of the scalp P3 (Squires et al. 1975; Snyder and Hillyard 1976). However, note that the depth P3a is neither exclusively frontal, nor is it preferentially evoked by rare distractors as compared to rare target stimuli.

The task correlates of the depth N2a/P3a/SW (rare or novel stimuli, regardless of whether they are task-relevant or directly attended, in both the visual and auditory modalities) are consistent with those representing the cerebral

ing to microstimulation and to unit recording in primates (Goldman-Rakic 1988; Anderson 1989; Olson et al. 1993).

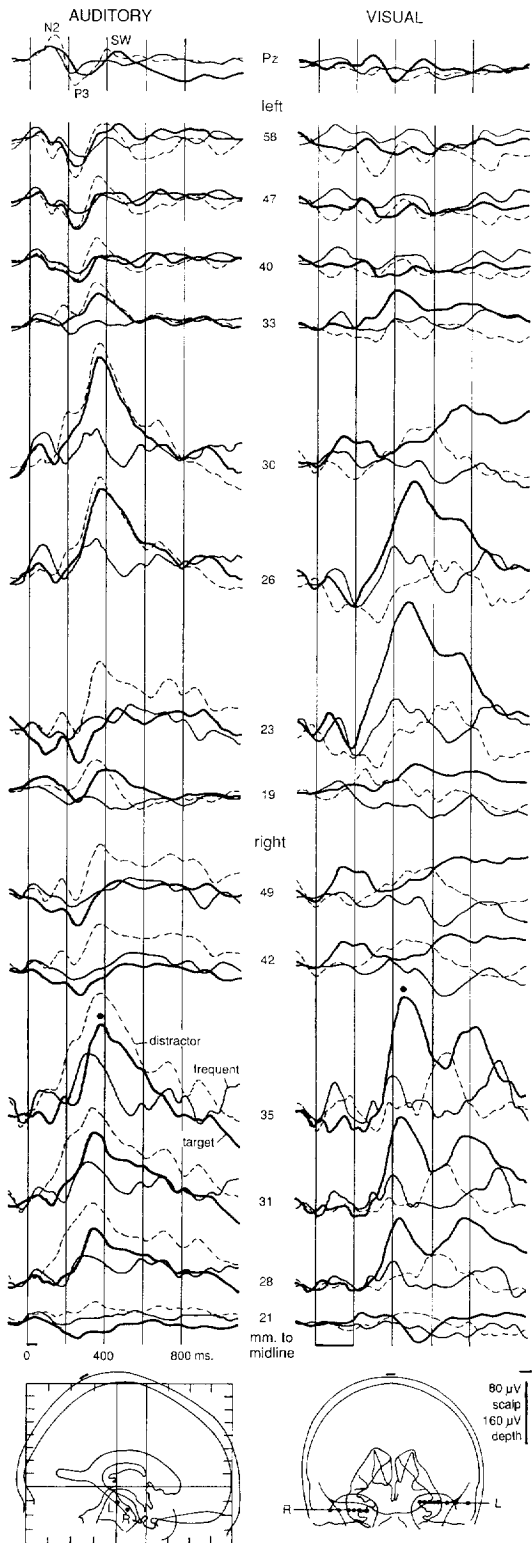These considerations suggest that probable N2a/P3a/

Fig. 9. Large polarity inverted focal P3bs in both the left and right hippocampi to both auditory and visual, rare target and distract stimuli. The large (> −200 μV) negativities in the left HC (upper, 26 mm to midline) and right HC (lower, 35 mm, ●) both achieve peak amplitude to both auditory and visual rare stimuli about 80 msec later than the simultaneously recorded scalp P3. The HC negativity declines rapidly in amplitude or even inverts at more medial (left 19; right 21), as well as more lateral (left 40; right 42) sites. AD and VD tasks. Pt. no. 19.
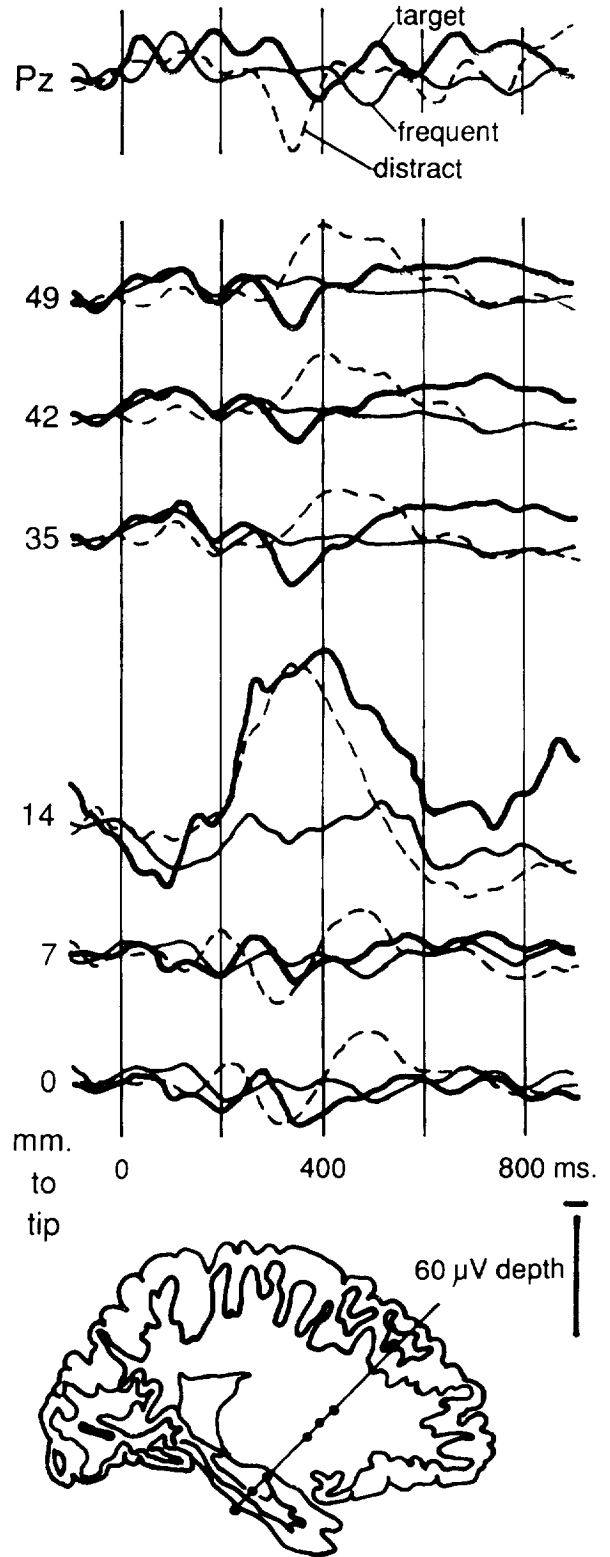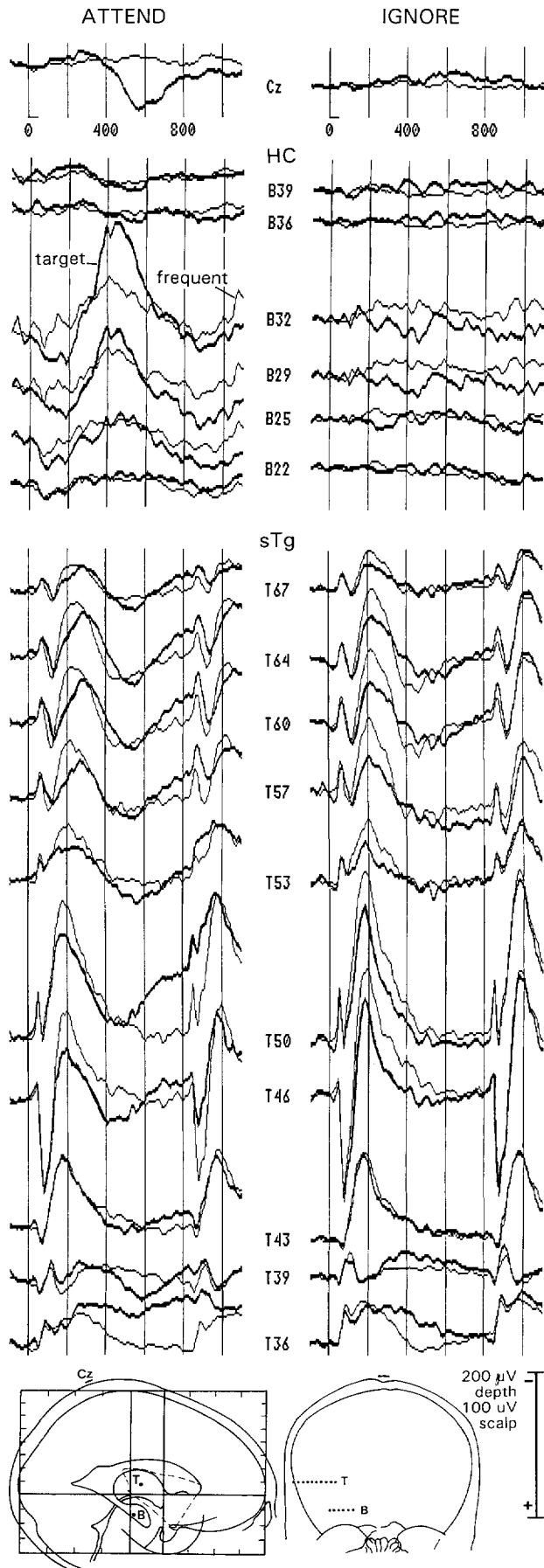
Fig. 10. Dorsoventral topography of the hippocampal P3b. A focal large negative P3b is observed in the middle HC (14 mm to tip) to rare target or distractor tones. Only small positive potentials are observed at the same latency in the more dorsal or ventral leads. AD task. Pt. no. 8.

