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Spatio-temporal stages in face and word processing. 1. Depth recorded potentials in the human occipital, and parietal lobes

temporal

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Summary – Evoked potentials (EPs) were used to help identify the timing, location, and intensity of the information-processing stages applied to faces and words in humans. EP generators were localized using intracranial recordings in 33 patients with depth electrodes implanted in order to direct surgical treatment of drug-resistant epilepsy. While awaiting spontaneous seizure onset, the patients gave their fully informed consent to perform cognitive tasks. Depth recordings were obtained from 1198 sites in the occipital, temporal and parietal cortices, and in the limbic system (amygdala, hippocampal formation and posterior cingulate gyrus). Twenty-three patients received a declarative memory recognition task in which faces of previously unfamiliar young adults without verbalizable distinguishing features were exposed for 300 ms every 3 s; 25 patients received an analogous task using words. For component identification, some patients also received simple auditory (21 patients) or visual (12 patients) discrimination tasks. Eight successive EP stages preceding the behavioral response (at about 600 ms) could be distinguished by latency, and each of 14 anatomical structures was found to participate in 2–8 of these stages. The earliest response, an N75–P105, focal in the most medial and posterior of the leads implanted in the occipital lobe (lingual g), was probably generated in visual cortical areas 17 and 18. These components were not visible in response to words, presumably because words were presented foveally. A focal evoked alpha rhythm to both words and faces was also noted in the lingual g. This was followed by an N130–P180–N240 focal and polarity-inverting in the basal occipitotemporal cortex (fusiform g, probably areas 19 and 37). In most cases, the P180 was evoked only by faces, and not by words, letters or symbols. Although largest in the fusiform g this sequence of potentials (especially the N240) was also observed in the supramarginal g, posterior superior and middle temporal g, posterior cingulate g, and posterior hippocampal formation. The N130, but not later components of this complex, was observed in the anterior hippocampus and amygdala. Faces only also evoked longer-latency potentials up to 600 ms in the right fusiform g. Words only evoked a series of potentials beginning at 190 ms and extending to 600 ms in the fusiform g and near the angular g (especially left). Both words and faces evoked a N150–P200–PN260 in the lingual g, and posterior inferior and middle temporal g. A N310–N430–P630 sequence to words and faces was largest and polarity-inverted in the hippocampal formation and amygdala, but was also probably locally-generated in many sites including the lingual g, lateral occipitotemporal cortex, middle and superior temporal g, temporal pole, supramarginal g, and posterior cingulate g. The P660 had the same distribution as has been noted for the P3b to rare target simple auditory and visual stimuli in 'oddball' tasks, with inversions in the hippocampus. In several sites, the N310 and N430 were smaller to repeated faces, and the P630 was larger. Putative information-processing functions were tentatively assigned to successive EP components based upon their cognitive correlates, as well as the functions and connections of their generating structures. For the N75–P105, this putative function is simple feature detection in primary visual cortex (V1 and V2). The N130–P180–N240 may embody structural face encoding in posterobasal inferotemporal cortex (homologous to V4?), with the results being spread widely to inferotemporal, multimodal and paralimbic cortices. For words, similar visual-form encoding (in fusiform g) or visual-phonemic encoding (in angular g) may occur between 150 and 280 ms. During the N310, faces and words may be multiply encoded for form and identity (inferotemporal), emotional (amygdala), recent declarative mnestic (hippocampal formation), and semantic (supramarginal and superior temporal sulcal supramodal cortices) characteristics. These multiple characteristics may be contextually integrated across inferotemporal, supramodal association, and limbic cortices during the N430, with cognitive closure following in the P630. In sum, visual information arrives at area 17 by about 75 ms, and is structurally-encoded in occipito-temporal cortex during the next 110 ms. By 150–200 ms after stimulus onset, activation has spread to parietal, lateral temporal, and limbic cortices, all of which continue to participate with the more posterior areas for the next 500 ms of event-encoding. Thus, face and word processing is serial in the sense that it can be divided into successive temporal stages, but highly

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parallel in that (after the initial stages where visual primitives are extracted) multiple anatomical areas with distinct perceptual, mnestic and emotional functions are engaged simultaneously. Consequently, declarative memory and emotional encoding can participate in early stages of perceptual, as well as later stages of cognitive integration. Conversely, occipitotemporal cortex is involved both early in processing (immediately after V1), as well as later, in the N430. That is, most stages of face and word processing appear to take advantage of the rich 'upstream' and 'downstream' anatomical connections in the ventral visual processing stream to link the more strictly perceptual networks with semantic, emotional, and mnestic networks.

N400 / P300 / memory / hippocampus / fusiform g

Introduction

The goal of this study is to identify, time and locate some of the major neural information-processing stages evoked by visually-presented works and faces, by recording electrical potentials from electrodes directly implanted into the human brain. Psychological studies have suggested that words (Morton and Patterson, 1980; Coltheart, 1987; Just and Carpenter, 1987) and faces (Bruce, 1988; Bruce *et al*, 1992) pass through formally similar processing stages: 1) sensory analysis; 2) feature detection; 3) integration of features; 4) individual identification; and 5) integration of the individual into the current context. Anatomical studies in macaques have demonstrated about 32 visual or visual association cortical areas (Ungerleider and Mishkin, 1982; Zeki and Shipp, 1988; Felleman and VanEssen, 1991). On the basis of the laminar origin and destination of their interconnections, these areas have been placed into 10 hierarchical levels, from V1 to the parahippocampal areas TF/TH. It has been hypothesized that these anatomical levels correspond to functional levels, with activation passing from primary visual cortex to visual association areas devoted to progressively more complex feature extraction, then matching of these features in anterior inferotemporal cortex with templates stored in long-term memory in order to identify objects, thence to higher level sensory and multimodal association cortex for identification of individuals and relation to long-term semantic memory, and finally passage to supramodal association areas for integration with the cognitive context, and to the hippocampus and amygdala for relation to declarative memory and emotion. This is broadly consistent with single-unit studies in primates demonstrating progressively more complex feature detectors in posterior visual association areas (VanEssen and Maunsell, 1983; Marrocco, 1986; Tanaka *et al*, 1991), culminating in units firing to hands, eyes, mouths, and ultimately faces in the superior temporal sulcus and inferotemporal cortex, and amygdala (Gross, 1973; Perrett *et al*, 1982; Rolls *et al*, 1987; Rolls, 1992; Perret *et al*, 1992). Units responsive to particular faces and words in a given context have also been found in the human amygdala and hippocampus (Heit *et al*, 1988). This apparent anatomic and functional progression also corresponds to progressively more complex pattern recognition deficits after progressively more anterior lesions in primates (Mishkin, 1982; Ungerleider and Mishkin, 1982) and humans (Luria, 1966; Hecaen and Albert, 1978; Damasio *et al*, 1990).

At the same time that the anatomical studies indicate a sequential organization, they also suggest that within each level, there are several areas that could be involved in parallel, and indeed physiological studies indicate that different types of features (shape, motion, color, etc) may be extracted in parallel by different areas (Zeki and Shipp, 1988). Furthermore, many anatomical connections skip levels so that, for example, the first level (V1) projects to the tenth level (parahippocampal areas TF/TH) *via* a single relay in V4 (Felleman and VanEssen, 1991). This is a total distance of about 7 cm in humans, and should require about 13 ms with typical myelinated fibers (diameter 1 μ: Patton, 1982), plus a synaptic delay of 2 ms. This estimate is consistent with the interhemispheric transmission times indicated by evoked potentials (Saron and Davidson, 1989). Humans require about 550 ms to recognize an individual face. Subtracting the time required for information to reach V1 (estimated as 70 ms, the latency to the peak of the first cortical visual EP component), and the time to proceed from decision to movement (80 ms), one arrives at about 400 ms of processing time. Thus, the anatomy could be consistent with anywhere from a single processing stage lasting 400 ms and uniting all of the visual areas, to 10 processing stages each involving one level of the hierarchy. Similarly, neither lesion nor unit-recording studies have been

sufficiently fine-grained to distinguish more than about three levels of analysis (corresponding roughly to simple features in V1, complex shapes in IT, and intermediate features in intermediate areas).

If multiple physiological levels (or stages) do actually exist, then there arise the further questions as to when each one starts, and how long it lasts. Finally, given the multiple feedback, feedforward, and lateral interconnections between visual areas, it is quite possible for any given physiological stage to involve multiple anatomical areas, and conversely, for multiple successive stages to be present in a single structure.

The location and timing of physiological stages clearly cannot be directly deduced from behavioral studies of the effects of brain lesions in humans ('classical' neuropsychology), both because such studies only measure the end-product of the cerebral information-processing sequence, and because they only indicate the areas that are essential for the impaired behavior. Metabolic measures such as PET can reveal structures that are activated during a given behavior even if they are not essential, and can be performed in normal subjects. However, PET integrates the brain response over a 1–35-min period, whereas the processing stages sought here last less than 400 ms. Although functional MRI is more rapid than PET, it cannot be faster than the 1–2-s reaction time of the underlying physiological process (cerebral bloodflow or perfusion) that it measures.

For these reasons, it is important to make complementary measures in order to arrive at a functional view of the areas involved in face and word processing. When synaptic currents are sufficiently synchronous (as might be expected in a stage of information-processing) and spatially aligned (as often happens in cortical structures), the net extracellular current produces a field that can be recorded locally as the depth EP (Wood, 1987). Depth EPs have the advantages of great temporal resolution (equal to the sampling rate, 5 or 6 ms in this study), high spatial resolution (equal to the electrode spacing, 3.5 mm in this study), and a direct relation to synaptic current-flows. If the generating structure has an appropriate internal geometry ('open field'), cerebral location and orientation, then the depth EP may passively propagate to the scalp. Thus, depth EPs have the additional advantage that their cognitive correlates can be inferred from those of the associated scalp EPs, which have in general been extensively studied (Halgren, 1990b). It is important to emphasize that, unlike scalp EP or MEG measures, depth recordings can unambiguously identify EP generators. For example, if the locally-recorded EP component is much larger than in adjacent structures, and changes amplitude and polarity over short distances, then that component is without question generated locally.

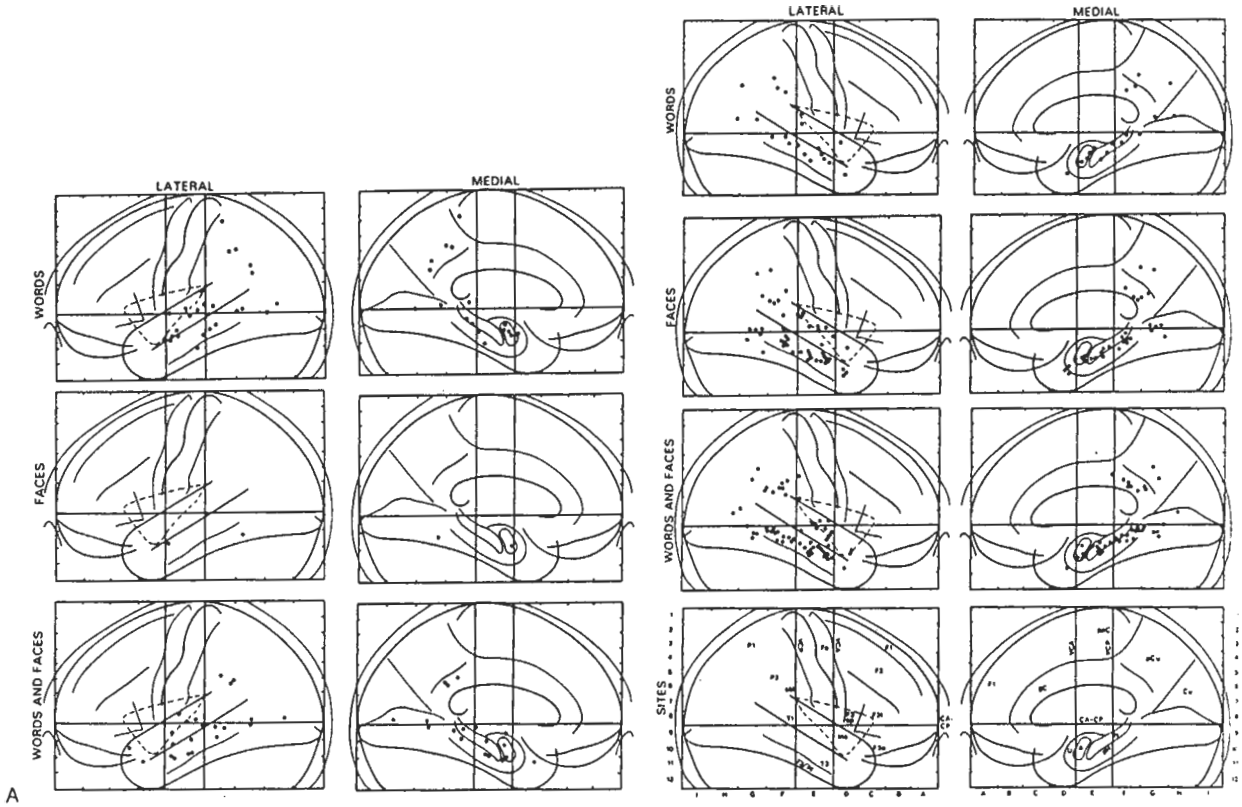
Depth recordings must be interpreted with caution, inasmuch as electrodes are only implanted for strictly clinical purposes usually in patients with long-standing epilepsy. However, most such patients perform in the normal range on cognitive tasks, and their epileptiform activity is localized in time and space. Thus, it is possible to select patients, sites and epochs for analyses that appear to be normal. Depth recordings are also limited in that they are primarily sensitive only to locally-generated activity, and only a limited number of electrodes are implanted in each subject. Thus, results from multiple subjects must be collated to arrive at an adequate sampling of cerebral activity. Furthermore, EPs may be blind to important information-processing stages if they involve synaptic activity which is non-overlapping, and/or occurs in a non-cortical structure. Finally, an important weakness of all the cognitive neurophysiological studies is that the small number of tasks given does not allow the precise cognitive correlate of each EP stage to be determined with certainty.

The current study attempts to distinguish the EP components evoked by words and/or faces in posterior cortex, define their latency and time-course, localize them to neocortical and/or limbic areas, and characterize their changes across task conditions. An attempt is then made to identify the EP components with cognitive processing stages, and using neural data regarding the connections and functions of the generating areas, a crude neural model is proposed. A clear sequence of physiological stages is observed with multiple but often focal generators, suggesting a combination of parallel and sequential processing.

Materials and methods

Patients

Adequate recordings were obtained from 33 patients with grossly normal personality and intelligence, suffering from epilepsy that had proven resistant to trials of all appropriate anticonvulsant medications (Bancaud, 1975). Electrodes were implanted for 5 to 14 days in order to localize the sites of seizure onset, at the Neu-



A

Fig 1. Location of electrode implants. The entry-points of electrodes are indicated on Lateral views of the patients' heads (left column), with the terminations of those electrodes that passed to the inner surface of the temporal, occipital or parietal lobes shown on the Medial views (right column). The inner table of the skull and the outlines of the ventricles are traced from lateral teleradiographs obtained under stereotaxic conditions during ventriculography (Talairach *et al*, 1967). Vertical and horizontal lines pass through the anterior and posterior commissures (AC and PC). Each electrode contained five to 15 separate contacts. All electrodes took a lateral to medial course perpendicular to the midline plane, except for two approximately vertical electrodes in patient no 8, one passing from the parietal lobe to the posterior cingulate g, and the other from the frontal lobe to the posterior hippocampal formation (not illustrated). The schemas from individual patients were superimposed using the proportional system of Talairach *et al* (1967), relative to a coordinate system based on AC–PC and the size of the brain. **A.** Location of electrodes implanted in the left hemisphere, where recordings were obtained only during Words (top row), only during Faces (middle), or during both Words and Faces (bottom). **B.** Locations of electrodes in the right hemisphere during the same tasks. At the bottom of the figure, the anatomical regions that statistically correspond to the proportional coordinates are indicated. It must be emphasized that these locations are approximate, being true only on the average. Confirmation of electrode sites in individual subjects was accomplished with reference to gyri outlined by stereotaxically visualized blood vessels (Szikla *et al*, 1977). Abbreviations: A, amygdala; Cu, cuneus; CA–CP, horizontal line passing through the anterior and posterior commissures; gC, cingulate gyrus; F1, superior frontal gyrus; F2, middle frontal gyrus; F3o, inferior frontal gyrus, pars orbitalis; F3op, inferior frontal gyrus, pars opercularis; F3t, inferior frontal gyrus, pars triangularis; Fa, precentral gyrus; H, hippocampus; Ins, insula (indicated by dashed lines); P1, superior parietal lobule; P2, inferior parietal lobule; paC, paracentral lobule; pCu, precuneus; pH parahippocampal gyrus; sM, supramarginal gyrus; T1, superior temporal gyrus; T2, middle temporal gyrus; T3/4 inferior temporal and fusiform gyri; U, uncus; VCA, vertical line passing through the anterior commissure; VCP, vertical line passing through the posterior commissure.

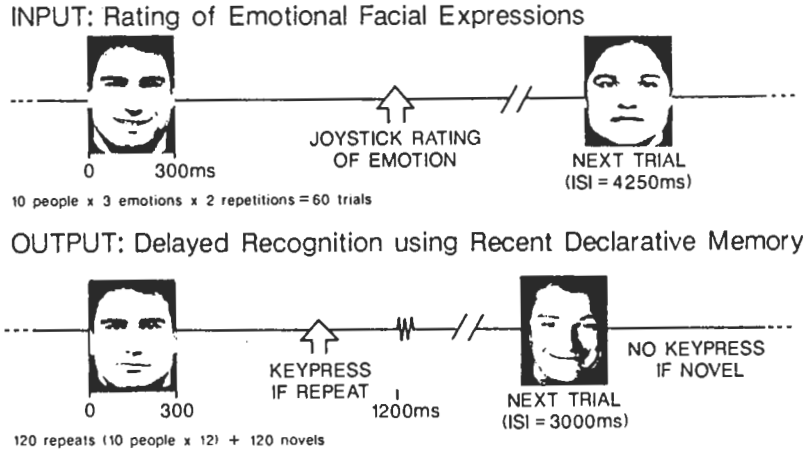


Fig 2. Face and word recognition tasks.

rosurgical Services of Hôpital Sainte-Anne in Paris (Pr JP Chodkiewicz, Chief), or of Hôpital Pontchaillou in Rennes (Pr J Faivre, Chief). While awaiting spontaneous seizure onset, recordings were obtained during cognitive tasks. Patients were not recorded if they were having frequent or major seizures, or within 1 h after a complex partial seizure. Data were rejected from patients and/or sites which exhibit chronic slow waves or interictal spikes, or when a patient was unable to perform within the normal range in speed and accuracy on the cognitive tasks. Selection of patients and sites to implant, as well as the duration of implantation, were made without reference to the experimental protocol. Cognitive recordings were made only after fully informed consent, monitored by the appropriate subject protection committees.