SW generators in the temporal lobe can be grouped with parieto-frontal N2a/P3a/SW generators into 3 multilobar systems: (1) a paralimbic cortex system consisting of the subicular complex and uncinate region together with the posterior and anterior cingulate gyrus and gyrus rectus; (2) a multimodal association cortex system concerned with the orientation of attention and including parts of the sTs and pHg as well as the inferior parietal lobule and dorsolateral prefrontal cortex; and (3) a pathway concerned with the orientation of visual attention, mainly lying in the dorsal visual stream, but highly related to parts of the ventral visual stream such as V4 and sTs.

N2b / P3b

Distinguishing characteristics. In addition to the auditory-specific endogenous potentials in the superior temporal plane (STP-P3; Halgren et al. 1995), and to the depth N2a/P3a/SW, an often large (usually) positive endogenous component was recorded in several depth sites. Like the scalp P3b (Pritchard 1981; Verleger 1988), this depth P3b component had a broad waveform, was evoked equally to auditory versus visual stimuli, and was abolished when the subject's attention was directed away from the stimulus. These characteristics allowed the depth P3b to be distinguished from the STP-P3 in that: (1) the depth P3b was abolished when the stimulus stream was ignored, whereas the STP-P3 was completely preserved; (2) the depth P3b was generated in different areas from the STP-P3; and (3) the depth P3b was equal to visual and auditory rare stimuli whereas the STP-P3 was only evoked by auditory stimuli. Similarly, the depth P3b could be distinguished from the P3a of the depth N2a/P3a/SW on several grounds: (1) the depth P3b had a longer latency than the scalp P3, whereas the P3a had a shorter latency; (2) the depth P3b was abolished when the stimulus stream was ignored, whereas the P3a was relatively preserved; (3) the depth P3b was a broad, long-duration (about 300 msec) waveform whereas the P3a was a sharp short-duration (about 80 msec) waveform; (4) the depth P3b was generated in different areas than the P3a; (5) the depth P3b frequently was extremely focal and polarity-inverted over

Fig. 11. Contrasting effects of attention on endogenous potentials in the hippocampus (HC) and the superior temporal gyrus (sTg). In the HL task, rare stimulus repetitions evoke a large response at about 400 msec in the HC (B32), but only if they are attended (left column). A greater positivity to rare tones is seen in the lateral leads of an electrode near Heschl's gyrus (T64-T46) from 110 to 320 msec post-stimulus onset. This response is unaffected by attention. Note also that the HC response is absent in leads that lie more medially (B22) or laterally (B36). In leads T50 and T36, a focal negativity is seen only to attended stimuli from 550 to 900 msec (T50, T36). This negativity appears to be related to the act of key-pressing to the target stimuli and may be propagated from the Rolandic cortex, superior to the recording electrode. Pt. no. 47.

short distances, whereas this was seldom observed for the P3a; and (6) the depth P3b was evoked equally by visual and auditory stimuli, whereas the P3a was preferentially evoked by auditory stimuli.

Hippocampal generator. The depth P3b was recorded in the hippocampus, amygdala, superior temporal sulcus and postero-superior parietal lobe (Halgren et al. 1995). It was often preceded by a negativity termed here "N2b." The hippocampal P3b has been extensively described in previous publications (Halgren et al. 1980, 1983, 1986; Stapleton and Halgren 1987; McCarthy et al. 1989; Heit et al. 1990). The current study confirms previous findings that the hippocampal P3b is evoked by both distractor and target rare stimuli (Stapleton and Halgren 1987), and by both visual and auditory stimuli (Squires et al. 1983; McCarthy et al. 1989), but not by ignored stimuli (Stapleton and Halgren 1987; McCarthy et al. 1989). It also confirms previous findings that the latency of the hippocampal P3b is about 35 msec longer than that recorded at the scalp in the same patients (Stapleton and Halgren 1987; McCarthy et al. 1989). Finally, the current recordings confirm that the P3b is usually very large and negative in the hippocampus, becoming always much smaller and usually positive in leads immediately inferior, superior, posterior and anterior (Stapleton and Halgren 1987; McCarthy et al. 1989). In addition, the current study demonstrates that the mediolateral extent of the P3b in the anterior hippocampus may be quite large (up to 20 mm). Comparing these results with the spatial distribution of the hippocampal anatomical fields (Duvernoy 1988; Amaral and Insausti 1990), it is clear that the zone of negativity most probably corresponds to the apical dendrites of the fields of Ammon's horn, a possibility developed by McCarthy et al. (1989) and Halgren et al. (1986). Furthermore, the demonstration in the current study that the P3b is small and positive in leads immediately medial to the hippocampus makes it unlikely that the subicular complex or entorhinal cortex are major P3b generators, and further demonstrates that it is impossible for the hippocampal P3b to be volume-conducted from a thalamic generator.

At many sites, a large, usually negative, potential was recorded immediately preceding the P3b. In the hippocampus, this N2b potential was usually negative and thus could only be discerned as an inflection on the same negative wave as the hippocampal P3b. In some patients, the N2b appeared to be relatively larger in more medial sites, suggesting that the entorhinal cortex may have a role in its generation.

Possible propagation from the hippocampus to the scalp. Although the largest P3bs in the brain are generated in the HC, it remains uncertain as to whether they propagate significantly to the scalp. No significant decrement of the scalp P3b was found after unilateral anterior temporal lobectomy which included the anterior HC and thus most of the volume of the HC (Wood et al. 1982; Stapleton et al. 1987; Johnson 1988). Furthermore, extensive bilateral

HC lesions produced only small to moderate but non-significant decrements in the scalp P3 (Onofrj et al. 1992; Polich and Squire 1993). Similarly, the degree of propagation of HC epileptiform slow waves to the scalp suggests that if the HC makes a contribution to the scalp P3, then it is probably small (Altafullah et al. 1986). It is thus surprising that unilateral vascular lesions encompassing the posterior HC and adjacent inferior temporal neocortex produce large bilateral decrements in the P3a recorded over frontal sites (Knight 1991, 1994). The current results render it unlikely that this decrement is due to a unilateral lesion of a volume-conducting pHC generator. First, the pHC does not generate a P3a, but, like the aHC, the pHC generates a P3b. Second, like the aHC, the pHC appears to be a closed field, with only small potentials in adjacent areas. Admittedly, the sampling of sites immediately dorsal to the pHC is very limited, and so this conclusion must be considered as tentative. In any case, it seems more likely that lesions in critical areas producing this effect were in the pHg and Fg, which were both found in the current study to be probable P3a generators. Furthermore, these cortices (and especially the basal convexity of Fg) are orientated such that their fields could propagate towards the frontal scalp. However, given the large number of other prominent P3a generators that are much closer to the frontal scalp than Fg and pHg, it seems highly unlikely that a unilateral Fg/pHg lesion could directly produce a large bilateral scalp P3a decrement. Rather, it seems likely that the Fg and/or pHg influence the entire P3a system via their projections to the medial limbic cortex (from the subiculum in pHg), as well as to widespread neocortical association areas (from TF/ TH in pHg, and/or from V4 in Fg, as discussed above),

Amygdala (or rhinal) generator. A large N2b/P3b was also recorded in the amygdala. As in previous studies (Stapleton and Halgren 1987; McCarthy et al. 1989), the amygdala P3b was usually positive and shared latency as well as cognitive characteristics with the hippocampal P3b. Although the amygdala P3b could occasionally be negative, clear local polarity inversions were never observed. Indeed it may seem in these cases that the negativity in the amygdala was a prolongation of the large N2b that was invariably recorded locally. This later wave often attained its maximal amplitude in the amygdala, even though it also was never observed to polarity invert locally. It is in any case unlikely that large potentials are generated in the amygdala, inasmuch as its neurons are multipolar with dendrites passing in all directions (McDonald 1992), thus making it likely that local synaptic currents would cancel each other rather than spatially summate. Possible local generators of the N2b and P3b recorded in the amygdala include the entorhinal and perirhinal cortices which lie immediately inferior and medial to the human amygdala, encasing it like a shell. These areas are strongly interconnected with the amygdala, as well as the HC and orbital cortex (Amaral et al. 1992), both of which have been found to be generators of the depth P3b (Baudena et al.

1995). Furthermore, the rhinal cortex participates in the same functional system as the HC, i.e., in recent declarative memory (Murray 1992). Thus, circumstantial evidence suggests that rhinal cortex may participate in generation of the N2b/P3b.

Note that the limbic N2b is not modality-specific. Thus, the modality specificity of the N2b at the scalp (Vaughan et al. 1980) must be due to overlap with modality-specific N2b generators. Such modality-specific N2s were observed in occipito-temporal cortex to visual stimuli in this study, and in the supramarginal gyrus to auditory stimuli by Halgren et al. (1995).

Superior temporal sulcus generator. Like the hippocampal P3b, the P3b recorded near the sTs was multimodal and had a broad waveform. Local generation is suggested by the two polarity inversions observed, one in an electrode track penetrating the fundus of the sTs, and the other between two electrodes passing on opposite sides of the sTs. In addition, negative sTs-P3bs were sometimes observed without inversion, especially in relatively more posterior recordings. Typically, a large potential may be maintained for many millimeters in depth from the cortical surface, roughly corresponding to the depth of the sTs. In deeper leads the sTs-P3b usually declined in amplitude before sometimes increasing in medial limbic sites (a similar phenomenon was reported by Stapleton and Halgren 1987). These observations strongly suggest local generation, a possibility that is further supported by considerations that render unlikely generation by adjacent structures. First, the multimodality of the sTs-P3b clearly distinguishes it from endogenous potentials generated in the immediately superior STP. Second, the maximal potentials were observed in only a limited antero-posterior extent centered about 6 cm from the temporal tip. Thus, more anterior or more posterior lateral temporal neocortical generators are unlikely. Thirdly, the observation that the sTs-P3b typically decreased in amplitude at electrode contacts situated in the white matter between the sites close to the sTs and the HC argues against generation of the sTs-P3b by volume conduction from the HC. Hippocampal generation of the sTs-P3b is also rendered unlikely by the observation that they had distinct waveforms, and that the sTs-P3b was usually somewhat earlier in latency than the hippocampal P3b. However, the reliability of latency measures in the lateral recordings is decreased by the possible overlap with the N2a/P3a/SW, inasmuch as some recordings in this area were dominated by this potential sequence (see above). Thus, the cortex in a limited region of the sTs appears to generate large potentials to both auditory and visual stimuli in cognitive tasks. The location and task correlates of this generator suggest that it may be homologous to the multimodal region that has been identified in the depth of the monkey sTs (see above).