Electrodes and localization

Each patient received 1-6 electrodes in the temporal, occipital and/or parietal lobes (total 180 electrodes, 46 left, 134 right). Electrodes were 0.8 mm in diameter, blunt-tipped, and had five, 10 or 15 recording contacts. Each contact was 2.0 mm in length, and successive contacts were separated by 1.5 mm. Initial electrode trajectories are chosen using the method of Talairach *et al* (1967), which uses a standard baseline (the anterior commissure-posterior commissure line = the AC-PC line), and a proportional grid system to compensate for variations in the size and shape of the brain, and which indicates the average location and statistical variation for the major neocortical gyri and telencephalic subcortical structures. *(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) anterosposterior, mm to the AC line, positive anterior; (z) vertical, mm to the AC-PC line, positive dorsal. Electrode contacts are indicated by the letter of the electrode, followed by a prime if the electrode is in the left hemisphere, followed by the number of mm from the center of the contact to the interhemispheric plane.)* Brodmann (1909) areas are also indicated, as mapped in Talairach *et al* (1967) and Talairach and Tournoux (1988), but it must be emphasized that these are only approximate; cytoarchitectonic boundaries obviously cannot be confirmed *in vivo*.

Statistical localization was confirmed and refined by direct visualization of vessels tracing the structure's outlines, using stereoscopic stereotactic angiography (Szikla *et al*, 1977). Angiograms were made in the same stereotaxic frame as was used for electrode implantation, and at a distance of 4.85 M (thus eliminating significant parallax). This method also allowed avascular trajectories to be chosen for the electrodes. Stereotactic MRI, with planes parallel to the interhemispheric plane and with the AC-PC line indicated, was obtained in some patients after electrode withdrawal. This allowed direct visualization of electrode tracks, albeit at a lower accuracy than is currently possible with ventriculography and angiography (Musolino *et al*, 1990). Localization of electrode contacts was performed blind as to the results of recordings.

Electrode placement was individualized to test possible sites of seizure onset, and could include, in different patients, most regions posterior to Rolandic cortex (*cf* fig 1). The dorsal, posterior and ventral extremes of the hemispheres were relatively poorly sampled due to a technical reason: electrodes nearly always entered from the lateral surface and followed a trajectory that was perpendicular to the midline. Because of their ability to sample several areas frequently involved in epileptogenesis with a single electrode, certain trajectories were selected relatively more frequently, permitting some quantitative analysis of the more commonly implanted sites. These sites (and their approximate coordinates in the Talairach axes) include: lingual g (±20,–58,–4); fusiform g (±30,–55,–5); lateral occipotemporal cortex (±52,–62, 2); posterior parahippocampal g (±17,–31,–8); posterior hippocampus (±28, –31,–8); anterior hippocampus (±27,–16,–18); amygdala (±25,–5,–18); posterior middle temporal g (±55,–25, –10); anterior middle temporal g (±56,–5,–18); posterior superior temporal g (±60,–17,+3); anterior superior temporal g (±60,+5,–2); temporal pole (±35,+10,–30); posterior cingulate g (±4,–37,+25); and supramarginal g (±50,–37,+25). Sites in the postcentral g are discussed with other central and frontal sites in a different paper (Halgren *et al*, 1994). A total of 1198 posterior sites (367 left hemisphere, 831 right) were recorded.

Recording, averaging and analysis

After passing through a unity gain input stage, the signal was amplified 20000 × including optical isolation. Bandpass was 0.1 to 100 Hz. For each patient, simultaneous recordings were made from 29–105 depth contacts, 0–5 EEG electrodes (most often placed between Cz and Pz), and a vertical EOG derivation. In some patients, additional contacts were recorded in a subsequent session. Waveforms were digitized every 6 ms at 12 bit accuracy for 1200 ms beginning 117 ms before face onset. In most patients, a second 1200 ms digitization epoch was collected beginning 100 ms before the feedback tone. Only trials without wrong responses, eye movements or epileptiform EEG spikes were used in constructing averages. Eye movements were detected by amplitude criteria applied to the EOG channel. Epileptiform EEG spikes and other large transients were rejected on amplitude criteria set individually for each patient's data. The effectiveness of these artifact rejection routines was carefully monitored by visual inspection of the graphics display. Channels contaminated by very frequent epileptiform abnormalities or showing spikes time-locked to the stimulus were excluded from analysis.

The generalizability of the current results to normal subjects is extensively discussed in the companion paper (Halgren *et al*, 1994). The likelihood that the data reported here represent epileptiform activity is considered unlikely, given that evoked paroxysms are very rare (epileptogenic tissue and surrounding areas tend to the hypo- rather than hyper-responsive), and would have been eliminated by the analysis procedure. Furthermore, all of the responses were confirmed across several subjects with varying pathology, and all responses were generated by brains that were performing the task correctly. However, the possibility that abnormal connections or responsiveness could have contributed to the current results cannot be eliminated.

Peak measurements were made by finding the maximum, minimum or clear inflection in a given channel within the appropriate latency window, and subtracting the average value of that channel during the period prior to the stimulus onset. The contact in each structure with the largest amplitude EPs was chosen for measurements. Due to the orientation of the generating field, the components present varied across structures. Furthermore, due to variations in the exact placement of the recording contacts with respect to the generators, the components within a given structure varied across different patients. Thus, measurements were only made for clearly identifiable components.

Behavioral tasks

The principle tasks, Face and Word, required declarative recognition memory (fig 2). Simple auditory (AD)

Table I. Patient characteristics

Patient no	*Sex*	*Age*	*Implanted sites*[a]	*sz focus*[a]	*Dominance man (hemi)*[b]	*Tasks*[c]
1	F	22	RTP	RT	R	F,A,V
2	F	34	RTPCF	RT	R	F,W,A
3	M	20	RPCF, LCP	RFP, LFC		F,W,A,V
4	F	25	RTOP, LT	RT	R	F,A
5	F	39	RTPCF	RT	R	F,W,A
6	M	50	RTPCF	RT	L(L)	F,A,V
7	M	29	RPRF	RF	R	F,A,V
8	M	21	RTPF	RTP	R	F,W,A,V
9	M	37	RTPCF	RT	R	F,W,A
10	M	40	RTPF	RT	R	W,A,V
11	F	25	LTOP	LT	R	F,W,A
12	M	32	RTOPF	RT	L(R)	F,W,A,V
14	M	35	LTPCF	LT	R	F,W,A,V
16	F	26	RTF	RT	R	F,A,V
17	M	26	RTOPCF	RT	R	F,A
18	M	39	RTCF	RT	R	F,A
19	F	19	RTP, LT	RT	R	F,W,A,V
20	M	22	RTOCF	RT	R	F,W,A,V
21	M	31	RTOCF	RT	R	F,W,A,V
22	M	30	RTPF	RT	R	F,W,A,V
23	M	28	RTOPCF	RJ	R	F,W,A
24	M	24	RTF	RT	R	F,A
25	M	18	LTOP	LT	R	W,A
27	M	24	RTPCF	RT	R	F,W,A
28	M	26	LTOF	LT	L(L)	F,W,A
31	F	24	LTF, RTF	BF	R	W,A,V
32	M	20	RTF	RT	R	W,A
35	F	35	LTPOCF, RC	LC	L(R)	W,A
36	F	28	LTPF, RTPF	BP	R	W,A
37	F	32	LTF	LT	R	W,A
44	M	34	LT	LT	R(L)	W,A
46	F	24	RTPO, LT	RF	R	W,A
48	F	30	LPF, RPF	BF	R	W,A

[a]T, temporal; O, occipital; P, parietal; F, frontal; C, central; J, junction of TPO; R, right; L, left; B, bilateral.
[b]Hemispheric dominance was determined by language function after unilateral intracarotid amytal (Wada test) in left handed subjects.
[c]F, face recognition; W, word recognition; A, auditory discrimination; V, visual discrimination.

Table II. Average latency and amplitude of potentials evoked by faces in each region

Components	*Site*	*Lg*	*Fg*	*OT*	*pHg*	*pHc*	*sTs*	*aHC*	*aT2*	*Am*	*TP*	*pCg*	*sMg*	*pTl*	*aTl*	*CPz*	*Mean depth*
N75	N	5															
	LAT	78															78.4
	NEW	−9															
	RPT	−4															
P105	N	8	3														
	LAT	105	108														107
	NEW	22	12														
	RPT	20[e]	6														
N130	N	7	10	6	5	7	8	6	2	10	1	12	16			8	
	LAT	138	126	145	127	112	119	119	124	114	110	131	146			118	126
	NEW	−52	−36	−34	−26	−18	−17	−40	−28	−20	13	−17	−25			−3.2	
	RPT	−41[d]	−28[e]	−33[e]	−23[e]	−10[e]	−16[e]	−13[e]	−5	−14[e]	−7	−15[e]	−21[e]			−3.9	
P180	N	8	9	8	3	7	10		3			11	14			11	
	LAT	187	185	198	143	166	189		195			189	193			178	183
	NEW	30	76	39	18	8	14		8			14	19			5.8	
	RPT	36[e]	78[e]	37[e]	37	14[e]	16[e]		19			15[e]	20[e]			5.1[e]	
N240	N	6	8	5	5	5	8	3	6			14	15			9	
	LAT	236	253	259	228	244	245	205	244			262	254			235	243
	NEW	−53	−55	−50	−41	−48	−28	−41	−20			−34	−31			−4.1[e]	
	RPT	−47[e]	−46[c]	−49[e]	−34[b]	−35[d]	−18[e]	−6	−11[d]			−31[e]	−24[e]			−3.3[e]	
N310	N	5	3		5	6	6	7	6	17	4	4	5		2	8	
	LAT	331	294		322	303	344	285	324	287	318	304	303		314	307	311
	NEW	−49	−63		−40	−60	−29	−96	−45	−64	−64	−7	5		−30	−6.3	
	RPT	−37[e]	−37		−31[d]	−46[e]	−9[d]	−85[e]	−27[c]	−52[d]	−57	−3	16[e]		−44	−5.1[e]	
N430	N	8	9	8	7	5	11	9	13	17	3	16	16	5	5	13	
	LAT	443	421	427	424	430	435	459	440	468	464	407	415	424	443	437	436
	NEW	−35	−34	−36	−30	−60	−26	−95	−37	−49	−67	−33	−35	−42	−28	−4.6	
	RPT	−28[e]	−15[d]	−35[e]	−28[e]	−35[e]	−17[d]	−77[d]	−26[d]	−30[d]	−47	−26[e]	−27[e]	−29[e]	−22[e]	−4.7[e]	
abs	NEW							116									
	RPT							94									
P630	N	6	8	7	3	4	13	8	13	10	5			5	5	12	
	LAT	574	599	609	726	650	609	655	622	662	660			581	607	617	630
	NEW	21	30	19	17	1	23	−22	4	11	28			17	25	4.5	
	RPT	22[e]	46[e]	15[e]	21[e]	6[e]	29[e]	−61[c]	22[b]	32[e]	41[e]			27[a]	60[d]	6.4[e]	
abs	NEW			24		15		48									
	RPT			34		26		67									
N800	N													4	2		
	LAT													831	811		816
	NEW													25	−18		
	RPT													−3	−26		

N, no of patients measured; LAT, latency in ms; NEW, amplitude in μV to non-repeated faces; RPT, amplitude to repeated faces; abs, absolute value;
For abbreviations of sites see legend to figure 1.
Components are listed according to usual polarity (Positive; Negative) and approximate mean latency across sites.
Difference between repeated (RPT) and novel (NEW) faces tested with paired *t*-test (two-tailed). [a]$P < 0.001$; [b]$P < 0.01$; [c]$P < 0.02$; [d]$P < 0.05$; [e]ns (only tested for $n > 4$).

Table III. Average latency and amplitude of potentials evoked by words in each region

Components	*Site*	*Lg*	*Fg*	*OT*	*pHg*	*pHC*	*sTs*	*aHC*	*aT2*	*Am*	*TP*	*pCg*	*sMg*	*pTl*	*aTl*	*CPz*
N130	N	2	5	7		2	5	2	1	3	2	5	12			7
	LAT	131	139	171		102	137	122	122	147	115	135	152			142
	NEW	−14	−17	−36		−12	−17	−41	−16	−11	−15	−17	−16			−4
	RPT	−11	−13[e]	−37[e]		−2	1[c]	−27	1	−8	−4	−9[e]	−15[e]			−4[e]
P180	N	6	8			2	4		2		1	7	7			8
	LAT	181	201			185	179		186		226	198	212			190
	NEW	13	32			19	21		19		1	13	21			5
	RPT	14[e]	27[e]			4	12		11		−21	15[e]	19[e]			4[e]
N240	N	5	6	7			2	2	3			8	7			6
	LAT	245	242	246			250	277	250			259	260			241
	NEW	15	−33	26			−14	30	−9			−29	−23			−8
	RPT	17[e]	−28[e]	38[c]			0	78	−2			−13[c]	−18[e]			−1[e]
N310	N	6	6	4	1	4	2	2	7	14	3	5	9			8
	LAT	307	325	359	315	347	352	332	335	310	351	311	289			311
	NEW	−34	−23	−75	−22	−45	−32	−57	−29	−38	−50	16	17			−5
	RPT	−31[c]	−23[e]	−56	−8	−37	−11	−48	−11[e]	−23[d]	−27	23[e]	11[e]			−1[c]
N430	N	6	10	9	2	6	10	6	13	13	2	13	14	11	5	12
	LAT	430	430	472	373	405	439	449	444	486	537	409	431	449	439	470
	NEW	−23	−43	−60	−27	−72	−17	−74	−23	−55	−29	−30	−26	−22	−20	−4
	RPT	−12[b]	−30[d]	−49[c]	−23	−59[c]	−2[b]	−49[e]	−7[a]	−18[b]	14	−17[c]	−22[e]	−8[a]	−11[d]	−3
P630	N	4	6	5	2	6	11	6	11	11	3			5	5	11
	LAT	571	639	677	623	619	652	619	652	668	665			628	601	612
	NEW	9	33	21	2	−15	−25	−44	15	−3	22			4	−3	6
	RPT	31[c]	42[e]	39[e]	−1	−26[d]	−36[e]	−109[a]	24[e]	24[c]	48			15[b]	18[b]	6
abs	NEW				21	19				23						
	RPT				30	46				26						
N800	N													5	1	
	LAT													837	649	
	NEW													−2	−17	
	RPT													−57[e]	−26	

N, of patients measured; LAT, latency in ms; NEW, amplitude in μV to non-repeated words; RPT, amplitude to repeated words; abs, absolute value. For the abbreviations of sites see legend to figure 1. Components are listed according to usual polarity (positive or negative) and approximate mean latency across sites. Note that for pHC the *t*-test of repetition effects was conducted after having (re)inverted inverted components.

Difference between repeated (RPT) and novel (NEW) faces tested with paired *t*-test (two-tailed). [a]$P < 0.001$; [b]$P < 0.01$; [c]$P < 0.02$; [d]$P < 0.05$; [e]ns (only tested for $n > 4$).

and visual (VD) discrimination tasks with infrequent target and non-target distractor stimuli (*ie* auditory and visual 'oddball' tasks) were presented for comparison purposes. During all tasks, the patient reclined on a bed with his/her back elevated, and maintained fixation on a target in front of him or her. Stimulus presentation was controlled and behavioral responses were monitored for latency and accuracy using a microcomputer.

FACE (21 patients)

The faces were presented every 3 s as color slides on a back projection screen tachistoscopically for 300 ms each. The images subtended a visual angle of 5.5 degrees horizontal by 8.3 degrees vertical. The patient was required to press a microswitch held in the dominant hand within 1200 ms after presentation of a repeating face. At 1200 ms post-stimulus, a 55 ms sawtooth feedback tone was presented indicating

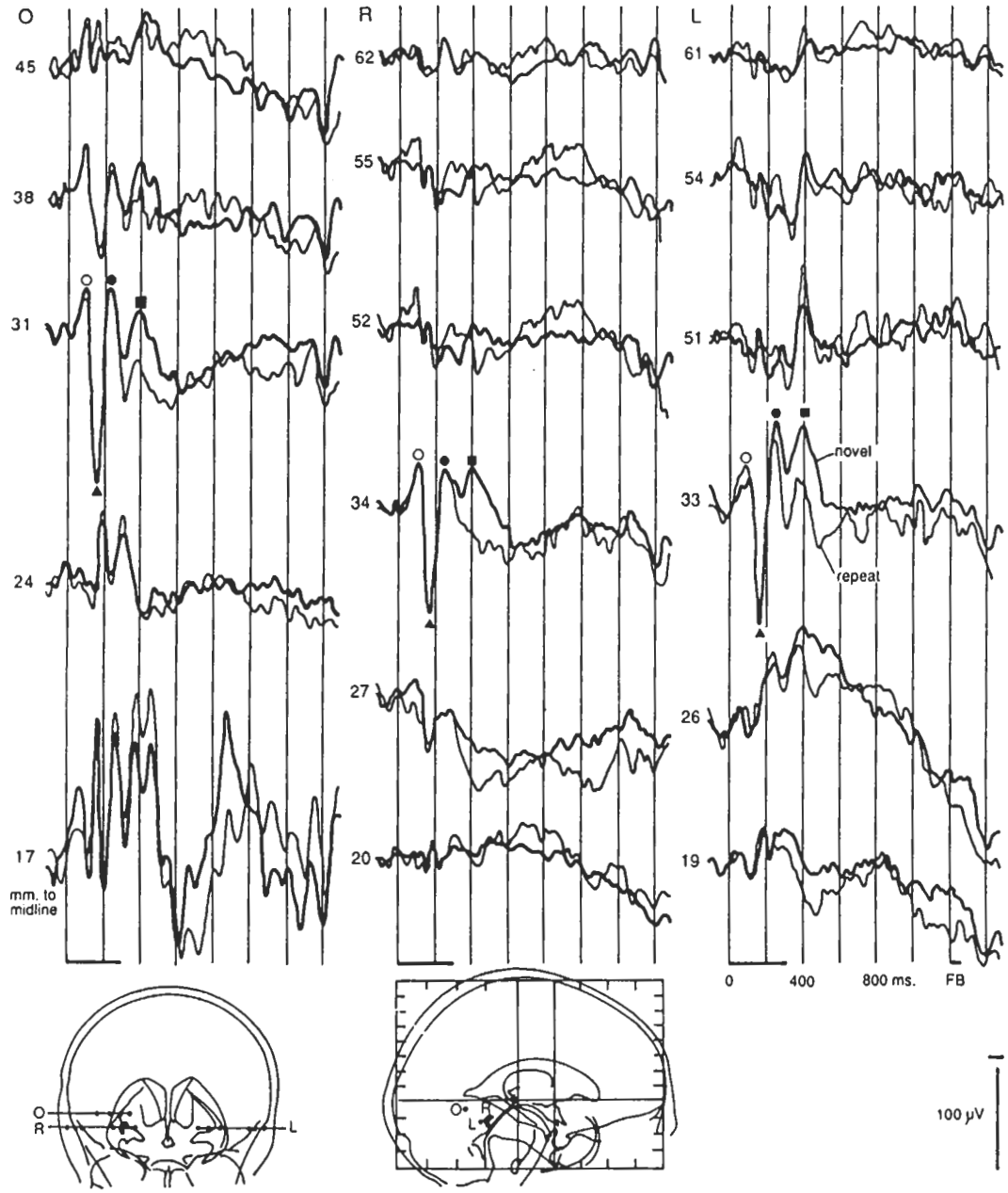


Fig 3. Early potentials recorded by three electrodes in occipito-temporal cortex, and evoked by faces in a recognition task. All three electrodes (O and R in the right, L left) show a similar sequence of four peaks: N90(○)–P170(▲)–N220 (●)–N400(■), with labels indicating polarity (N = negative, P = positive) and latency in ms from stimulus onset to peak response. Responses are maximal in the electrode contacts located in the fusiform g (O, 31 mm from midline; R, 34 mm; L, 33 mm). These peaks are very focal and large, and in some cases polarity invert more medially in the lingual g (the N90–P170–N220–P300–N400 in electrode O between 31 and 24 mm from midline, the N400 in electrode R between 34 and 27 mm). The earlier potentials are very similar to novel *vs* repeated faces, but the N400 is clearly larger to novel stimuli. Note also that although these potentials all are generally maximal in the same leads, that their topographies (especially that of the N400 in electrode L) are clearly distinct. A small P200–N280 to the auditory feedback tone is seen in the external leads of electrode O. Finally, the most medial posterior contact (O, 17 mm) records prominent rhythmic activity at 9.1 Hz, whose synchronization with stimulus onset is shown by the superimposition of the peaks to repeated and novel stimuli. In this and following figures, recordings from successive contacts of each electrode are displayed in one column, with the most superficial contact at the top, and the distance of each contact from the midline indicated in millimeters on the left of each trace. Waveforms evoked by novel faces (thick lines) and repeated faces (thin) are superimposed after equating their prestimulus baseline levels. All contacts are recorded simultaneously, and each represents the average of 50 to 100 trials. Negative is up with the scale as indicated. The first vertical line indicates stimulus onset, with successive lines every 200 ms. Face stimulus presentation is indicated by the first thick horizontal line below the waveforms, and feedback (FB) by the second line. The anatomical positions of the electrodes are indicated as lines below on tracings of the antero-posterior (left) and lateral (right) radiographs, with the recorded contacts indicated by filled circles (note that since the convention is to present radiographs as if viewing the body, the electrode is implanted in the *right*). Patient no 4.