Possible propagation from the sTs to the scalp. Given the difficulties that post-lesional scalp recordings have posed for generation of the scalp P3b in the HC, as well as

the lack of striking and consistent parietal P3bs (Halgren et al. 1995), the possibility that an sTs generator may propagate significantly to the scalp deserves serious consideration. It appears that the critical sTs zone generating the P3b was partially or completely lesioned in the group of temporo-parietal patients with severe decrements in the auditory P3b over much of the midline scalp (Knight et al. 1989). Furthermore, dipoles located in the upper or lower banks of the sTs, bilaterally, would be expected to propagate to the scalp with a broad midline topography maximum near the vertex, similar to that which is observed for the P3b. However, arguing against a large sTs contribution to the midline scalp P3 is the fact that recordings from the STP, which lie between the sTs and the midline central scalp, reveal a P3 with different task correlates from the sTs-P3, and thus which could not result from volume conduction from the sTs. This difficulty (a lack of volume-conducted potentials in intervening areas) would not apply to a dipole in the fundus of the sTs, because it would be expected to propagate to the lateral temporal scalp, and the potentials lateral to the fundus of the sTs have the same characteristics as in the fundus. Consistent with this possibility, a small but significant decrease in P3 amplitude over the ipsilateral temporal scalp has been observed in one series of patients who had undergone unilateral anterior temporal lobectomy (McCarthy et al. 1987). The classical "standard anterior temporal lobectomy" would be expected to remove about half of the sites where the sTs-P3b was recorded on the right side (where it extends to a point about 6 cm from the temporal tip), but a minority of such sites on the left (where it extends to about 4.5 cm from the tip; Falconer 1976). Further studies correlating in individual patients the extent of the excision (and in particular whether it appeared to remove the areas where the sTs-P3b had been recorded) with post-surgical changes in temporal scalp topography are necessary to test this hypothesized propagation from the sTs generator.

In summary, definite large N2b/P3b generators are found in the MTL, especially in the HC proper (P3b) and perhaps also rhinal cortex, especially for the N2b. A P3b generator in the sTs is also highly likely.

Functional significance. Studies of the cognitive correlates of the scalp P3b have led to the hypothesis that it reflects the closure of cognitive processing of an event, i.e., at the completion of controlled or conscious processing (Posner 1975; Desmedt 1981; Donchin et al. 1983; Näätänen and Picton 1986; Hillyard and Picton 1988; Hoffman 1990). For example, the P3b is present if, and only if, independent behavioral data show that the stimulus has captured the subject's attention and reached his or her awareness. The peak of the P3b occurs at about the same latency as the subject's response, indicating that the stimulus has been accurately classified (Kutas et al. 1977; McCarthy and Donchin 1981). Since the time from P3b onset to P3b peak is about equal to the time from motor command to behavioral response, this suggests that the

P3b begins when the stimulus has been sufficiently processed to be accurately perceived (Desmedt 1981). The finding that the depth P3b is generated in multiple limbic and multimodal association cortex areas is also consistent with this hypothesis.

Note that although both the N2a/P3a/SW and N2b/P3b/SW sequences have generators in widespread cortical multimodal association regions, these regions are different for the two sequences. This suggests a functional dichotomy between multimodal cortices concerned with directing and maintaining the focus of attention (a more dorsal stream consisting of cingulate, inferior parietal and dorsolateral prefrontal cortices, with contributions from subicular and superior temporal sulcal cortices), and those concerned with the transmodal integration of diverse semantic information into cell assemblies encoding specific complex meaningful events (a basal stream consisting of the medial temporal lobe, part of the superior temporal sulcus, and the ventrolateral prefrontal cortex). The finding that the systems engaged by the P3a versus the P3b are to a large extent anatomically distinct thus confirms the assertion by Posner and Petersen (1992) that the attention system is anatomically separate from the data-processing system.

Implications of multiple generating structures

Dipole localization from extracranial recordings. The results of this and our other studies (Baudena et al. 1995; Halgren et al. 1995) imply that attempts to model depth generators of the N2, P3 or later waves as a single dipole are misguided. First, there are multiple generating structures simultaneously involved. For example, the current studies found approximately 12 probable P3 generators in each hemisphere, eight of which displayed local polarity inversions. These generators are found in the temporal, parietal and frontal lobes. Second, each of these P3 generating structures has a complex geometry that should be represented as a convoluted plane of dipoles rather than a single dipole (simulation studies have demonstrated that when an extended dipole sheet is represented as a single dipole, then that dipole may be spatially shifted from the true generator's location; Ary et al. 1981). It should be noted that the successes of source modelling (i.e., "inverse problem" solutions) have been for the early sensory potentials. These potentials tend to have a single generator with a topographically mapped and thus restricted cortical field. The current results demonstrate that the later cognitive potentials do not fit this model and will probably require the development of other analytic techniques.

One family of such techniques attempts to remove the smearing effects of the skull and estimate the field that would have been recorded had the electrodes been placed on the cortical surface (Nunez 1990). Unfortunately, such techniques are insensitive to generators that are very extended and/or that lie in deep sulci or midline or basal structures. Since (as the current paper demonstrates) such

extended and deep generators are prominent during the N2/P3, these techniques might expect relatively little success in their localization (e.g., Curran et al. 1993). More promising are inverse methods that use anatomical constraints as well as spatio-temporal MEG and EEG to estimate dipole strength in all cortical areas simultaneously (Dale and Sereno 1993).

Full employment as the brain processing policy. The current and companion (Baudena et al. 1995; Halgren et al. 1995) studies demonstrate that many cortical and limbic areas generate prominent potentials to rare stimuli in the simple auditory discrimination task. Given that simple sensory discriminations can be performed in the absence of a neocortex (Bitterman 1975; Tuber et al. 1980) many or even most of the brain areas "activated" in this task are unnecessary for basic task performance. A similar observation was made in a task where the subjects were presented with simple stimuli in the left or right hemifield and needed to respond with either the left or right hand. Again, even when both stimulus and response needed to involve only one and the same hemisphere, depth recording indicated that, outside of the specific sensory and motor areas, both hemispheres were about equally involved (Clarke et al. 1992). Thus, the brain seems to adopt the strategy of engaging all potentially useful areas, even though the probability that they will contribute to immediate task performance is very low.

The potential benefit of engaging multiple structures is that incidental learning can occur, behavioral accuracy and consequences can be monitored and, more generally, stimulus information achieves a widespread integration with context and memory. While such "conscious" processing is intentionally rendered superfluous in many psychological tasks, it could be essential for survival and reproduction in the natural environment. In comparison to these benefits, the cost of such a strategy would seem to be minimal, given that in homeotherms all brain areas must be metabolically supported in any case, regardless of whether they are engaged by the task or not (cf. the classical studies which failed to find changes in overall cerebral metabolic rate between slow wave sleep, mental arithmetic, and LSD-induced hallucinations; Lassen 1959).