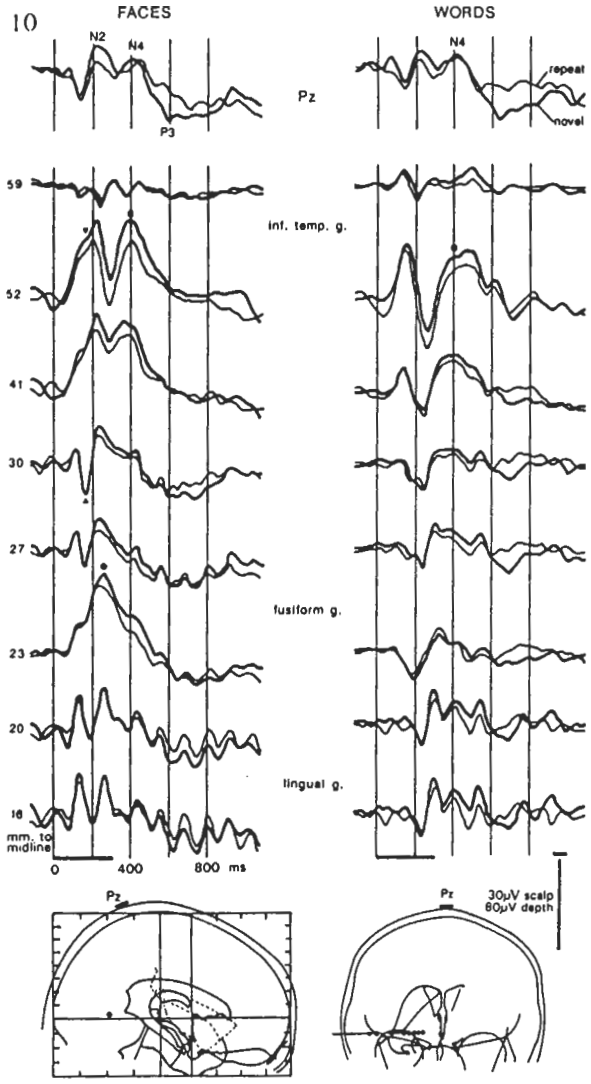


Fig 4. Contrasting potentials evoked in the posterobasal inferotemporal cortex by faces *vs* words. The left and right columns display waveforms recorded from the same contacts, but in response to faces or words, respectively. The earliest potential is a P90/N120 recorded by the most medial leads (16 and 20 mm) in the lingual g to faces only. This is followed in the lingual g by a rhythmic activity at about 8.9 Hz and synchronized to the exposure of both words and faces. The most striking aspect of these waveforms is an N120–P170 (▲)–N220 sequence evoked in the fusiform g by faces only. The P170 inverts laterally (▼, from 30 to 41 mm from midline), and medially (27 ↔ 23 mm) from the fusiform g. The N220 extends laterally to the inferior temporal g. Other potentials (N150–P280–N400) in the most lateral lead in the inferior temporal g (52 mm) are evoked by both words and faces. Still in the fusiform g and also specific to faces, but more medially is a focal large (−100 μV) N260 (●). Finally, an N420 specific to faces is evoked in the fusiform g (23 mm) at the same time that a non-specific N400 is evoked by both words and faces (■) in the superficial inferior temporal g site (52 mm). The top traces were recorded simultaneously with the depth recordings from an electrode placed on the scalp on the midline near the position shown as the horizontal bar on the radiographs. Patient no 20.

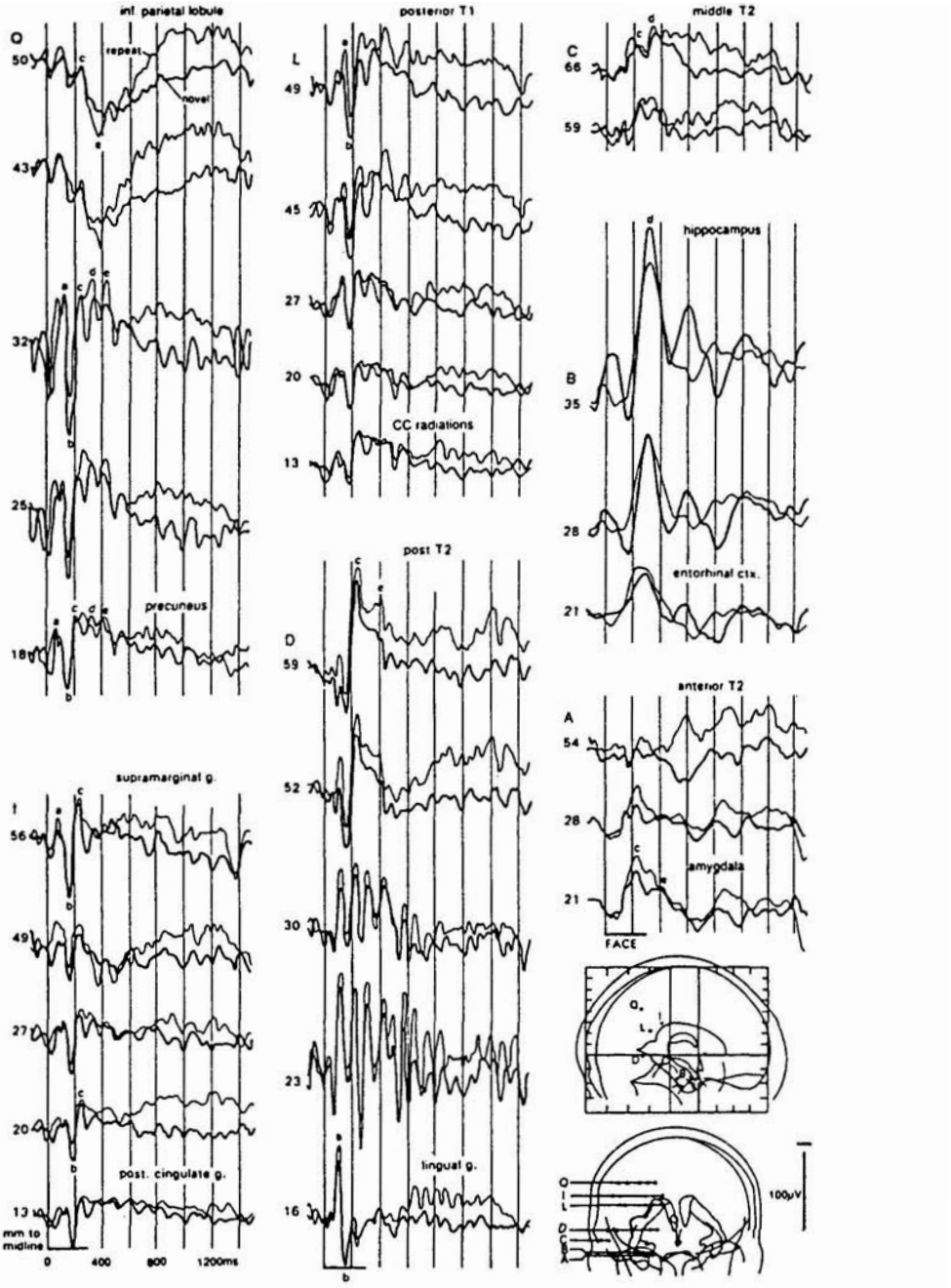
whether the response (or lack thereof) had been correct (1000 Hz) or wrong (200 Hz). Responses to feedback tones were collected in most subjects but are discussed in another paper in relation to the N2/P3 in 'auditory oddball' tasks.

The face stimuli were comprised of photographs of previously unfamiliar young adults of European descent who lacked beards or mustaches. The background was black, and the clothing was obscured by a black drape. Glasses, jewelry and other unnatural identifying objects were removed, and hair was pulled back from the face prior to photography. Subjects posed in each photograph as happy, sad, or neutral, according to instructions and after practice.

Six hundred slides from 260 individual subjects were included, divided into two equivalent sets. In each set, 10 individuals were chosen to be targets and presented repeatedly ('repeats'), with the remaining 120 presented only once ('non-repeats'). During the input phase, each of the repeating individuals was shown six times (twice each for each of three emotions), and the subject was required to rate the valence and intensity of the facial expression with a joystick. EEG was not digitized during input and the behavioral results will not be discussed in this paper. During the output phase, 240 slides were presented every 3 s with rests after 80 and 160 slides. Of these 240 slides, 120 were the non-repeats, and the remainder were 12 repetitions of each of the 10 target faces. Repeat and non-repeats were presented in random order, except that no individual could be presented on two successive trials, no more than three repeats or three non-repeats could follow each other in a row, and each of the 10 targets occurred exactly once in each block of 20 slides. Consequently, the delay between successive presentations of a given face was filled with distractors, and has a duration of 6–117 s (average 61.5 s). The faces were 1/2 male and 1/2 female, and no more than five male or five female faces were presented in a row. The faces were 1/3 of each emotional expression, and no more than three faces with the same expression were presented in a row. Repetition, gender and expression were all completely crossed with each other. The influence of gender and expression on the waveforms will be presented in another paper.

WORD (14 patients)

The words were presented every 3 s as proportionally-spaced white letters on a computer monitor for 300 ms, where each subtended a visual angle of 1.24 to 1.49 degrees horizontal by 0.36 degree vertical. The 4–7 letter words were 1/2 of moderately low (31 to 162 occurrences per 10 million, average 100), and 1/2 of moderately high frequency (> 3193 occurrences per 10 million, average 15000). The patient was required to press a microswitch held in the dominant hand within 1200 ms after presentation of a repeating word. At 1200 ms post-stimulus, a 55 ms sawtooth feedback tone was presented indicating whether the response (or lack thereof) had been correct (1000 Hz) or wrong (200 Hz).



potentials in parietal and temporal cortices. The earliest response is a focal 90 μV N100/P150 (a/b) in the ling
18 or 19). Immediately lateral leads in the collateral s (D23 and 30) record an over 100 μV amplitude very
a (about 11.2 Hz). Early N110/P160 potentials (a/b) are also recorded in supramarginal g (156, in the posterior
ding ramus of the Sylvian f, area 40), precuneus (Q18), posterior superior temporal g (L49), and in the sulcus be
and inferior parietal lobules (Q32). This is followed by an N210 (c) in the same sites, plus the inferior parietal

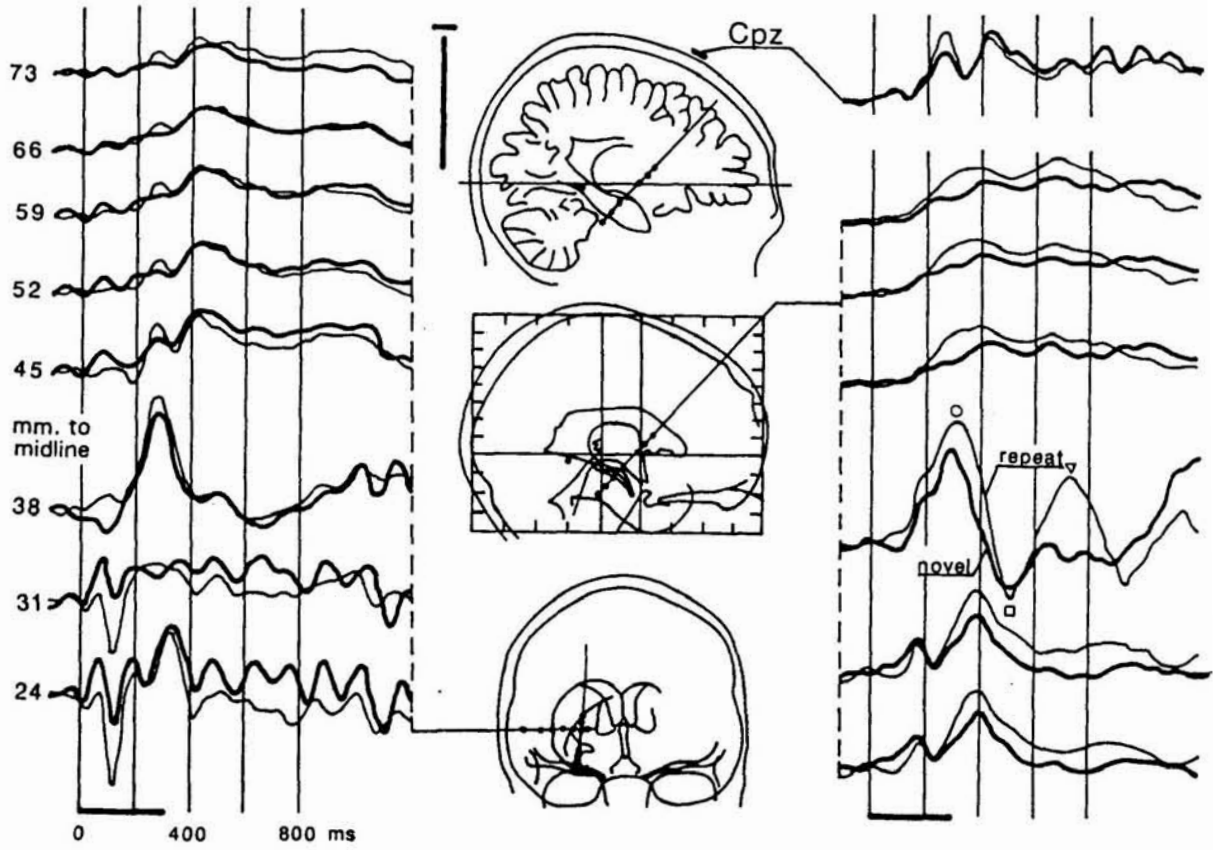


Fig 6. Hippocampal face potentials: Vertical approach. Potentials are recorded in response to faces by two electrodes, approaching the hippocampal formation vertically from the dorsal prefrontal cortex (right), or laterally from the posterior middle temporal g (left). A very focal N300 (○) is observed in both the posterior and middle hippocampus. In the middle hippocampus, a P500 (□) and N700 (▽) follow the N300. Medial to the posterior hippocampus, near the junction of the lingual and parahippocampal g, early potentials at 70 and 110 ms are observed. In the upper middle of the figure is a tracing of a saggital MRI at the level of the vertical electrode (conducted post-deplantation so that the edema surrounding the electrode tracks was visible). The three electrodes superior to the hippocampus were in the putamen, whereas those beneath the hippocampus were in the sulcus between the parahippocampal and fusiform gyri. Scale = 80 μV depth, 35 μV scalp. Patient no 8.

Responses to feedback tones were collected in most subjects but are discussed in another paper in relation to the N2/P3 in 'auditory oddball' tasks.

260 individual words were used, divided into two equivalent sets. In each set, 10 words were chosen to be targets and presented repeatedly ('repeats'), with the remaining 120 presented only once ('non-repeats'). During the input, each of the repeating words was shown for 10 s, and the subject was required to attempt to memorize it. EEG was not digitized during input. During output, 240 trials were presented every 3 s with rests after 80 and 160 trials. Of these 240 trials, 120 were the non-repeats, and the remainder were 12 repetitions of each of the 10 target words. Repeats and non-repeats were presented in random order, except that no individual word could be presented on two successive trials, no more than three repeats or three non-repeats could follow each other in a row, and each of the 10 targets occurred exactly once in each block of 20 slides. Consequently, the delay between successive presentations of a given word was filled with distractors, and had a duration of 6-117 s (average 61.5 s).