This finding that multiple brain areas are electrophysiologically engaged, even when task performance does not require their engagement, in turn has possible implications for the "subtraction strategy" used with metabolic techniques (PET and functional MRI) to identify the brain areas involved in particular cognitive tasks. This strategy subtracts the pattern of brain activation evoked by a "baseline" task from that evoked by an "active" task formally identical in all respects except that it is hypothesized to demand one additional cognitive process of interest. If areas tend to be engaged even if they have only a very slight probability of being needed, then it is likely that many of the essential areas in the "active" task will also be engaged in the "baseline" task, even though they

are not essential. The subtraction may not reveal such areas and thus greatly underestimate the extent of the brain involved in a given cognitive process.

Clinical utility. The fact that multiple generators are active during the P3 also has implications for the utility of scalp P3 recording in clinical diagnosis. First, it clearly implies that deducing precise anatomical localization of brain damage from a decrease in the P3 is unlikely. Nonetheless, it may be possible to probe *systems* of generators associated with P3a, P3b, or the auditory P3, respectively. It is important to note that all 3 systems are engaged by the rare target tones of the "auditory oddball task" used in most clinical settings. Dissociation of these systems can be achieved by using additional tasks: ignoring the stimuli eliminates the P3b but apparently not the P3a or P3 auditory; conversely, rare visual stimuli continue to evoke the P3b but not the P3 auditory, and the P3a is greatly diminished. The current results suggest the possibility that a change in scalp P3 topography (such as is observed in certain diseases; Faux et al. 1987) could be due to a change in the relative strengths of two or more generating systems (e.g. P3a vs. P3b), rather than indicative of focal brain dysfunction. This question could be resolved by using different tasks to dissociate the components.

Even when multiple tasks are used to isolate a single P3 *system*, the current results strongly suggest that a focal lesion is highly unlikely to eliminate all of the generating structures within that P3 system. Thus, when a global decrease *is* observed after a focal lesion, one must suspect that the lesion has interfered with either: (1) an essential antecedent process that is a prerequisite for that P3, or (2) a central (presumably brain-stem) modulatory trigger for that P3 system to be activated (Halgren et al. 1986). Interference with a precursor antecedent calculation would be indicated if a lesion eliminated the P3 in some but not all tasks. For example, left anterior lobectomy eliminates the P3b to repeated words but not to rare tones (Stapleton et al. 1987; Smith and Halgren 1989). In contrast, interference with a modulatory trigger would be constant across tasks.

Evidence exists suggesting that both the cholinergic (Meador and Loring 1989) and noradrenergic (Foote et al. 1991) systems are involved in modulating the P3. However, the relative effects of these systems on the P3a versus P3b systems in humans has not been examined. The suggestion that the P3 is modulated by a brain-stem trigger is supported by the fact that in patients with complete sections of the cerebral commissures and massa intermedia, the unilateral presentation of the rare stimulus evokes a partially bilateral response (Kutas et al. 1990). The current results (together with Baudena et al. 1995 and Halgren et al. 1995) are consistent with this possibility, inasmuch as especially the P3a system engages remarkably widespread cortical regions, more or less simultaneously.

In summary, these results suggest that there are serious

factors greatly complicating interpretation of changes in scalp-recorded P3s in pathological states. However, these results also suggest strategies that could be taken to resolve these ambiguities and thus (in the long term) reveal the dynamics of the P3a and P3b functional brain systems in pathological states. The apparent association (or even identity) between the P3a system and the attention-orientation system and between P3b system and the event-encoding system, suggests that such data may be useful.

Conclusions

The simple auditory discrimination task used here engaged 3 largely distinct cortico-limbic systems. The first system to be engaged was auditory-specific, localized to auditory cortex, and continued to be active until after the response was made (Halgren et al. 1995). The second (N2a/P3a/SW) system engaged diffuse association cortical generators, but was especially prominent in paralimbic (cingulate and postero-medial temporo-frontal) and attentional (inferior parietal and dorsolateral prefrontal) cortices (Baudena et al. 1995). It appears to embody the cortical component of the orienting complex and may assist in probing widespread cortical areas for rapid evaluation of the biological significance of simple but prepotent stimuli. The third (N2b/P3b/SW) system engaged the limbic medial temporal lobe and multimodal association cortex. It is related to the cognitive processing/closure cycle, with a longer latency that is related to the time necessary to process the stimulus.

Acknowledgements

Abbreviations

AC	= sensorily balanced auditory oddball task
AD	= auditory oddball task with unique distractors
aHC	= anterior hippocampus

Am   = amygdala
CA-CP   = line passing through the anterior and posterior
           commissures
EP   = evoked potential
Fg   = fusiform gyrus
HL   = task with rare tone repetitions amongst regular
           alternations
Lg   = lingual gyrus
MT   = mfsmiddle temporal gyrus (MTa, MTb, MTc,
           MTd represent different antero-posterior levels
           of MT – see Methods)
MTL   = medial temporal lobe
N2   = usually negative EP component near 200 msec
OM   = task with rare tone omissions
OT   = lateral occipito-temporal cortex
P3   = usually positive EP component near 300 msec
pHC   = posterior hippocampus
pHg   = posterior parahippocampal gyrus
STP   = superior temporal planes
Ts   = superior temporal sulcus
SW   = slow wave EP component
TP   = temporal pole
VD   = visual oddball task with distractors

References

Alain, C., Richer, F., Achim, A. and Saint-Hilaire, J.M. Human intracerebral potentials associated with target, novel and omitted auditory stimuli. Brain Topogr., 1989, 1: 237–245.

Altafullah, I., Halgren, E., Stapleton, J.M. and Crandall, P.H. Interictal spike-wave complexes in the human medial temporal lobe: typical topography and comparisons with cognitive potentials. Electroenceph. clin. Neurophysiol., 1986, 63: 503–516.

Amaral, D.G. and Insausti, R. The hippocampal formation. In: G. Paxinos (Ed.), The Human Nervous System. Academic Press, New York, 1990: 711–755.

Amaral, D.G., Price, J.L., Pitkänen, A. and Carmichael, S.T. Anatomical organization of the primate amygdaloid complex. In: J.P. Aggleton (Ed.), The Amygdala. Neurobiological Aspects of Emotion, Memory, and Mental Dysfunction. Wiley-Liss, New York, 1992: 1–66.

Anderson, R.A. Visual and eye movement functions of the posterior parietal cortex. Annu. Rev. Neurosci., 1989, 12: 377–403.

Ary, J.P., Darcey, T.M. and Fender, D.H. Locating electrical sources in the human brain. IEEE Trans. Biomed. Eng., 1981, 28: 1–5.

Başar-Eroglu, C., Başar, E. and Schmielay, F. P300 in freely moving cats with intracranial electrodes. Int. J. Neurosci., 1991.