AD (21 patients), VD (12 patients)

In the auditory and visual oddball tasks with distractors, the patient responded to rare target rare stimuli by incrementing a silent count and by pressing a microswitch in the patient's dominant hand. Frequent and non-target (but rare) distracting stimuli were also presented, and were to be ignored. In AD, a 48 ms sound (including a 12 ms rise and 12 ms fall) was presented every 1600 ms at a comfortable level binaurally through a speaker located 2 m behind the patient's head. Rare (11% of trials), frequent (78%), or distractor (11%) trials, occurred in random order except that at least two

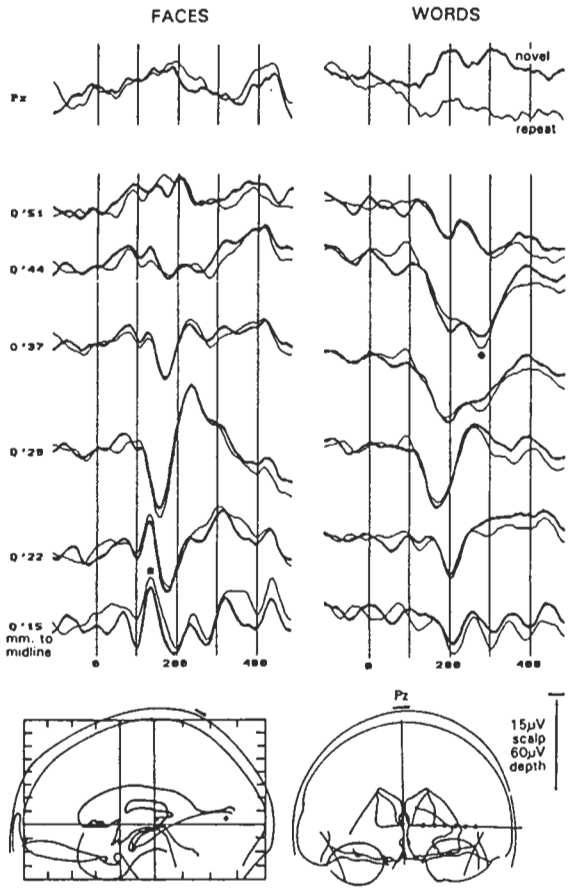


Fig 7. Left lateral occipito-temporal cortex word potentials. Positive potentials at 200 ms (60 μV) and 270 ms (70 μV) are recorded by the superficial leads (especially Q'44, 44 mm from the midline) of an electrode penetrating the left inferior temporal g/middle occipital g. The same leads show no activity evoked by faces. A more medial lead of the same electrode (Q'29, near the sulcus separating the fusiform and lingual g) shows a biphasic P160/N250 to both words and faces. The most medial leads (Q'22 and Q'15, near the precuneus) record a P100/N140 to faces only, and a P200 to both words and faces. (Note that a two-fold expanded timebase is used in this figure only). Patient no 18.

frequents occurred after each rare or distractor. The rare stimuli were tones ascending from 700 to 1000 Hz. The frequent stimuli were tones at a constant pitch of 670 Hz. The distracting stimuli were unique on each trial, with varying waveshape, pitch, and envelope. About 227 trials were presented per block, with 25 rares, 25 distractors, and 25 frequents (half each occurring just before a rare or a distractor), chosen for analysis. In VD, single letters or symbols subtending 0.43 degrees of visual angle were presented in white on a video monitor for 200 ms every 1600 ms. Rare stimuli were the symbol*, frequents were O, and distractors were capital letters. Between stimuli, fixation was maintained on a +. Details of these tasks and the potentials evoked by them are presented elsewhere (Halgren *et al*, submitted). We present these results here only insomuch as they help explicate the potentials evoked by faces and words.

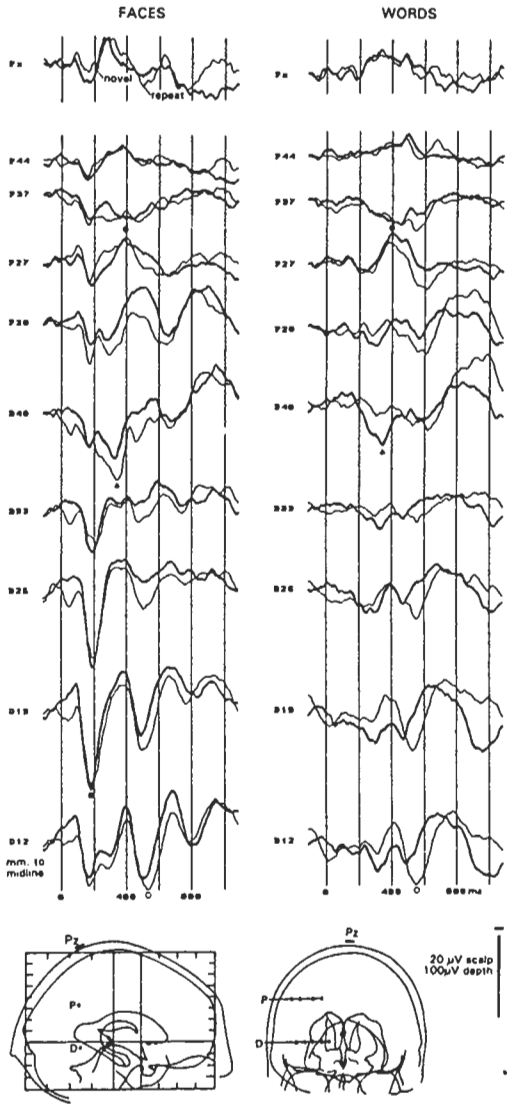


Fig 8. Face and word potentials in the right supramarginal and fusiform g. A small (about 50 μV) negative potential at 400 ms is recorded 27 mm from the midline in the supramarginal g (●), where it polarity-inverts more laterally (P37), and then back again in the most lateral lead (P44). This potential is about equal to words and faces, as is a P350 recorded focally deep to the posterior middle temporal g (▲: D40) and an N400-P550 (○) recorded in the lingual g (D12). In contrast, simultaneous recordings from near the sulcus separating the lingual and fusiform gyri (D19) demonstrate a large (100 μV) focal P190 to faces only (■). The earliest components (N100-P180) recorded in the most medial lead (D12: lingual g) also are specific to words. Patient no 23.

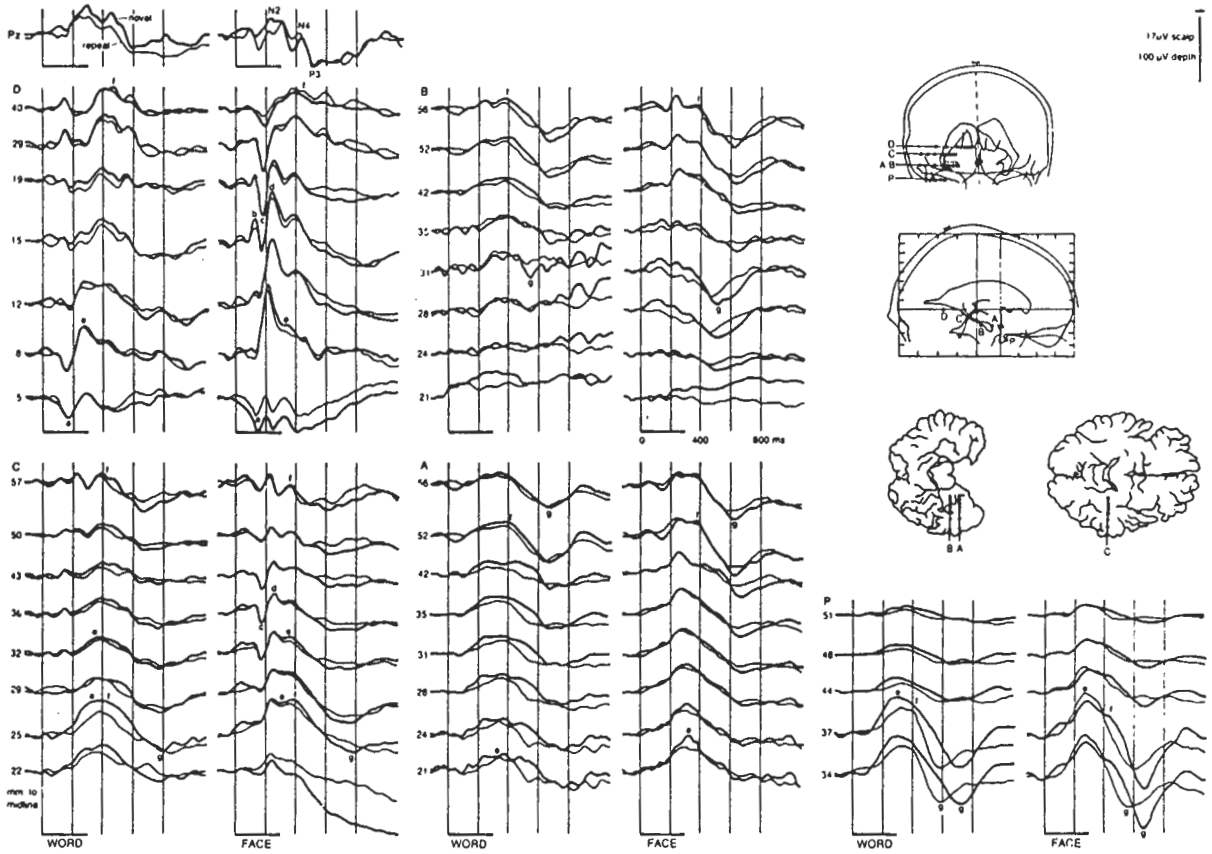


Fig 9. Medial and inferior temporal word and face potentials. Potentials were recorded simultaneously from 36 contacts on five electrodes in the right temporal lobe, plus the midline scalp (Pz) during word and face memory tasks. The earliest potentials are seen in the most posterior electrode D. Medially, in the lingual g (a, D5 and 8), a positivity at 150 ms to words and faces, is followed by a large negativity at 200 ms to faces only. Faces only also evoke a N140–P180–N220 in the fusiform g (D15 and 19, a-b-c), and extending to the surface of the posterior middle temporal g (D40) and the posterior hippocampal region (C32). Negativities at about 320 and 410 ms (e, f) are observed equally to both faces and words in all electrodes and many sites, including lingual g (note the small size but apparent inversion of the N410 between D5 and D8), fusiform g (despite the fact that earlier potentials in the same region are distinct to words and faces, D15 and 19), middle temporal g (posterior, D40, C50 and 57; and anterior, B52 and 56, A52 and 56), posterior hippocampus (C22–32), amygdala (A21–28), and temporal pole (P). A late positive component at 500–800 ms post-stimulus onset (g) is recorded in many of these same sites (especially posterior and anterior hippocampus, C25 and 29, B28 and 31; middle temporal g, C57, B52 and 56, A42–56; and temporal pole, P). The late negativities (N320–N410) are generally larger to the novel stimuli (especially when recorded medially to words), and the late positive component (P620) is generally shorter latency to repeated stimuli (especially in the temporal pole). Note that the N320–N410–P620 in the temporal pole are maximal medially (P34 and 37), and are larger than those simultaneously recorded in the amygdala (A21, 24 and 28), or anterior hippocampus (B21, 24, 28 and 31). The small potentials in the later structure could be related to the hippocampal cell-loss that was noted in the lobectomy specimen. Patient no 21.

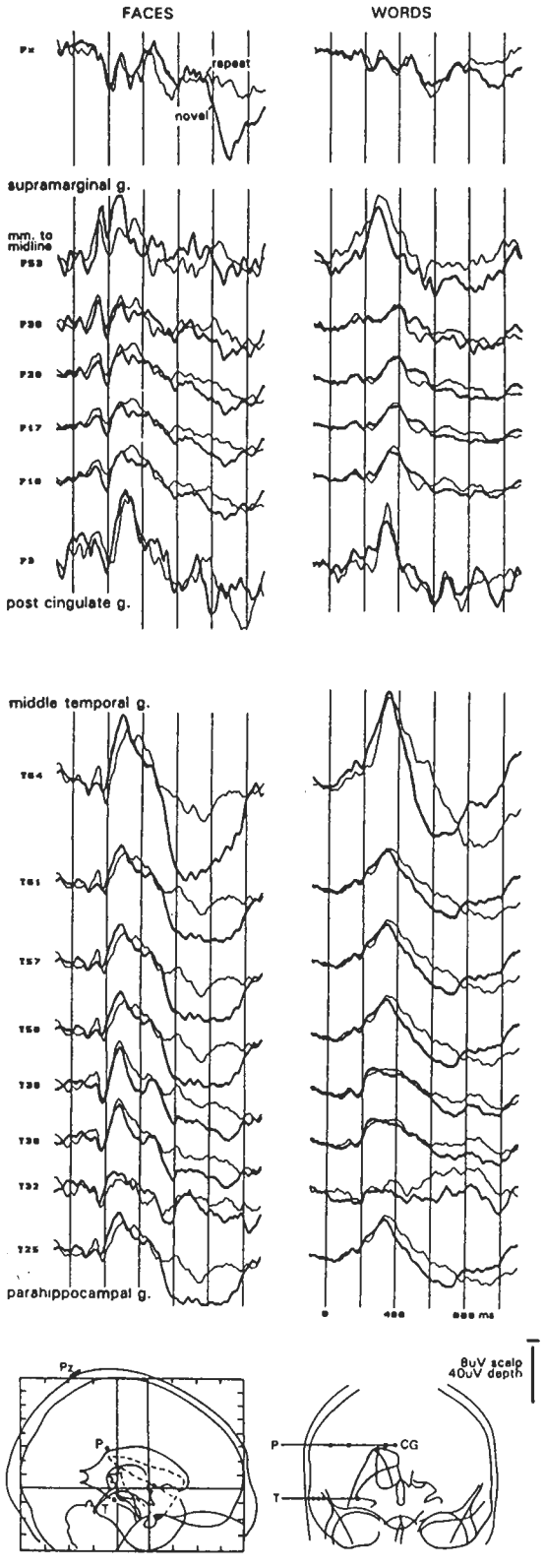
Results

Behavioral

Average reaction time was 626 ± 79 ms to correctly identified repeating faces, and 637 ± 67 ms to repeating words. Of the repeating faces, 78 ± 16% were correctly identified ('hits'), and 21 ± 18% of the non-repeating faces were falsely identified as having repeated ('false positives'). Performance for the words was 85 ± 18% hits and 17 ± 22% false positives.

Physiological

Visual inspection of the waveforms revealed a regular series of evoked potential components



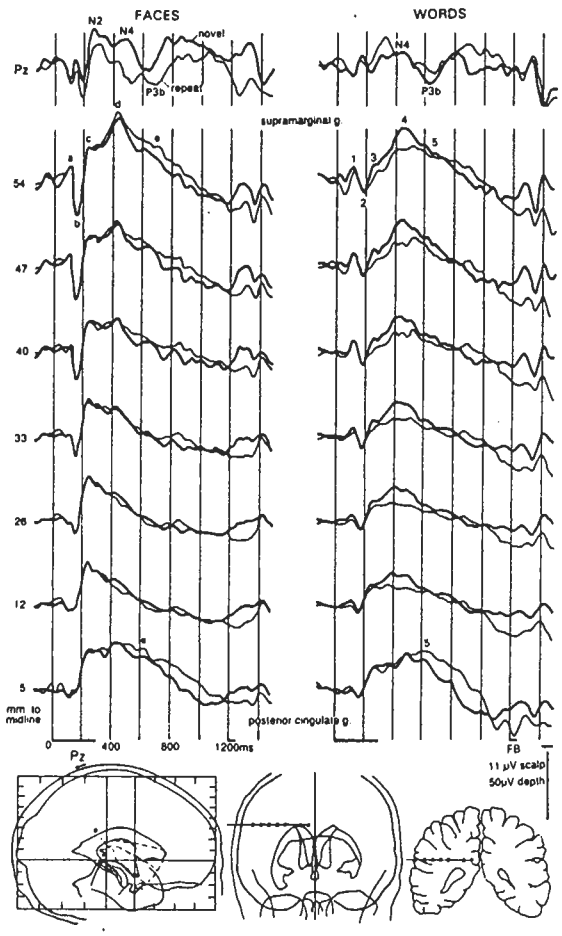


Fig 11. Parietal word and face potentials. A similar sequence of five components (N120–P190–N220–N430–N670) is observed both to faces (left: a, b, c, d, e) and to faces (right: 1, 2, 3, 4, 5). These potentials are recorded simultaneously by lateral leads (upper: 54, 47) in the right supramarginal g. and by medial leads (lower: 5, 12) in posterior cingulate g. The early potentials (N120–P190) are larger to faces and in lateral sites, where, however, they show no large voltage gradients. In contrast, the N430 (d, 4) is equal to words and faces, and shows significant voltage gradients both medially (5 ↔ 12 mm) and laterally (47 ↔ 54 mm.) Patient no 9.

Fig 10. Focal N300s in multiple sites. Somewhat focal negativities at about 310 ms were recorded at the scalp (Pz), and simultaneously in supramarginal g (P53), posterior cingulate g (P3), middle temporal g (T64), and posterior hippocampus (T25) during face and word recognition tasks. To faces only is seen a somewhat focal N160 in the supramarginal g, and a more diffuse P200 in both the parietal and temporal electrodes. Patient no 22.

with peak latencies from 70 to 1000 ms after stimulus onset. Certain early components were quite distinct for faces and words, whereas the later components tended to be similar in latency and localization (tables II, III).

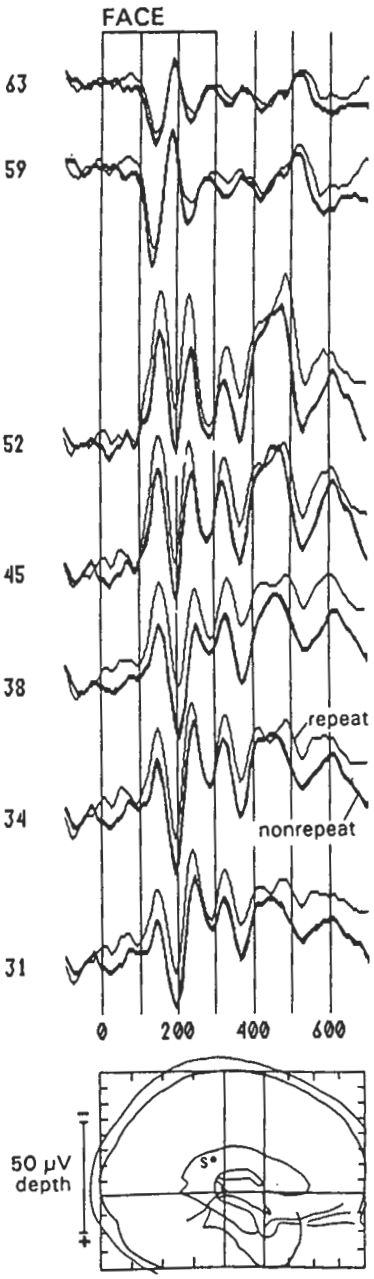


Fig 12. Inversion of the face P140–N190–P240 in the supramarginal g. A P140 (40 μV) – N190 (25 μV)–P240 (30 μV) evoked by faces in lateral leads (63, 59) of an electrode in the supramarginal g inverts in polarity in more medial leads (52, 45) to an N150 (65 μV)–P200 (5 μV) – N240 (65 μV) (marked as peaks 1, 2, 3). Later peaks at 290 and 450 ms are focal but do not clearly invert (4, 5). Patient no 2.

Components evoked by faces

N75–P105

Lingual gyrus. Faces initially evoked specific visual potentials which were focal in medial posterior leads, localized to the lingual g, areas 18 and 19 of the medial occipital lobe (fig 3, O17; fig 4, 16, 20; fig 5, D23, D30: note that recorded waveforms illustrated here are referred to by their figure number, then electrode, then distance in mm to midline: 3-O17 refers to a contact 17 mm from midline on electrode O in fig 3). In one case, the same response was observed more anteriorly in the posterior parahippocampal g (fig 6-24: note that 'lingual' and 'parahippocampal' are two names for different segments of a single gyrus stretching between the occipital and temporal poles). This first component had a latency

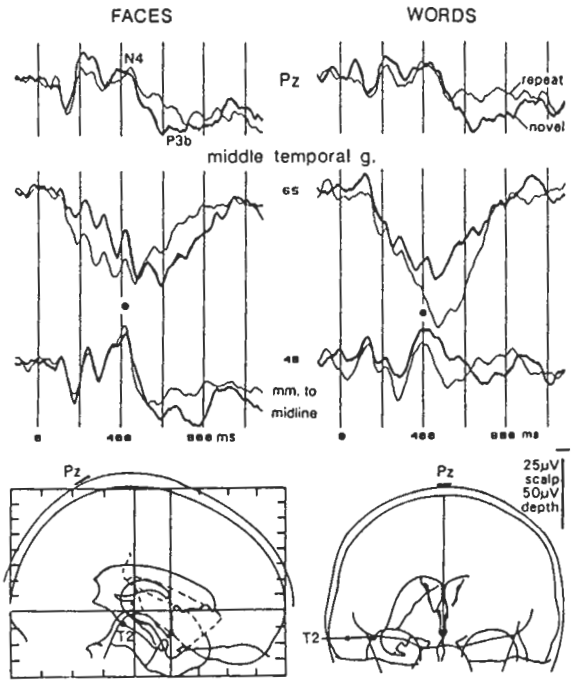


Fig 13. N400 polarity-inversions near the superior temporal sulcus. An inversion is noted of a potential evoked by faces and words at about 410 ms in the right middle temporal g (area 21), between leads 48 and 65 mm from the midline (C48 and 65). Words especially also evoke a large positive LPC-like component at slightly longer latency in C65. An N4/P3b with similar latencies are seen in simultaneous scalp recordings (Pz). Patient no 20.

to peak of 65–80 ms and could be either negative (table II: fig 3-O17; fig 7-Q'15) or positive (fig 4-16, 20; fig 5-D23, D30; fig 6-24). This component was always followed by a second component of opposite polarity peaking at about 105 ms (this component was also occasionally recorded in the fusiform g). The N75–P105 did not polarity invert across successive contacts of the same electrode. However, the polarity of these potentials seemed to vary between patients (*ie* a P75–N105 instead of a N75–P105). Furthermore, these potentials were quite focal, and were followed by a large focal alpha rhythm (see below). Sites recording focal N75–P105 had the approximate coordinates: ± 24 (lateral, mm to midline, positive right), −58 (anteroposterior, mm to the AC line, positive anterior), −4 (vertical, mm to the AC–PC line, positive up). Also note that the zone with focal N75–N105 is not necessarily the most medial contact, which may instead display an N130–P180 like the fusiform g (see below: fig 5-D16; fig 8-D12).

N130-P180-N240

A negative-positive-negative EP sequence was recorded in several sites in all lobes. The first peak had a latency of 90–150 ms, the second of 140–200 ms, and the third of 200–280 ms. These potentials were most prominent in the basal occipito-temporal cortex. The three peaks usually occurred together, with the initial negative peak several times smaller in amplitude, especially in recordings outside the mediobasal temporo-occipital cortex. In nearly all cases, the initial two potentials are evoked only by faces, not by words. However, the N240 had a wider distribution than the P180–N240, and also was either less specific for faces (as compared to words), or overlapped with other components with different topographies and task correlates but similar latencies. Distinguishing between these possibilities was sometimes not possible in this study, and will require further recordings with additional tasks.

Fusiform g. The N130 was usually largest in the fusiform g (up to 60 μV: fig 3-O31, R34, L33) at the basal occipito-temporal junction (areas 19 and 37). Because the electrodes took in nearly all cases a horizontal medial-to-lateral trajectory, gray matter recordings were from the sulci penetrating the ventral occipito-temporal surface, rather than from the ventral surface itself. Clear potentials were recorded from contacts with coordinates of about ± 15 to 34, −45 to −65, +2

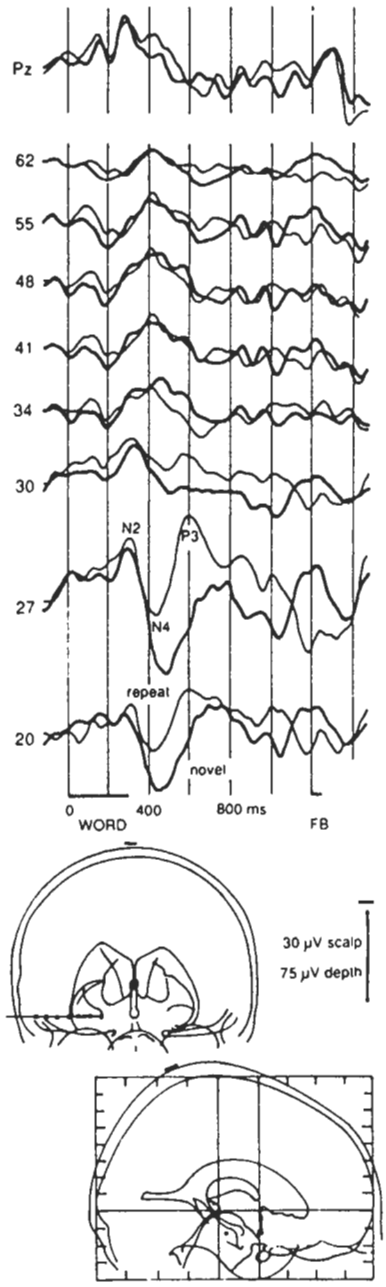


Fig 14. Hippocampal word potentials: Lateral approach. In the anterior hippocampus (20 and 27 mm to midline), a focal N310-P460 N600 sequence is observed. The P460 is larger to novel words, and inverts as the electrode crosses into the lateral ventricle (30), white matter (30, 34), and then middle temporal g (41–62). In contrast, the N600 is larger to repeated stimuli, and has a less clear inversion in more lateral leads. Finally, the N310 is about equal to repeated and nonrepeated stimuli, and does not polarity invert but is somewhat focal in the hippocampus. Patient no 10.

to −12, with the largest potentials tending to be recorded at around ± 30,−58,−5. The topography of this field can be appreciated in figure 3, where at the mediolateral level of the fusiform g, both posterior (O31) and anterior sites (right R34, and left L33) produce large N130s, but more medial and lateral sites do not. In most cases, words evoked no activity from the same electrode contacts (fig 4-30; fig 8-D19; fig 9-D19).

Like the N130, the P180 is usually largest in the fusiform g (up to 165 μV: fig 3, O31, R34, L33) at the basal occipito-temporal junction, and these potentials displayed a very similar topography (areas 19 and 37). Possible polarity inversions of the P180 were observed along successive contacts of an electrode, inverting to a negativity more medially (fig 3, O31 to O24; fig 4, O27 to 23). Again, in most cases, words evoked no activity from the same electrode contacts (fig 4-30; fig 8-D19; fig 9-D19).

The N130–P180 to faces in the fusiform g was nearly always part of a triphasic complex which included also the N240. The N240 was prominent in the fusiform g, where it was often highly focal and up to 93 μV in amplitude (fig 3-O31, R34, L34). When recordings were obtained from the same contacts in response to words and faces, the N220 was then only evoked by faces (fig 4-23; fig 7-Q'29; fig 9-D15, 19). The N240 tended to have a wider distribution in this region than the preceding N110–P170 (fig 3-L26).

Supra marginal g and other parietal sites. The supramarginal g was recorded from 22 (18 right, four left) electrodes implanted in 21 patients. Recordings were obtained during WORD only (three right, two left), FACE only (six right, one left), and both (nine right, one left). Recorded sites were mainly in the right hemisphere, in the post-

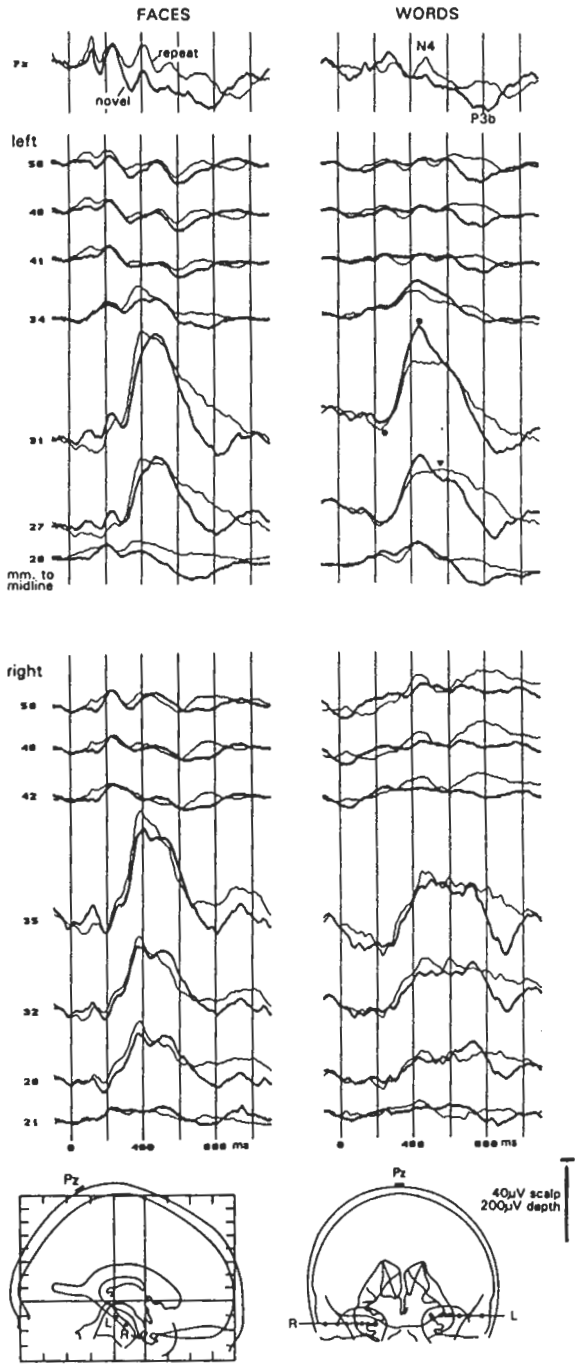


Fig 15. Large bilateral negativities evoked by both words and faces simultaneously in the left and right hippocampi. As is typical for recordings passing through the hippocampus from lateral to medial, the potentials are very large (up to −280 μV), and show steep voltage gradients both medially and laterally. However, the largest potentials, peaking at about 400 ms, do not, strictly-speaking, polarity-invert. In contrast, possible inversions of the N280 to words on the left (between 20 and 27, and again between 31 and 34 mm, from the midline), and of the N200 to faces on the right between 20 and 27, and 35 and 42 mm). The P280 (●)–N400 (■)–N600 (▲) sequence is substiantially the same to faces and words, and similar in the left *versus* right hemispheres. Comparison of the electrode tracts with respect to the lateral ventricles (Talairach *et al*, 1958, 1967) indicated that on the left, the electrode contacts were located in the cisterna ambiens (left 20 mm, to midline), middle hippocampus (27, 31), lateral ventricle (34), white matter (41), and superior temporal sulcus (48, 58); and on the right the medial four contacts were located in the anterior hippocampus (21, 28, 32, 35), and the lateral three in the middle temporal g or underlying white matter (42, 48, 59). Patient no 19.

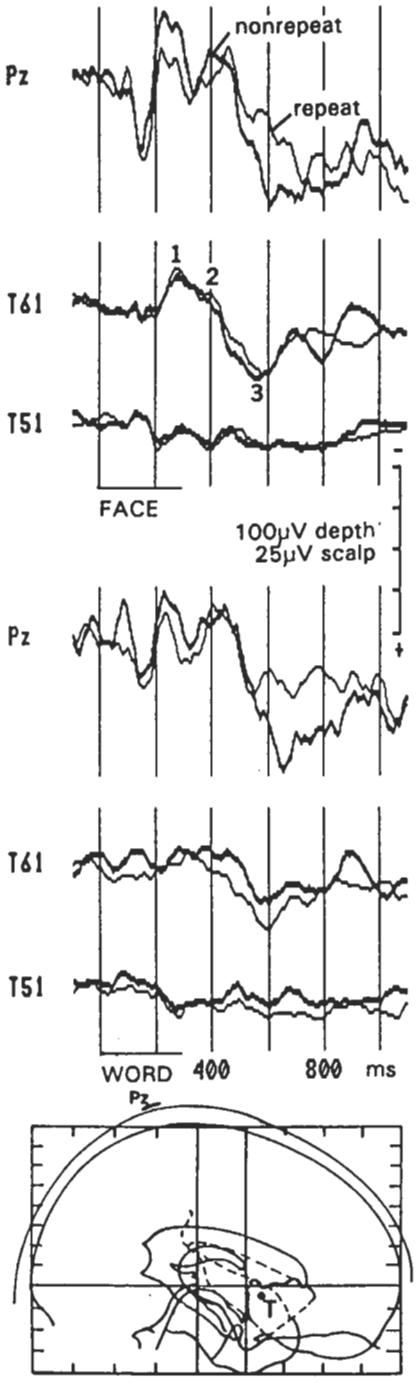
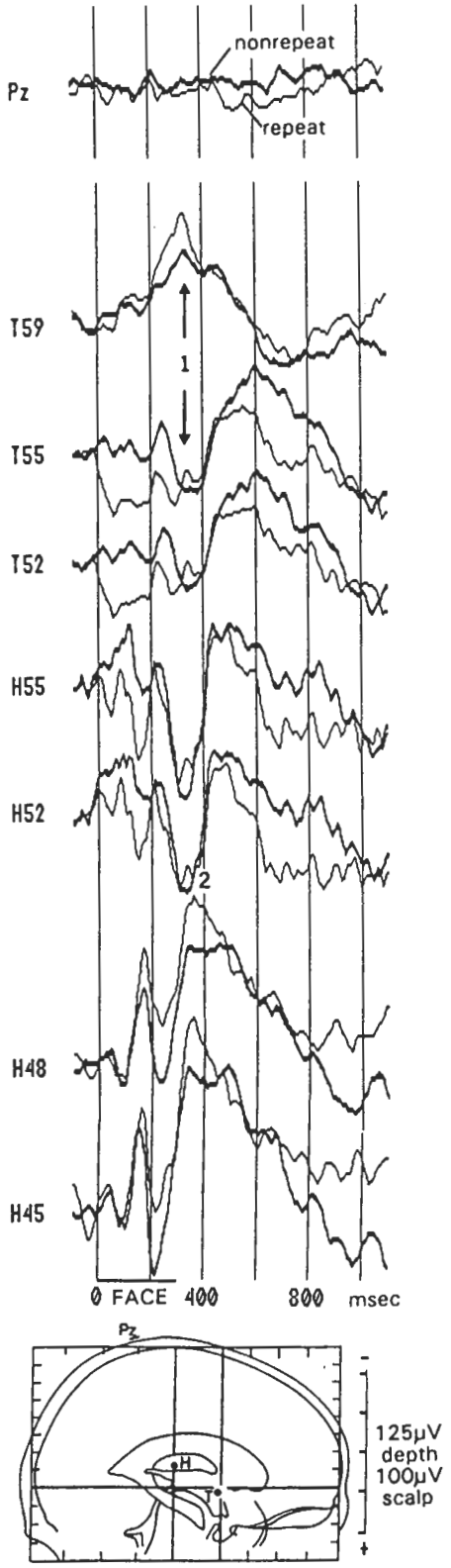


Fig 16. N2-N4-P3b to faces and words in the right anterior superior temporal g. Negativities at about 280 ms (1) and 400 ms (2), followed by a positivity at 560 ms (3) are clearly evoked by faces and perhaps by words in the superior temporal g, and at similar latencies at the scalp. Even through the depth potentials are small, they are absent 10 mm medially, suggesting generation may be in the overlying superior temporal plane or in the underlying superior temporal sulcus. Patient no 20.

erior bank of the ascending ramus of the Sylvian fissure (area 40: coordinates +50, −40, +25). A clear N130–P190 was observed in the supramarginal g, mainly to faces (fig 5-I56; fig 8-P37; fig 10-P53), but also to a small degree to words (fig 11-54). The N130 was seen in all 22 electrodes with an average latency of 146 ms to faces and 152 ms to words (tables II, III). Of the 10 patients with recordings during both faces and words, the N130 was about equal in two patients, the N130 was greater for faces in five (including the one patient with a left implant), and the N130 was evoked exclusively by faces in three. The P180 was seen in 15 electrodes in 15 patients with an average latency of 193 ms to faces and 212 ms to words. Of the six patients with a P190 and with recordings during both tasks, the P190 was about equal to faces and words in one patient, the P190 was greater for faces in three (including the one patient with a left implant), and the P190 was evoked exclusively by faces in two. Again, the N240 was more equivalent to faces and words. Its latency in these structures was about 260 ms.

In one patient, an N150–P200–N250 sequence to faces (words were not recorded) was observed to polarity-invert in more lateral contacts (fig 12-S52 to S59). Although polarity inversions were rare, the responses were often large (up to 60 μV) and sometimes displayed moderately steep voltage gradients. A much smaller and possibly volume-conducted N120–P190 was often recorded by the deeper contacts of the same electrodes, in the posterior cingulate g (fig 10, P3; fig 11-5). In the one patient in whom recordings were obtained in the sulcus between the superior and inferior parietal lobules, a large (> 100 μV) focal N130–P180 was recorded (fig 5, Q32: area 7 or 40). Again, deeper contacts near the precuneus recorded smaller but similar potentials (fig 5-Q18).

Lateral temporo parietal cortex. A large number of recordings were made in the middle temporal g, from about +5 to −65 (with respect to the AC–PC line), but relatively little responsiveness was observed during this latency window. The only partial exception were recordings in the vicinity of the PC line (−25) where small (about 15 μV) N130–P180s were recorded (fig 9-B56; fig 10-T64; fig 13-48). An interesting contrast with parietal recordings is seen in figure 5, where the N130–P180 in the posterior superior temporal g (L49: area 40 or 22) is much larger than the simultaneously recorded potentials in the posterior middle temporal g (D59: area 21).



The face-specific N240 was present in many of the same sites where the earlier P180 was observed, *ie* in the region of the middle superior temporal sulcus (fig 9-B56; fig 13-48), and the posterior superior temporal g (L49; area 40 or 22). Contacts in the posterior middle and inferior temporal g (area 37; approximate coordinates ± 55,–60, 0) sometimes recorded a large N240, only to faces, and without necessarily a large preceding N130–P180 (fig 4-52; fig 5-D52, 59).

Medial temporal lobe. In addition to clear early responses in the posterior parahippocampal g (see above), the P180 component was sometimes recorded by contacts in the hippocampal formation. Although this can be seen to both words and faces, it is far greater to faces (fig 9-C32; fig 10-T36). These potentials are clearly more prominent in the posterior than in the anterior portion of the hippocampal formation (figs 6, 9, 10), where it is either not seen at all (figs 6, 9, 10, 14), or difficult to distinguish from the background noise (fig 5, B35; fig 15, R35 faces). Convincing components in this latency range were not observed in more anterior medial temporal sites (amygdala and temporal pole). However, in these sites as well as in the anterior hippocampus, an early N130 was sometimes observed (fig 9-A27, P34). Again, these potentials were not always clearly distinguishable from the noise, but occurred in enough subjects that they appear to represent a real phenomenon.

Within the posterior hippocampal formation, the P180 often changes very markedly in amplitude from medial to lateral recording sites. In six cases with a typical placement (a mean of 7.7 mm posterior to the PC line, and 0.7 mm superior to the inferior limit of the lateral ventrical), the P170 is maximal in the contacts just lateral to the hippocampal formation, in the lateral ventrical or white matter of the temporal stem, directly superior to the collateral sulcus between the parahippocampal and fusiform gyri (fig 9-C32; fig

Fig 17. Inverting N330-420 to faces in the right superior temporal g. Recordings from two electrodes, one near Heschl's g (H), and one in the anterior superior temporal g (T), both showing possible inversions of a potential peaking about 400 ms after face onset (1, 2). Note that the larger potentials are observed in posterior sites, and the polarity of the more lateral potentials may be either positive (1) or negative (2). Patient no 16.