Baudena, P., Halgren, E., Heit, G. and Clarke, J.M. Intracerebral potentials to rare target and distractor auditory and visual stimuli. III. Frontal cortex. Electroenceph. clin. Neurophysiol., 1995, 94: in press.

Bitterman, M.E. The comparative analysis of learning. Science, 1975, 188: 699–709.

Brodmann, K. Vergleichende Lokalisation Lehre der Grosshirnrinde in ihren Prinzipien dargestellt auf Grund des Zellenbaues. Barth, Leipzig, 1909.

Bruce, C.J., Desimone, R. and Gross, C.G. Visual properties of neurons in a polysensory area in superior temporal sulcus of the macaque. J. Neurophysiol., 1981, 46: 369–384.

Buchwald, J.S. Animal models of cognitive event-related potentials. In: J.W. Rohrbaugh, R. Parasuraman and R. Johnson, Jr. (Eds.), Event-Related Potentials of the Brain. Oxford University Press, New York, 1990: 57–75.

Clarke, J.M., Chauvel, P., Scarabin, J.M. and Halgren, E. Intracerebral measures of lateralized processing in humans: effects of visual field, response hand, and processing stage. Soc. Neurosci. Abst., 1992, 18: 336.

Curran, T., Tucker, D.M., Kutas, M. and Posner, M.I. Topography of the N400: brain electrical activity reflecting semantic expectancy. Electroenceph. clin. Neurophysiol., 1993, 88: 188–209.

Dale, A.M. and Sereno, M.I. Improved localization of cortical activity by combining EEG and MEG with MRI cortical surface reconstruction: a linear approach. J. Cogn. Neurosci., 1993, 5: 162–176.

Desmedt, J.E. Scalp-recorded cerebral event-related potentials in man as point of entry into the analysis of cognitive processing. In: F.O. Schmitt, F.G. Worden, G. Edelmann and S.D. Dennis (Eds.), The Organization of the Cerebral Cortex. MIT, Cambridge, MA, 1981: 441–473.

Donchin, E., McCarthy, G., Kutas, M. and Ritter, W. Event-related potentials in the study of consciousness. In: R.J. Davidson, G.E. Schwartz and D. Shapiro (Eds.), Consciousness and Self-Regulation. Advances in Research and Theory, Vol. 3. Plenum, New York, 1983: 81–122.

Duvernoy, H.M. The Human Hippocampus: an Atlas of Applied Anatomy. Bergmann, Munich, 1988.

Falconer, M.A. Anterior temporal lobectomy for epilepsy. In: C. Rob and R. Smith (Eds.), Operative Surgery. Butterworth, London, 1976: 142.

Faux, S.F., Torello, M.W., McCarley, R.W., Shenton, M.E. and Duffy, F.H. P300 topographic alterations in schizophrenia: a replication study. In: R. Johnson, Jr., J.W. Rohrbaugh and R. Parasuraman (Eds.), Current Trends in Event-Related Potential Research. EEG Suppl. 40. Elsevier, Amsterdam, 1987: 688–694.

Felleman, D.J. and Van Essen, D.C. Distributed hierarchical processing in the primate cerebral cortex. Cereb. Cortex, 1991, 1: 1–47.

Foote, S.L., Berridge, C.W., Adams, L.M. and Pineda, J.A. Electrophysiological evidence for the involvement of the locus coeruleus in alerting, orienting, and attending. Prog. Brain Res., 1991, 88: 521–532.

Goldman-Rakic, P.S. Topography of cognition: parallel distributed networks in primate association cortex. Annu. Rev. Neurosci., 1988, 11: 137–156.

Halgren, E. Evoked potentials. In: A.A. Boulton, G. Baker and C. Vanderwolf (Eds.), Neuromethods. Vol. 15. Neurophysiological Techniques – Applications to Neural Systems. Humana, Clifton, NJ, 1990: 147–275.

Halgren, E. and Marinkovic, K. Neurophysiological networks integrating human emotions. In: M. Gazzaniga (Ed.), The Cognitive Neurosciences. MIT Press, Cambridge, MA, 1993: 1137–1151.

Halgren, E., Squires, N.K., Wilson, C.L., Rohrbaugh, J.W. and Babb, T.L. Endogenous potentials generated in the human hippocampal formation and amygdala by infrequent events. Science, 1980, 210: 803–805.

Halgren, E., Wilson, C.L., Squires, N.K., Engel, J., Walter, R.D. and Crandall, P.H. Dynamics of the human hippocampal contribution to memory. In: W. Seifert (Ed.), Neurobiology of the Hippocampus. Academic Press, London, 1983: 529–572.

Halgren, E., Stapleton, J.M., Smith, M.E. and Altafullah, I. Generators of the human scalp P3s. In: R.Q. Cracco and I. Bodis-Wollner (Eds.), Evoked Potentials. Liss, New York, 1986: 269–289.

Halgren, E., Baudena, P., Heit, G., Clarke, J.M. and Marinkovic, K. Spatio-temporal stages in face and word processing. 1. Depth-recorded potentials in the human occipital, temporal and parietal lobes. J. Physiol. (Paris), 1994, 88: 1–50.

Halgren, E., Baudena, P., Clarke, J.M., Heit, G., Liégeois-Chauvel, C., Chauvel, P. and Musolino, A. Intracerebral potentials to rare target and distractor auditory and visual stimuli. I. Superior temporal plane and parietal lobe. Electroenceph. clin. Neurophysiol., 1995, 94: 191–220.

Hari, R. and Lounasmaa, O.V. Recording and interpretation of cerebral magnetic fields. Science, 1989, 244: 432–436.

Heit, G., Smith, M.E. and Halgren, E. Neuronal activity in the human

medial temporal lobe during recognition memory. Brain, 1990, 113: 1093–1112.

Hillyard, S.A. and Picton, T.W. Electrophysiology of cognition. In: F. Plum (Ed.), Handbook of Physiology – The Nervous System V. American Physiological Society, Bethesda, MD, 1988: 519–584.

Hoffman, J.E. Event-related potentials and automatic and controlled processes. In: J.W. Rohrbaugh, R. Parasuraman and R. Johnson, Jr. (Eds.), Event-Related Brain Potentials: Basic Issues and Applications. Oxford University Press, New York, 1990: 145–157.

Johnson, Jr., R. Scalp-recorded P300 activity in patients following unilateral temporal lobectomy. Brain, 1988, 111: 1517–1529.

Kaga, K., Harrison, J.B., Butcher, L.L., Woolf, N.J. and Buchwald, J.S. Cat "P300" and cholinergic septohippocampal neurons: depth recordings, lesions, and choline acetyltransferase immunohistochemistry. Neurosci. Res., 1992, 13: 53–71.