10-T36: approximate coordinates ± 37,–31,–8: above area 20 or 36). However, in two electrode trajectories positioned more postero-inferiorly (a mean of 16.5 mm posterior to the PC line, and 3.3 mm inferior to the inferior limit of the lateral ventrical), the P170 was maximal in the medial contact, in the medial part of the posterior parahippocampal g, corresponding to area TF/TH, entorhinal ctx, and/or subicular complex (fig 6, left 24). A small (especially relative to other potentials recorded later from the same sites) but clearly present N240 was sometimes recorded in the posterior or middle hippocampus, to faces and not to words (fig 6, right; fig 9-C32; fig 15, left 31).

N300-N450-P600

Right fusiform g When recordings were made in the right fusiform g to words and faces, it was usually observed that the N310–N430–P630 were evoked largely or exclusively to faces rather than words (fig 4-23: coordinates +23, –64, +3; area 19). It is interesting that this face specificity could be observed in the same electrode track where more medial contacts in the lingual g (fig 4-16, 20), and more lateral contacts in the inferior temporal g (fig 4-52), lacked any obvious specificity in the N430 for faces over words. In other cases, however, the N450 within the fusiform

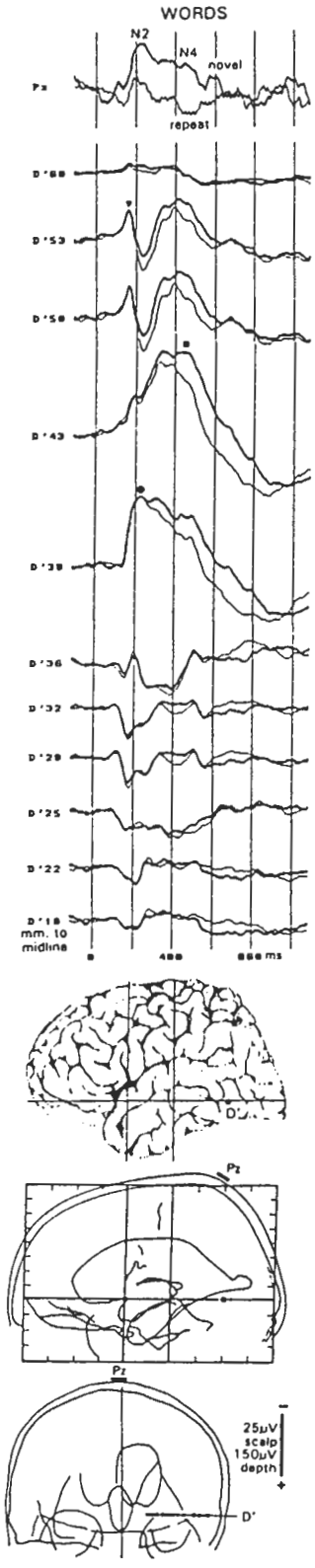


Fig 18. Anatomically distinct inversions of the N220, N330 and N460 evoked by words in the left inferior temporal, fusiform and lingual gyri. The electrode entered the inferior temporal gyrus (D'53, 50), passed through the fusiform g (D'43, 39, 36, 32), and terminated in the lingual g (D'25, 22: locations were confirmed using serial 5 mm MRI sections). The largest potentials (up to 170 μV) are a N210–N330–N460 sequence recorded in the fusiform g at about the same time as the scalp (Pz) N2–N3–N4. These potentials are maximal in the part of the fusiform g lying within the inferior temporal sulcus, with the N120 maximal slightly more medial (D'39; ●) than the N330 (D'43) and N450 (D'43; ■). The N210–N330–N460 invert to a small positivity medially within the white matter of the fusiform g, again at slightly different levels (D'32 for the N210, D'36 for the N330-N450). These late potentials are larger to novel than to repeated words as are the simultaneously-recorded scalp potentials (Pz). More medially, the 330-N450 are much smaller, but seem nonetheless to undergo another polarity inversion from the collateral sulcus (D'29) to the lingual g (D'25). Laterally, within the inferior temporal g, an N170 (D'53; ▼), then P240, and finally N330-N450 are observed. MRI sections were used by Dr Bertrand Devaux to trace the gyral pattern in the lateral view, below the EP traces. Patient no 25.

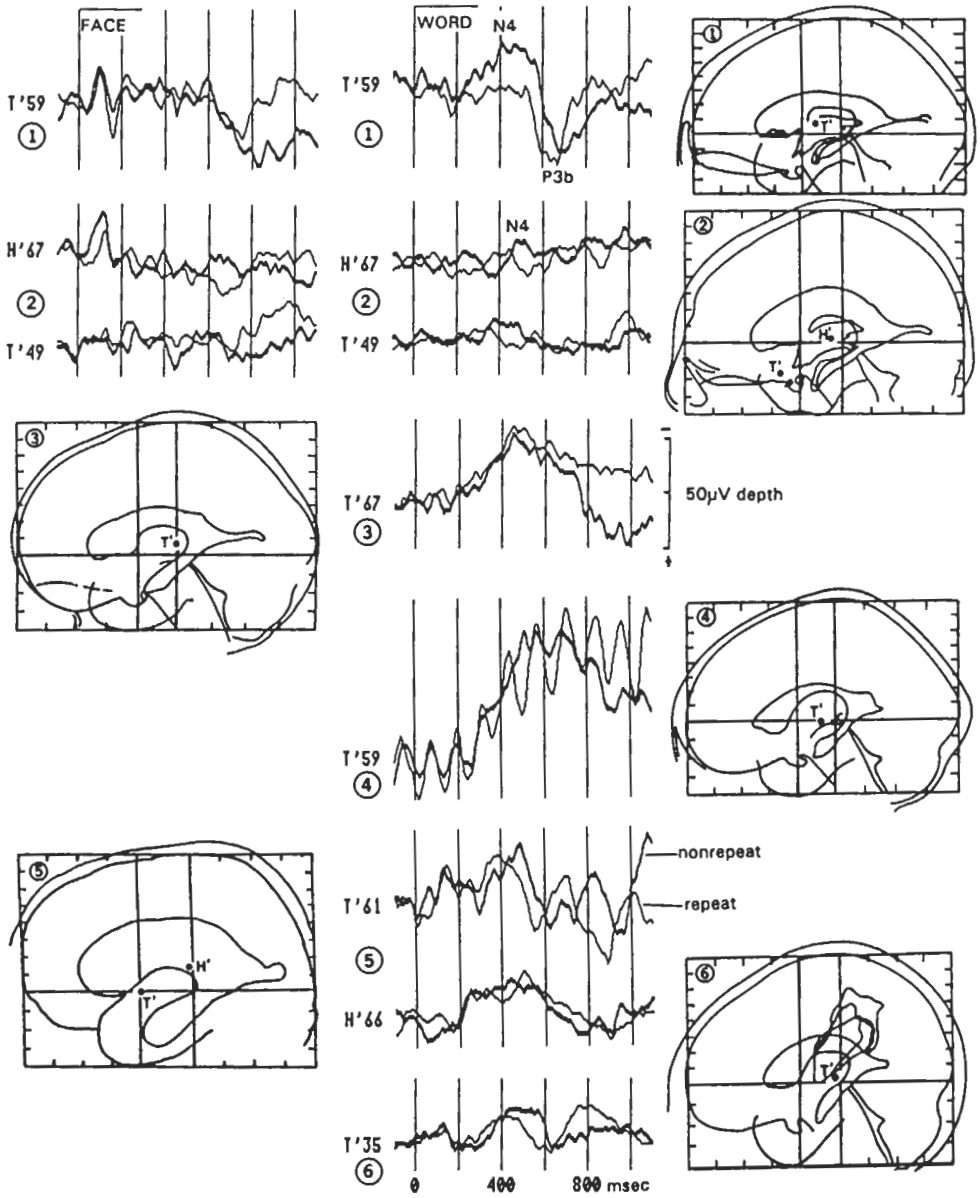


Fig 19. Lack of large endogenous activity to words in the left superior temporal g. Potentials evoked by words in the left posterior temporal g are from 10 to 30 μV in six patients (1, T'; 2, H'; 3, T'; 5, H'; 6, T'), and larger but superimposed on large alpha activity in one subject (4, T'). Potentials from more anterior superior temporal sites (2, T'; 5, T'), and from the same sites in response to faces (1, 2), are also small. In one patient (1, T'59), the N4-P3b sequence appears to be larger to words than to faces. Patients nos 11, 28, 46, 40, 25, 38.

g was also about identical in amplitude to words and faces. These cases are described below.

Right superior temporal lobe. In one patient, a small but typical and focal N280–N400–P560 sequence was evoked by faces but not by words (fig 16-T61). In another patient, the N330 evoked by faces was large (up to 100 μV) and polarity-inverted over short distances (fig 17-T59 to 55, H48 to 52), but potentials to words were not recorded in this patient. These electrodes penetrated the superior temporal g, and they may have recorded potentials from the overlying superior temporal plane, or from the underlying superior sulcus.

Components evoked by words

P190–P220

Fusiform g. Early potentials recorded in the fusiform g were usually strikingly different for words as compared to faces. Whereas occasionally both evoked a positivity at about 190 ms, their distinct topographies indicate that they are distinct components (on the right, fig 4-30; on the left, fig 7-Q'29; fig 9-D15, 19). This P190 was usually followed by a P220 to words only (on the right, fig 4-30; on the left, fig 7-Q'29).

In one patient, a 160 μV negativity peaking at 210 ms was evoked by words in the part of the left fusiform g lying in the sulcus between it and the inferior temporal g (fig 18-D'39: coordinates –39,–63, 0: area 19 or 37). This potential was very focal, inverting to a 40 μV positivity at the site 7 mm medial to the sulcus (within the white matter of the fusiform g itself). This site was not recorded during the FACE task, so the specificity of the response for words remains to be demonstrated.

Left lateral occipito-temporal cortex. In one patient, with an electrode lying in the most posterior part of the left superior temporal g (or the most anterior part of the middle occipital g, below the angular g, probably area 37) a P200 was evoked by words, but not by faces (fig 7, Q'44: coordinates –44,–56,+2).

250

Left lateral occipito-temporal cortex. The left posterior superior temporal g (near angular g) electrode that recorded the P200 (described just above) also recorded a P270 to words, but not to faces (fig 7, Q'44). Overall, at a latency of about 270 ms in the lateral occipitotemporal cortex, words tended to evoke a positivity (table III), whereas faces tended to evoke a negativity (table II), as in other sites.

Supramarginal g. The supramarginal g (area 40) was recorded in 21 subjects (22 electrodes: figs 5, 7, 10, 11, 20). A potential with latency to peak at about 290 ms was recorded in the supramarginal of 13 electrodes (12 subjects). Usually, this potential was positive, low amplitude, and appeared to be volume conducted from another location. However, in two subjects, this potential was found to be quite focal and about 50 μV in amplitude (fig 10, P53). The P290 was recorded in six subjects presented with both the WORD and FACE tasks, all with implants in the right hemisphere. It was about equal in one subject, was greater for words in two subjects, and was evoked exclusively by words in three subjects. In one patient, an N150–P210 to words (potentials to face were not recorded) polarity-inverted in the left supramarginal g (fig 20, Q'37 to 44).

N310–N460–N600

Left posterior superior temporal g. This region, part of the classical Wernicke's area, produced only small potentials to words, which, however, could occasionally appear to be larger to words than to faces (fig 19).

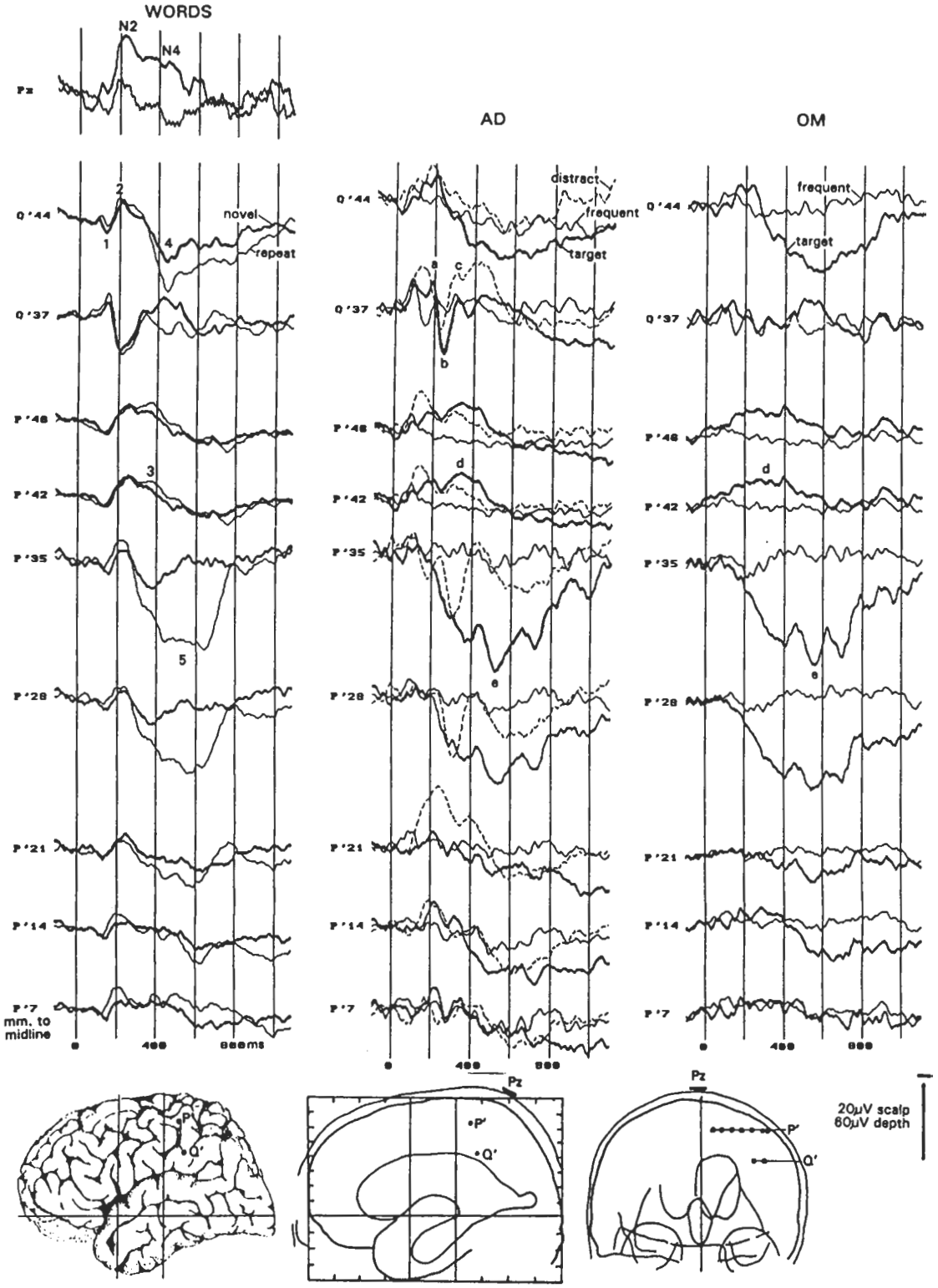
Left fusiform g. Very large (about 170 μV) negative potentials with peaks at 310 and 460 ms were recorded in one patient in the left fusiform g, in the inferior temporal sulcus between the fusiform and inferior temporal g (fig 18, D'43, 39: coordinates –41, –63, 0: area 19 or 37). These components polarity-inverted in the lead 7 mm medial to the sulcus in the white matter of the fusiform g (fig 18, D'36). Since the FACE task was not given to this subject, the specificity of this response for words rests unconfirmed. However, similar very large and focal potentials were often observed in the homologous areas of the right hemisphere in response to faces (see above), but only small responses were evoked in the right fusiform g to words (*eg* fig 4, 30; fig 8, D26; fig 9, D19).

Components evoked by both faces and words

N150–P200–PN260

Early components evoked both by words and by faces were small, and often were obscured by larger N130–P180–N240 potentials evoked by faces only. In addition, the N150–P200–PN260 did not constitute a widespread characteristic waveform like the N110–P170–N220, and many sites lacked one of its components, as noted below.

Lingual gyrus. Following the N74–P105 evoked in the lingual g only by faces, later components tended to be similar to words as compared to faces. These consisted of a positivity between 160 and 220 ms, followed by a negativity peaking between 230 and 270 ms. Often, the latency of the corresponding peaks was about 10 ms earlier for faces than words. Similar components were observed in the left (fig 7-Q'15, 22; fig 18-D'18)


WORDS
N2
N4
Pz
AD
OM
novel
repeat
distract
frequent
target
mm. to midline
20μV scalp
60μV depth

and right (fig 4-16, 20; fig 13-D5, 8) hemispheres. These potentials were small, but distinct from those recorded in adjacent structures.

Lateral occipito-temporal cortex. An N150–P250 was the most commonly observed pattern in this area (generally consisting of area 37 at the junction between the posterior parts of the inferior and middle temporal g, and in the inferior temporal sulcus, coordinates ± 52, –62, 2). However, in one case, these components were observed more medially, in the left fusiform g (fig 7, Q'29).

Both faces and words were observed to evoke an N150–P250, and in both the right and left hemispheres (fig 4, 52; fig 18, D'50, 53). These potentials were often large (up to 75 μV) and very focal. In several cases, it appeared that the N150 to faces in this region was difficult to appreciate due to cancellation by a volume-conducted P150 from the immediately medial fusiform g (fig 9-D40). Similarly, it appeared that the P250 to faces could be obscured by the N220 (fig 4-52).

N310–N430–P630

Lingual g. Moderate N310 (up to 70 μV), N430 (up to 50 μV), and/or P630 (up to 60 μV) components were commonly observed in the lingual g (fig 3-O17, R20, R27, L19, L26; fig 4-16, 20; fig 8-D12, D15; fig 9-D5, D8). These components were sometimes focal, and polarity inversions in this polarity range were often observed, seeming most related to the N430 (fig 3-L19 to 26; fig 9-D5 to 8; fig 18-D'22 to 25). This N310–N430–P630 in the lingual g could occur alone (fig 3-R27, L26), or could occur with a superimposed alpha rhythm (fig 3-O17; see below).

Fusiform g. As described above, face-specific N310–N430–P630 sequences were observed in the right fusiform g, and a possibly word-specific sequence was observed in one left fusiform g. In other cases, however, the N430 to words and faces was about identical in amplitude, even when earlier potentials were much larger to faces (fig 8-D19, 26; fig 9-D15, 19). These non-specific responses were smaller than the word- or face-specific potentials in the fusiform g, being up to 70 μV for the N430, and up to 60 μV for the P630 (fig 3-O31, R34, L33; fig 4-27; fig 9-15, 19). A possible inversion of a small non-specific N390 was observed in this region (fig 8-D26 to D40).