Knight, R.T. Neural mechanisms of event related potentials: evidence from human lesion studies. In: J.W. Rohrbaugh, R. Parasuraman and R. Johnson, Jr. (Eds.), Event-Related Brain Potentials: Basic Issues and Applications. Oxford University Press, New York, 1990: 3–18.

Knight, R.T. Effects of hippocampal lesions on the human P300. Soc. Neurosci. Abst., 1991, 17: 657.

Knight, R.T. Attention regulation and human prefrontal cortex. In: A.M. Thierry (Ed.), Motor and Cognitive Functions of the Prefrontal Cortex. Springer, Berlin, 1994: 160–173.

Knight, R.T., Scabini, D., Woods, D.L. and Clayworth, C.C. Contributions of temporal-parietal junction to the human auditory P3. Brain Res., 1989, 502: 109–116.

Kutas, M., McCarthy, G. and Donchin, E. Augmenting mental chronometry: the P300 as a measure of stimulus evaluation time. Science, 1977, 197: 792–795.

Kutas, M., Hillyard, S.A., Volpe, B.T. and Gazzaniga, M.S. Late positive event-related potentials after commissural section in humans. J. Cogn. Neurosci., 1990, 2: 258–271.

Lassen, N.A. Cerebral blood flow and oxygen metabolism in man. Physiol. Rev., 1959, 39: 183–238.

Lewine, J.D., Foeder, S.B.W., Oakley, M.T., Arthur, D.L., Aine, C.J., George, G.S. and Flynn, E.R. Generators of the neuromagnetic P3. Soc. Neurosci. Abst., 1989, 15: 478.

McCarthy, G. and Donchin, E. A metric for thought: a comparison of P300 latency and reaction time. Science, 1981, 211: 77–80.

McCarthy, G., Darcey, T.M., Wood, C.C., Williamson, P.D. and Spencer, D.D. Asymmetries in scalp and intracranial endogenous ERPs in patients with complex partial epilepsy. In: J. Engel, G. Ojemann, H. Lüders and P.D. Williamson (Eds.), Fundamental Mechanisms of Human Brain Function. Raven Press, New York, 1987: 51–59.

McCarthy, G., Wood, C.C., Williamson, P.D. and Spencer, D.D. Task-dependent field potentials in human hippocampal formation. J. Neurosci., 1989, 9: 4253–4268.

McDonald, A.J. Cell types and intrinsic connections of the amygdala. In: J.P. Aggleton (Ed.), The Amygdala. Neurobiological Aspects of Emotion, Memory, and Mental Dysfunction. Wiley-Liss, New York, 1992: 67–96.

Meador, K.J. and Loring, D.W. Current perspectives on the relationship of the P3 evoked potential and disorders of memory. Neuropsychiat. Neuropsychol. Behav. Neurol., 1989, 2: 161–174.

Meador, K.J., Loring, D.W., King, D.W., Gallagher, B.B. and Gould, M.J. Cholinergic modulation of human limbic evoked potentials. Int. J. Neurosci., 1988, 38: 407–414.

Meador, K.J., Loring, D.W., King, D.W., Gallagher, B.B., Gould, M.J., Flanigan, H.F. and Smith, J.R. Limbic evoked potentials predict site of epileptic focus. Neurology, 1989, 37: 494–497.

Mesulam, M.M. Large-scale neurocognitive networks and distributed processing for attention, language, and memory. Ann. Neurol., 1990, 28: 597–613.

Morecraft, R.J., Geula, C. and Mesulam, M.M. Architecture of connectivity within a cingulo-fronto-parietal neurocognitive network for directed attention. Arch. Neurol., 1993, 50: 279–284.

Murray, E.A. Medial temporal lobe structures contributing to recognition memory: the amygdaloid complex versus the rhinal cortex. In: J.P. Aggleton (Ed.), The Amygdala. Neurobiological Aspects of Emotion, Memory, and Mental Dysfunction. Wiley-Liss, New York, 1992: 453–470.

Musolino, A., Tournoux, P., Missir, O. and Talairach, J. Methodology of "in vivo" anatomical study and stereo-electroencephalographic exploration in brain surgery for epilepsy. J. Neurorad., 1990, 17: 67–102.

Näätänen, R. and Picton, T.W. N2 and automatic versus controlled processes. In: W.C. McCallum, R. Zappoli and F. Denoth (Eds.), Cerebral Psychophysiology Studies in Event-Related Potentials. Electroenceph. clin. Neurophysiol., Suppl. 38. Elsevier, Amsterdam, 1986: 169–186.

Neshige, R. and Lüders, H. Recording of event-related potentials (P300) from human cortex. J. Clin. Neurophysiol., 1992, 9: 294–298.

Nunez, P.L. Electric Fields of the Brain. Oxford University Press, New York, 1981.

Nunez, P.L. Localization of brain activity with electroencephalography. In: S. Sato (Ed.), Advances in Neurology, Vol. 54. Magnetoencephalography. Raven Press, New York, 1990: 39–65.

Okada, T.C., Kaufman, L. and Williamson, S.J. The hippocampal formation as a source of the slow endogenous potentials. Electroenceph. clin. Neurophysiol., 1983, 55: 417–426.

Olson, C.R., Musil, S.Y. and Goldberg, M.E. Posterior cingulate cortex and visuospatial cognition: properties of single neurons in the behaving monkey. In: B.A. Vogt and M. Gabriel (Eds.), Neurobiology of Cingulate Cortex and Limbic Thalamus. Birkhäuser, Boston, MA, 1993: 366–380.

Onofrj, M., Fulgente, T., Nobiolio, D., Malatesta, G., Bazzano, S., Colamartino, P. and Gambi, D. P3 recordings in patients with bilateral temporal lobe lesions. Neurology, 1992, 42: 1762–1767.

Paller, K.A., Zola-Morgan, S., Squire, L.R. and Hillyard, S.A. P3-like brain waves in normal monkeys and in monkeys with medial temporal lesions. Behav. Neurosci., 1988, 102: 714–725.

Paller, K.A., McCarthy, G., Roessler, E., Allison, T. and Wood, C.C. Potentials evoked in human and monkey medial temporal lobe during auditory and visual oddball paradigms. Electroenceph. clin. Neurophysiol., 1992, 84: 269–279.

Perrett, D.I., Hietanen, J.K., Oram, M.W. and Benson, P.J. Organization and functions of cells responsive to faces in the temporal cortex. Phil. Trans. Roy. Soc. Lond. B, 1992, 335: 23–30.

Pineda, J.A., Foote, S.L. and Neville, H.J. Effects of locus coeruleus lesions on auditory, long-latency, event-related potentials in monkey. J. Neurosci., 1989, 9: 81–93.

Polich, J. and Squire, L.R. P300 from amnesic patients with bilateral hippocampal lesions. Electroenceph. clin. Neurophysiol., 1993, 86: 408–417.