Lateral occipito-temporal cortex. Electrodes in the posterior part of the middle or inferior temporal gyri, areas 37 and 21, consistently recorded N430 potentials, usually small (fig 3-O45, R55, L54; fig 5-L49; fig 9-D40), but sometimes fairly large (fig 4-52; fig 5-D59; fig 18-53). Sites recording large potentials had approximate coordinates of ± 53, –63, 0. In one case, a possible polarity inversion of a potential with a latency of 330 ms was noted in this region (fig 8-D40 to D26). These potentials were in all cases approximately equal in amplitude to words and faces. For example, note the similarity of the N310–N430 potentials evoked by words in the posterior inferior temporal g, in the right (fig 4, 52 mm from midline) and left (fig 18, 50 mm from midline) hemispheres.

In general, potentials recorded more anteriorly in the middle temporal g were small (fig 5-C66; fig 6-73; fig 9-C57, B56, A56, P51; fig 14-62; fig 15-L58, R59; fig 21-60; fig 22-A'58). In all of these cases, the potentials observed in the middle temporal g tended to resemble those recorded simultaneously at the scalp in waveform, polarity and latency. However, a second focus of

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Fig 20. Long-duration, moderately-large positive P3b-like activity recorded in the left parietal lobe. In response to words, the initial potentials at 140 and 200 ms (1-2) as well as the N4-like potential at 420 ms (4) invert polarity in the left supramarginal g (between Q'37 and Q'44). A potential at 350 ms (3) also inverts more superiorly between P'42 and P'35, just posterior to the postcentral g. Also polarity-inverting between the same two sites is a P3-like potential (d) evoked by rare target as well as rare non-target tones in an auditory oddball task (AD), as well as by rare target stimulus omissions (OM). In contrast, in the supramarginal g (Q'37), rare target and nontarget tones evoke a negative-positive-negative waveform with peaks (to targets) at 190, 260 and 320 ms (a, b, c), and associated in other studies with the N2/P3a/SW (as is often observed in the SMG, there is a second positive peak following the SW, with a latency of about 370 ms). Following the potential at 300 ms is a large late positivity to repeated words or rare target events that is maximal in P'35, where it extends from about 280 to 800 ms (5,e). It is smaller in more medial leads of the same electrode (P'28, P'21), and is absent more laterally. In another task given to the same patient, this positivity was noted only to trials when the response key-press was made by the right hand, suggesting that it is related to somatosensory feedback from the behavioral response. Consistent with this interpretation, note that the late positivity does not occur to rare nontarget events. Patient no 25.

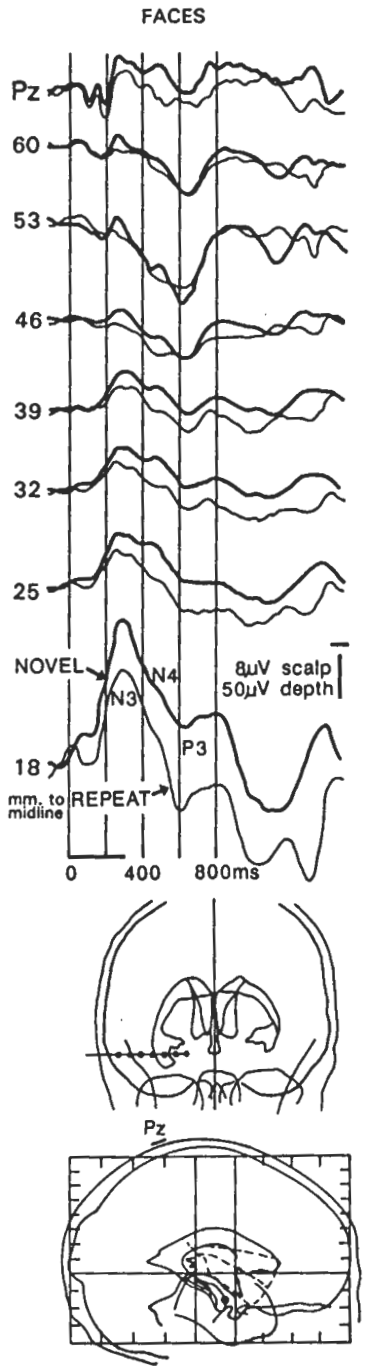


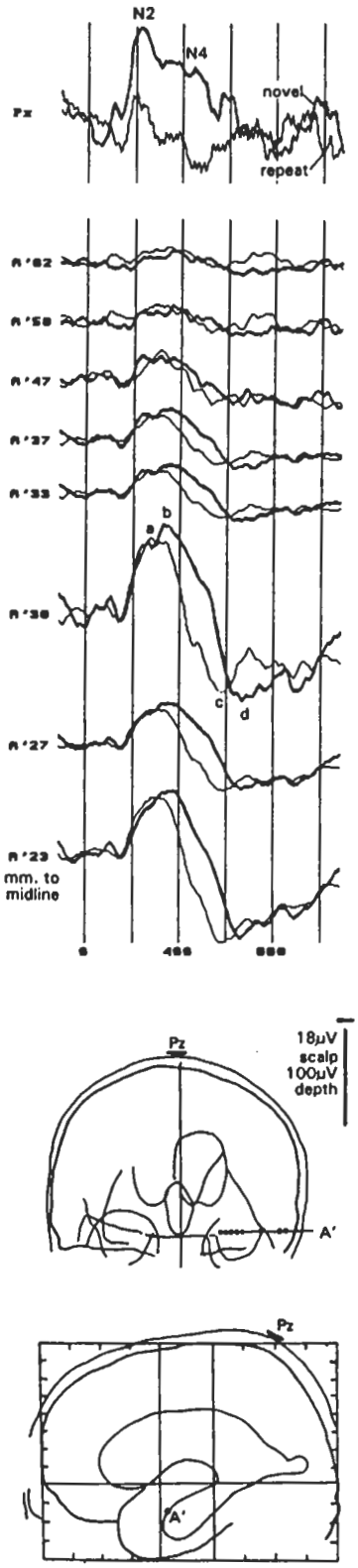
Fig 21. Amygdala face potentials. A −150 μV N290 peak (N3), an N440 inflection (N4), and a P600 peak (P3), are evoked focally in the amygdala (at the tip of the electrode, 18 mm to midline). The N290/N440 are larger to novel faces, and the P600 to repeated faces. Peaks with similar latency are recorded also in the lateral contacts of the same electrode lying in the anterior middle temporal g, where the P600 is more prominent. Patient no 9.

large or inverting potentials was noted in a small number of patients at about the level of the PC line (approximate coordinates ± 64, −26, −8: area 21). In these sites, the N310, N430, and/or P630 were found to have very steep gradients, or even polarity-reversals, although their maximum amplitude was only about 80 μV (fig 10, T64; fig 13, 65).

Hippocampal formation. Recordings were obtained from 26 patients with electrodes implanted in the anterior hippocampus, including one with bilateral implants. Of these 27 electrodes, clear endogenous responses were observed in only 13. In the unresponsive electrodes, high noise levels were observed. On the other hand, if a response was observed, it was usually high amplitude, and the largest responses observed in this study were recorded in the hippocampal formation. The posterior hippocampus was implanted in 18 patients (19 electrodes), and endogenous responses were visible in 18 electrodes. Previous studies suggest that the absence of potentials in the hippocampus reflects sclerotic or other pathology (Squires *et al*, 1983; Wood *et al*, 1988; Puce *et al*, 1989). Such pathology is more common in more anterior levels of the hippocampus.

The waveforms of the responses recorded in the hippocampus were extremely variable. Broadly speaking, three components could be identified, peaking between 250 and 360 ms (N310), 360 and 520 (N430), and 520 and 760 ms (P630) post-stimulus onset, respectively. The polarity of these components could be either positive or negative, but were usually negative. In any case, the largest potentials were negative, and exceeded 200 μV in amplitude for all three components. Often, the N310s were difficult to distinguish from the following N430, which in turn merged with the inverted P630 often recorded in this structure.

When considering the largest response in a given electrode track penetrating the anterior hippocampal formation, 9/9 N310 responses, 10/13 N430 responses, and 11/13 P630 responses were negative. A similar proportion of negative and positive responses was observed in the posterior hippocampus. When considering the anterior and posterior hippocampus together, in seven cases the most prominent potential is the N310 (figs 5, 6, 10), in six cases the N430 (figs 14, 15), and in seven cases they about equal (fig 9, C). The topographies of the N310 and N430 were clearly different, and could invert or change between leads independently (fig 23). These potentials are



large both left and right, anteriorly and posteriorly, to both words and faces. There was no obvious difference in the locations within the hippocampus where the N310 and/or N430 were positive (*eg* fig 15), as opposed to negative (*eg* figs 6, 14). Inversions of the N310 in the course of a single electrode trajectory were observed in three patients (fig 23). In the anterior and middle hippocampus, the N310/N430 is usually maximal in the contact immediately medial to the ventricle (*eg* fig 15, left 31, right 35), whereas in the posterior hippocampus, the N310/N430 may be larger relatively more medially (fig 23). In either case, the N310/N430 in that trajectory was found to be maximal within the hippocampal formation, and to be smaller both medially and laterally (figs 15, 23).

Amygdala. The amygdala was recorded with 27 electrodes in 26 patients. With the exception of one patient with noisy data, all electrodes showed endogenous potentials. Three components were consistently observed: N310, a negativity peaking between 250 and 370 ms post-stimulus onset (maximum amplitude 168 μV); N430, a negativity peaking between 410 and 560 ms (maximum 158 μV); and P630, a positivity between 560 and 780 ms (maximum 63 μV: fig 21, 18; fig 22, A'30, A'23; fig 24). The N310 and N430 were each observed in all 27 electrodes, and showed focal or substantial voltage gradients in 21. The P630 was seen in 23 electrodes with voltage gradients in 19.

No polarity inversions were observed across successive contacts of the electrodes penetrating the amygdala. Indeed, the polarity of each of the components was very consistent. However, in the five patients with the steepest voltage gradients within the amygdala, the largest amplitudes were always in the most medial three contacts (figs 21, 22, 24). Furthermore, in one of these five patients, a very steep gradient was observed at

Fig 22. Amygdala word potentials. A large N280–N390–P600 (a-b-c/d) recorded at multiple sites by an electrode that penetrates the left amygdala, is large in the most medial lead (A'23), then becomes smaller (A'27) and then larger again (A'33). MRI indicates that lead 23 was 3 mm lateral to the cisterna ambiens, and that lead 33 was in the lateral ventricle. The double voltage gradient within the amygdala suggests that the electrode is relatively close to a complex generator configuration. As is commonly observed, the N390 is larger to the novel stimuli (b), and the P600 is much earlier to the repeated (c) as compared to novel (d) stimuli. Patient no 25.

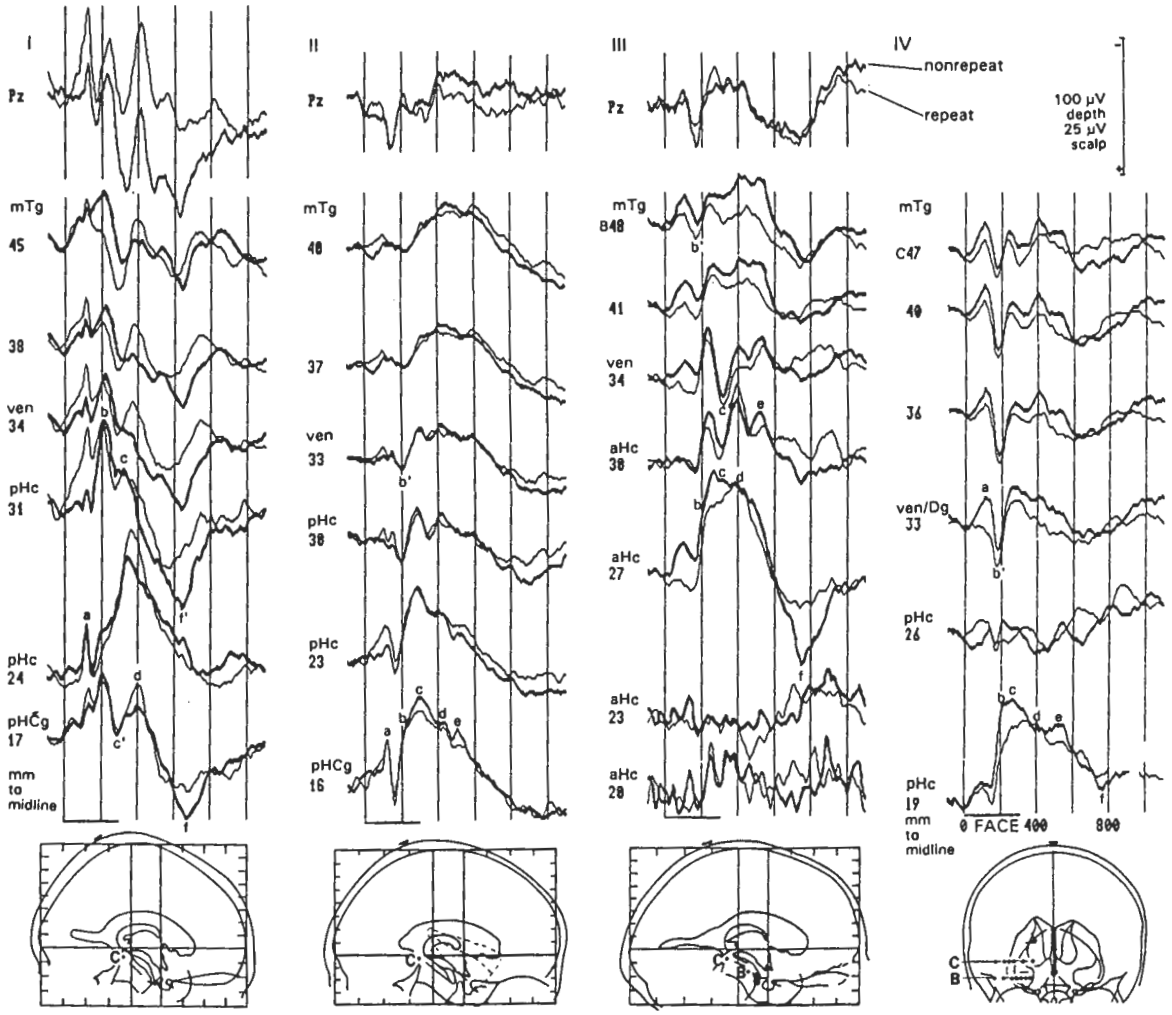


Fig 23. Medio-lateral topography of hippocampal face potentials. Recording from four electrodes are shown, all passing from white matter of the right middle temporal gyrus (mTg, inferior to the superior temporal sulcus, in external leads 40 to 48 mm to midline), thence through the temporal horn of the lateral ventricle (ven, 33–34 mm to midline), the anterior or posterior hippocampus (aHC or pHC, 19–31 mm to midline), and may extend into the posterior parahippocampal gyrus (pHCg, 16–17 mm to midline). The voltage topographies of multiple components change rapidly over small distances within the hippocampal formation, suggesting local generation. Note particularly: the often large and focal early (130 ms) negativity in posterior hippocampal formation sites (peak a: I, 24, II, 16, IV, 19); the focal and large N200 medially (peak b: I, 31, II, 16, III, 27, IV, 19), often polarity-inverted from potentials at similar latencies more laterally in the same electrode tracks (b': II, 33, III, 48, IV, 33); the multiple negative peaks (c, d, e) between 280 and 510 ms, and positivity (f) at about 660 ms, that change amplitude rapidly and independently between adjacent contacts in the hippocampal formation. The sites within the medial temporal lobe where recordings were made were determined by localizing electrode contacts with respect to the lateral ventricle: (Talairach *et al*, 1958). Column I, Patient no 19; II, 27; III and IV, 24).

the most medial contact, which recorded very small potentials (fig 24). This electrode was more basal and anterior than the usual amygdalar placements, and its most medial lead (at 17 mm from the midline, S31) could easily have passed through the periamygdaloid cortex into the cisterna ambiens.

In order to evaluate the possibility that the potentials recorded in the amygdala were actually generated in the hippocampus, the absolute value

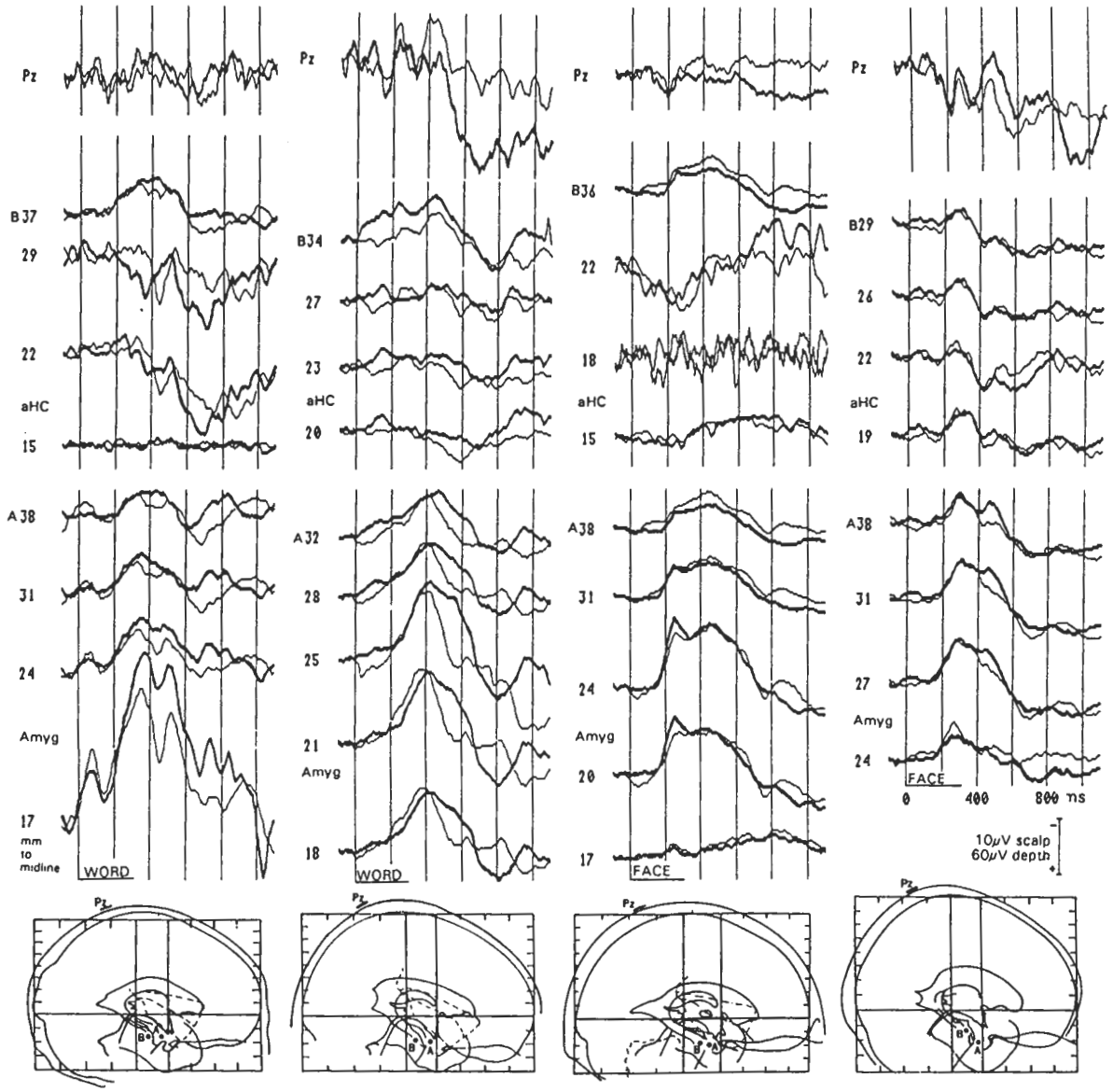


Fig 24. Large amygdala N4 in the absence of hippocampal N4. Large potentials are observed to faces and words in the amygdala (Am: internal contacts of electrode A), but not in simultaneous recordings from electrodes implanted in the anterior hippocampus (aHC: internal contacts of electrode B) in the same four patients. The lack of endogenous potentials in the hippocampus of these patients presumably reflects their involvement in the epileptogenic zone, and were noted to show cell-loss upon histological examination of tissue removed in therapeutic surgery (Wood *et al*, 1988; Puce *et al*, 1989). Moderate potentials are also observed in the anterior part of the middle temporal g (external contacts of electrodes A and B). Patients nos 9, 20, 17, 22 (left to right).

of the maximal response to words and/or faces between 200 and 700 ms that was recorded in the amygdala was compared to the maximal response recorded in the ipsilateral anterior hippocampus of the same patient (fig 24). It was found that the amygdala response was larger in eight cases, the hippocampal response was larger in six, and they were about equal in three. Furthermore, some of the largest amygdala potentials (up to 165 μV in amplitude) were found in four patients in whom no endogenous potentials could be observed with simultaneous multilead hippocampal recordings due to presumed hippocampal sclerosis. These observations are thus consistent with a generator in

the rhinal cortex that covers the medial and basal surfaces of the amygdala like a shell.