Posner, M.I. Psychobiology of attention. In: M. Gazzaniga and C. Blakemore (Eds.), Handbook of Psychobiology. Academic Press, New York, 1975: 441–480.

Posner, M.I. and Petersen, S.E. The attention system of the human brain. Annu. Rev. Neurosci., 1992, 13: 25–42.

Pritchard, W.S. Psychophysiology of P300. Psychol. Bull., 1981, 89: 506–540.

Pritchard, W.S., Shappell, S.A. and Brandt, M.E. Psychophysiology of N200/N400: a review and classification scheme. In: P.K. Ackles, J.R. Jennings and M.G.H. Coles (Eds.), Advances in Psychophysiology. JAI Press, Greenwich, CT, 1988.

Puce, A., Kalnins, R.M., Berkovic, S.F., Donnan, G.A. and Bladin, P.F. Limbic P3 potentials, seizure localization, and surgical pathology in temporal lobe epilepsy. Ann. Neurol., 1989, 26: 377–385.

Renault, B., Ragot, R., Lesèvre, N. and Rémond, A. Onset and offset of brain events as indices of mental chronometry. Science, 1982, 215: 1413–1415.

Richer, F., Johnson, R.A. and Beatty, J. Sources of late components of the brain neuromagnetic response. Soc. Neurosci. Abst., 1983, 9: 656.

Rogers, R.L., Baumann, S.B., Papanicolaou, A.C., Bourbon, T.W., Alagarsamy, S. and Eisenberg, H.M. Localization of the P3 sources using magnetoencephalography and magnetic resonance imaging. Electroenceph. clin. Neurophysiol., 1991, 79: 308–321.

Rosene, D.L. and Van Hoesen, G.W. Hippocampal efferents reach widespread areas of cerebral cortex and amygdala in the rhesus monkey. Science, 1977, 198: 315–317.

Selemon, L.D. and Goldman-Rakic, P.S. Common cortical and subcortical targets of the dorsolateral prefrontal and posterior parietal cortices in the rhesus monkey: evidence for a distributed neural network subserving spatially guided behavior. J. Neurosci., 1988, 8: 4049–4068.

Seltzer, B. and Pandya, D.N. Afferent cortical connections and architectonics of the superior temporal sulcus and surrounding cortex in the rhesus monkey. Brain Res., 1978, 149: 1–24.

Smith, M.E. and Halgren, E. Dissociation of recognition memory components following temporal lobe lesions. J. Exp. Psychol.: Learn. Mem. Cogn., 1989, 15: 50–60.

Smith, M.E., Halgren, E., Sokolik, M., Baudena, P., Mussolino, A., Liégeois-Chauvel, C. and Chauvel, P. The intracranial topography of the P3 event-related potential elicited during auditory oddball. Electroenceph. clin. Neurophysiol., 1990, 76: 235–248.

Snyder, E. and Hillyard, S.A. Long-latency evoked potentials to irrelevant, deviant stimuli. Behav. Biol., 1976, 16: 319–331.

Squires, N.K., Squires, K.C. and Hillyard, S.A. Two varieties of long-latency positive waves evoked by unpredictable auditory stimuli in man. Electroenceph. clin. Neurophysiol., 1975, 83: 387–401.

Squires, N.K., Halgren, E., Wilson, C.L. and Crandall, P.H. Human endogenous limbic potentials: cross-modality and depth/surface comparisons in epileptic subjects. In: A.W.K. Gaillard and W. Ritter (Eds.), Tutorials in ERP Research: Endogenous Components. North-Holland Publ., Amsterdam, 1983: 217–232.

Stapleton, J.M. and Halgren, E. Endogenous potentials evoked in simple cognitive tasks: depth components and task correlates. Electroenceph. clin. Neurophysiol., 1987, 67: 44–52.

Stapleton, J.M., Halgren, E. and Moreno, K.A. Endogenous potentials after anterior temporal lobectomy. Neuropsychologia, 1987, 25: 549–557.

Szikla, G., Bouvier, G., Hori, T. and Petron, V. Angiography of the Human Brain Cortex. Springer, New York, 1977.

Talairach, J. and Tournoux, P. Co-Planar Stereotaxic Atlas of the Human Brain. Thieme Medical Publishers, New York, 1988.

Talairach, J., Szikla, G., Tournoux, P., Prossalentis, A., Bordas-Ferrer, M., Covello, L., Jaco, M. and Mempel, E. Atlas d'Anatomie Stéréotaxique du Télencéphale. Masson, Paris, 1967.

Taube, J.S., Muller, R.U. and Ranck, Jr., J.B. Head-direction cells recorded from the postsubiculum in freely moving rats. 1. Description and quantitative analysis. J. Neurosci., 1990, 10: 420–435.

Tuber, D.S., Berntson, G.G., Bachman, D.S. and Allen, J.N. Associative learning in premature hydranencephalic and normal twins. Science, 1980, 210: 1035–1037.

Ungerleider, L.G. and Mishkin, M. Two cortical visual systems. In: D.J. Ingle, M.A. Goodale and R.J.W. Mansfield (Eds.), Analysis of Visual Behaviour. MIT Press, Cambridge, MA, 1982: 549–586.

Van Hoesen, G.W. The parahippocampal gyrus: new observations regarding its cortical connections in the monkey. Trends Neurosci., 1982, 5: 345–350.

Vaughan, Jr., H.G., Ritter, W. and Simson, R. Topographic analysis of auditory event-related potentials. In: H.H. Kornhuber and L. Deecke (Eds.), Progress in Brain Research. Vol. 54. Motivation, Motor and Sensory Processes of the Brain: Electrical Potentials, Behaviour and Clinical Use. Elsevier, Amsterdam, 1980: 279–290.

Velasco, M. and Velasco, F. Subcortical correlates of the somatic, auditory and visual vertex activities. II. Referential EEG responses. Electroenceph. clin. Neurophysiol., 1986, 63: 62–67.

Verleger, R. Event-related potentials and cognition: a critique of the context updating hypothesis and an alternative interpretation of P3. Behav. Brain Sci., 1988, 11: 343–427.

Wise, S.P. and Desimone, R. Behavioral neurophysiology: insights into seeing and grasping. Science, 1988, 242: 736–741.

Wood, C.C. and McCarthy, G. A possible frontal lobe contribution to scalp P300. Soc. Neurosci. Abst., 1985, 11: 879–880.

Wood, C.C., McCarthy, G., Allison, T., Goff, W.R., Williamson, P.D. and Spencer, D.D. Endogenous event-related potentials following temporal lobe excisions in humans. Soc. Neurosci. Abst., 1982, 8: 976–970.

Wood, C.C., McCarthy, G., Kim, J.H., Spencer, D.D. and Williamson, P.D. Abnormalities in temporal lobe event-related potentials predict hippocampal cell loss in temporal lobe epilepsy. Soc. Neurosci. Abst., 1988, 14: 5.