Temporal pole. Early (N130) as well as late (N310–N430–P630) responses were recorded within the temporal pole. As noted above, the N130 was small and lacked sharp gradients, suggesting it was volume-conducted from another area, presumably the basal occipitotemporal cortex. In contrast, the later responses are consistently large and moderately focal, strongly implying that they are generated locally or in nearby structures. In general, the temporal pole N310/N430/P630 potentials achieved largest amplitude medially.

Local polarity-inversions were difficult to observe due to the small number of subjects sampled (eight), and to the large size of the recording contacts in comparison to the cortical thickness. On the other hand, in the three other patients with simultaneous orbital and temporal pole recordings, the potentials were larger in the temporal pole.

To test whether the amygdala might generate the potentials recorded in the temporal pole, the relative amplitude of potentials recorded in the two structures was compared in the six subjects where both the temporal pole and amygdala were recorded and displayed similar waveforms. In four out of these six, the temporal pole potentials were larger than those recorded in the amygdala. Similarly, cases were identified (including the one illustrated in fig 9) where the anterior hippocampus did not generate field potentials (presumably due to local sclerosis) but where large temporal pole potentials were nonetheless observed. In contrast, orbitofrontal leads frequently record potentials to words and faces that have a similar waveform to those observed in the temporal pole, but with substantially larger amplitudes and clear polarity inversions (see Halgren *et al*, 1994).

Supramarginal g. A negativity peaking between 360 and 500 ms (*ie* the N430) was observed in all subjects with supramarginal g recordings. Although this potential was usually rather small, it could reach an amplitude of greater than 100 μV. Furthermore, the N430 inverted polarity in the supramarginal g in three subjects (fig 5-I56 to I49; fig 8-P44 to P37 to P27; fig 20-Q'44 to Q'37), and in nine others showed at least a moderate voltage gradient (fig 11-54, peaks d, 4). The N430 was recorded in 10 subjects presented with both the WORD and FACE tasks, nine with implants in the right hemisphere. It was about equal in five subjects (all right), was greater for words in two subjects (one left, one right), and was greater for faces in two subjects (both right).

The N430 rarely was prolonged with what might be an additional component at about 650 ms (*ie* the same latency as the P3b: fig 11-54, peaks 5, e). However, this was not seen with sufficient regularity to allow quantitative evaluation.

Inferior and superior parietal lobules. Recordings in the parietal lobe outside of the inferior supramarginal g were rare, but consistently revealed small but probably locally-generated potentials. In one patient, a small (20 μV) N380 was recorded in the sulcus behind the postcentral g, at the junction of the superior and inferior parietal lobules (areas 40, 5 and 7). This potential polarity-inverted to positive deeper in the sulcus (fig 20, P'46, 42 to 35: coordinates –40, –43, +61). In this deep lead, the inverted N380 was followed by a large (100 μV) long-lasting positivity to targets only, that subsequent analysis revealed to be related to somatosensory feedback. In another patient, an electrode in the inferior parietal lobule passing near the sulcus separating the supramarginal and angular gyri recorded a moderate positivity peaking at 390 ms, which polarity-inverted in deeper leads (fig 5, Q50, 43 to 32: coordinates +40, –50, +40: area 40). The deepest leads of this electrode were just lateral to the precuneus, where a gradient in the N380-N450 are observed. In the one other patient with an electrode in this region, a focal but small (40 μV) N420 was recorded.

Posterior cingulate g. The region of the posterior cingulate gyrus (approximate coordinates ± 4, –33, 25: area 23) was recorded in 22 subjects. However, in only 15 of these patients was the deepest recorded lead 7 mm or less from the midline. A more lateral contact could not be expected to lie in the gray matter, unless it by chance lay in a sulcus. In nine subjects, a potential, usually positive, was observed to peak between 250 and 380 ms post-stimulus onset. In four patients, this component had a focal topography (fig 10-P3). More consistently observed was a negativity peaking between 330 and 470 ms, the N430, discernable to some degree in all subjects (figs 5, 10, 11). This potential was either focal or showed a clear gradient in 14 subjects (fig 11-5). In most cases, late potentials in this region were small, but they could reach an amplitude of 100 μV.

Table IV. Evoked potential stages in the cerebral processing of faces and words

Evoked potential component[a]	**Principal** and secondary generators[b]	Functional brain region	Putative cognitive function
N75	lingual g	Early visual cortex	Simple feature extraction
–P105[c,e]			
N130	**fusiform g**	Basal occipitotemporal (R > L?)	Face-specific feature-extraction
–P180	occip-temp ctx		
–N240[d]	supramarginal g		
P190–**P250**[c]	**fusiform g**	Basal and lateral occipitotemporal (L > R?)	Word-specific feature-extraction
	angular g		
N310	supramarginal g	Polymodal assoc ctx	Semantic association
–N430	sup temp s		Contextual integration and closure (memory, emotion)
–P630	**hippocampal form**	Medial temporal (limbic)	
	amyg, temp pole		
	lingual g	Basal occipitotemp	Feedback to sensory ctx
	fusiform g		

[a]The principal component in a sequence is indicated with bold type.
[b]Principal generators contained frequent polarity-inversions of the indicated components and are printed in bold faced type. Focal large potentials were observed in the other structures.
[c]Although these potentials were primarily evoked by faces, this is thought to be due to electrode placement rather than face-specificity. Note that the generating zone may extend anteriorly to the posterior parahippocampal g.
[d]Components that were primarily evoked by faces and not by words or by simple visual or auditory stimuli (the significance of this specificity needs to be confirmed with word and face stimuli that are balanced on sensory characteristics).
[e]Components that were primarily evoked by words and not faces.

Alpha rhythm

Lingual gyrus. Very large focal oscillations in the alpha range (9–11 Hz), synchronized to stimulus onset, and lasting over a second were recorded in the same sites as the N75–P105 evoked by faces (fig 3-O17; fig 4-16, 20; fig 5-D23, D30; fig 6-24; fig 7-Q'15: approximate coordinates: ± 27, –58, –4). In contrast to the clear absence of the N75–N105 in response to words, the post-stimulus alpha occurred to both faces and words but was larger to faces (figs 4, 7). Large alpha was not recorded in all sites with similar coordinates, presumably because it is related to idiosyncratic factors of arousal and medication levels (Regan, 1989). Again note that the zone with focal alpha is not necessarily the most medial contacts (fig 5-D16; fig 8-D12). Recordings from the same lingual g sites were compared between faces and/or words on the one hand, and auditory discrimination on the other, in seven subjects. An alpha rhythm was also present in the auditory task, with the same topography as the word/face task. However in the auditory task, the alpha is not synchronized to stimulus onset, and thus is generally considerably smaller in amplitude.

Changes with repetition

Significant effects of word and face repetition were noted in several sites (tables II, III). With a single exception, these effects consisted of a decreased processing negativity or an increased P630. The earliest effects were on the N130 component. However, these effects were only seen in one site (lingual g for faces, superior temporal sulcus for words) and need to be replicated with more measures. The N240 to faces significantly decreased with repetition in the fusiform g, posterior parahippocampal g, posterior hippocampus, and anterior middle temporal g. The N240 to words decreased with repetition in the posterior cingulate g, whereas a positivity of about the same latency in the lateral occipitotemporal cortex increased with repetition. The N310 to faces

decreased to repetition in the posterior parahippocampal g, superior temporal sulcal region, anterior middle temporal g, and amygdala; to words it decreased in the amygdala. The most widespread changes to repetition were observed during the N430, which decreased to repeated faces in the fusiform g, superior temporal sulcal region, anterior hippocampus, anterior middle temporal g, and amygdala; the N430 to repeated words decreased in the lingual and fusiform g, lateral occipitotemporal cortex, posterior hippocampus, superior temporal sulcal region, anterior middle temporal g, amygdala, posterior cingulate g, and anterior and posterior superior temporal g. Finally, significant increases in the P630 were noted to faces in the anterior hippocampus (where it was inverted in polarity), anterior middle temporal g, and anterior and posterior superior temporal g. The P630 to words increased with repetition in the lingual g, posterior and anterior hippocampus (where it was inverted), amygdala, and posterior and anterior superior temporal g. Thus, significant changes to delayed word or face repetition were seen in both medial limbic, and lateral and basal neocortical sites.

Discussion

Summary of results

Eight successive EP stages preceding the behavioral response (at about 630 ms) could be distinguished by latency, and evidence was found for the participation of each of 14 anatomical structures in two to eight of these stages. The largest potentials were found to follow the anatomical pathways of the basomedial part of the ventral visual processing stream. These pathways, established in primates, are concerned with object recognition, declarative memory, and emotional evaluation. The current results were also generally in accord with deficits after brain lesions in humans, and PET cognitive activation studies, both of which indicate that networks of multiple structures contribute to the appreciation of words (Petersen *et al*, 1989; Mesulam, 1990; Wise *et al*, 1991) and faces (Damasio *et al*, 1990; Sergent *et al*, 1992). However, many more structures were engaged in the electrical response than have been identified with metabolic or lesion techniques as involved in face or word processing. Furthermore, the current study demonstrated that each structure is involved in multiple processing stages, and each processing stage involves multiple structures.

The responses could be divided into three groups, the first associated with sensory processing, the second with material-specific encoding, and the third with cognitive integration (table IV). The earliest components (N75–P105) were focal in the most medial and posterior occipital leads (lingual g), and appeared to be generated in areas 17/18 (*ie*, V1/V2). If so, this would explain why they were evoked mainly by faces, because electrodes were not placed sufficiently posterior to sample from the part of V1 where the foveally-presented words would be expected to project. A focal evoked alpha rhythm as well as later potentials (N150–P200–PN260) to both words and faces were also noted in this area.

The next sequence of potentials, N130–P180–N240, was large, focal and polarity-inverting in the basal occipitotemporal cortex (fusiform g, basal areas 19/37, putative area V4). In most cases, the P180 was evoked only by faces, and not by words, letters or symbols. Although largest in the fusiform g, this sequence of potentials (especially the N240) was also observed in the supramarginal g, posterior superior and middle temporal g, posterior cingulate g, and posterior hippocampal formation. The N130, but not later components of this complex, was observed in the anterior hippocampus and amygdala, but local generation was not clear. Seemingly analogous potentials to words occurred at slightly longer latencies (190 to 280 ms) in the fusiform g, and near the angular g (especially left).

A N310–N430–P630 sequence was largest and polarity-inverted in the hippocampal formation and amygdala, but was also probably locally-generated in many sites including the lingual g, lateral occipitotemporal cortex, middle and superior temporal g, temporal pole, supramarginal g, and posterior cingulate g. The P660 had the same distribution as has been noted for the P3b to rare target simple auditory and visual stimuli in 'oddball' tasks, with inversions in the hippocampus. In several sites, the N310 and N430 were smaller to repeated stimuli, and the P630 was larger. Although in the vast majority of sites, the N310–N430–P630 were equally evoked by words and faces, some material-specificity could be observed in the fusiform areas. An average reaction time of 626 ms to faces and 637 ms to words was

observed, indicating that all potentials before the late positivity could have been generated by neural activity contributing to the behavioral response.

The initial N75–P105 are hypothesized to embody simple feature detection. The N130–P180–N240 may embody structural face encoding in posterobasal inferotemporal cortex (homologous to V4?), with the results being spread initially to posterior inferotemporal, multimodal and paralimbic cortices. For words, visual-form encoding (in fusiform g) or visual-phonemic encoding (in angular g) may occur between 150 and 280 ms. During the N310, faces and words may be multiply encoded for form and identity (inferotemporal), emotional significance (amygdala), presence in recent declarative memory (hippocampal formation), and semantic associations (supramarginal and superior temporal sulcal supramodal cortices). These multiple characteristics may be contextually integrated across inferotemporal, supramodal association, and limbic cortices during the N430, with cognitive closure following in the P630. In the following discussion, the EP components will be discussed in turn, first those apparently simple visual, then those that might be specific for faces, then words, then those common to both.

Visual components

N75–P105 in posterior lingual g

The N75 potential was only recorded in the lingual g in the medial occipital lobe, where it was always followed by the P105. No polarity inversions were actually observed in the course of a single-electrode track, but potentials of both polarity were recorded in this region in different tracks (*ie* a P75–N105 was sometimes recorded instead of a N75–P105). It is possible that the potentials were actually generated locally, in areas 18 and 19. This possibility is supported by the focal distribution of the potential in the mediolateral dimension, and its long extension in the anterioposterior dimension. It is more likely, however, that the potentials were generated within the lingual g just posterior to the recording sites, in area 17. This interpretation is consistent with the observation that the largest potentials in this latency range were recorded in the most posterior lingual g placements.

The face stimuli were centrally-presented, subtending about 5.5 degrees horizontal by 8.3 degrees vertical. This would be expected to activate areas in the fundus and upper and lower banks of the calcarine fissure and extending 2 or 3 cm anterior to the occipital pole. In contrast, words were foveally presented (less than 1.5 degrees horizontal and 0.36 degrees vertical) and thus would activate only the part of area 17 on the occipital pole. Thus, the varying polarity but lack of polarity-inversions of this potential to faces would be explained by the varying orientations of the calcarine fissure, and the absence of this potential to words would be explained by the location of the foveal projection far from the recording sites. Furthermore, the mediolateral focus of the N75 at about 24 mm to midline would correspond approximately to the depth of the fundus of the calcarine fissure.

This interpretation of the generators of the N75–P105 is consistent with that given to prior depth recordings by Darcey *et al* (1980). In cats and monkeys, the potentials that are probably homologous to the human N75–P105 are thought to be generated by excitatory then inhibitory postsynaptic potentials in layer IV of V1, due to activation by geniculo-striate afferents (Arezzo *et al*, 1986; Mitzdorf, 1986; Zemon *et al*, 1986). Of course, the classical unit-recordings of Hubel and Weisel (1968) identify these as the first cortical stage in simple feature-detection.

A large focal alpha rhythm was evoked by face and word stimuli in many of the same lingual g sites where the N75-P105 were recorded. Even when there was no spontaneous alpha rhythm *per se*, the locally-recorded EPs consisted of successive positive and negative peaks at about alpha frequency. The same lingual g sites were also noted to generate an alpha rhythm during an auditory task, but it was not synchronized to the stimuli and therefore was smaller in amplitude in the averaged waveforms. Like the N75–P105, the lingual alpha could be generated locally in areas 18 and 19, and/or posteriorly in area 17. In either case, this finding seems to indicate that primary and/or juxta-primary visual cortex has a tendency to synchronize oscillations in the alpha range when it is activated, consistent with some prior scalp studies (Kooi and Bagchi, 1964; Dustman and Beck, 1965). This observation seems to contradict the notion that the alpha rhythm is necessarily an indicator of local disengagement.

It should be noted that the scalp topography of electrical (Srebro and Purdy, 1990; Hillyard, 1993) and magnetic (Aine *et al*, 1990) activity evoked by visual stimuli at about 100–110 ms is most consistent with multiple generators, most notably in occipital-temporal cortex. The current results sup-

port this view, and suggest that the medial occipital lobe (lingual g) also is active at this time.

Possible face-specific potentials

N130–P180–N240 in the fusiform g

The existence of face-specific brain processes has been predicted from the extraordinary abilities of normal humans to identify quickly, automatically, and nearly infallibly thousands of faces, regardless of view, illumination, or expression. Also remarkable is the number of attributes (*eg* age, gender, race, emotion, beauty) that can be extracted from even unknown faces. In this study, a large N130–P180–N240 sequence of EP components was evoked only by faces in many patients. These components were largest, and polarity-inverted focally in the fusiform g (basal occipitotemporal cortex). Adequate controls are lacking to permit the unambiguous assertion that the specificity of these responses is due to faces *per se*, and not to the size or color of the visual stimulus. In fact, this area has been implicated in color processing in humans by lesion (Meadows, 1974b; Zeki, 1991) and PET (Corbetta *et al*, 1990) studies, as has the possibly homologous area V4 in monkeys (Allman and McGuinness, 1988; Felleman and VanEssen, 1991).

However, several indirect arguments suggest that these potentials indeed reflect face-specific processing. First, specific deficits in familiar face identification (prosopagnosia) occur after lesions in the major generating structures of the N130–P180–N240: the fusiform g and surrounding structures in the basal occipito-temporal cortex (Meadows, 1974a; Damasio *et al*, 1990; Sergent and Poncet, 1990). Similarly, the right fusiform g is metabolically activated during face identification (Sergent *et al*, 1992). Unilateral right fusiform g region lesions have been reported to produce prosopagnosia, whereas the N130–P180–N240 is bilateral. However, most studies find that bilateral lesions are necessary to produce prosopagnosia, and in split-brain patients both disconnected hemispheres can recognize faces (Levy *et al*, 1972; Sergent, 1990).

The second argument suggesting that the N130–P180–N240 reflects face-specific processing derives from the task correlates of the apparently identical potentials when they are recorded from the scalp. Specifically, the same faces used in the current task evoke a prominent positivity at 160 ms that polarity-inverts over the posterobasal temporal lobe, consistent with generation in the region of the fusiform g (Marinkovic and Halgren, 1993). This potential appears to be absent to nonface visual stimuli that have been matched for color, size and intensity (Srebo, 1985; Potter *et al*, 1987; Jeffreys and Musselwhite, 1987; Botzel and Grüsser, 1989; Grüsser *et al*, 1990; Seeck and Grüsser, 1992). Furthermore, the magnetic field evoked specifically by faces at 150 ms has a topography consistent with generation on the inferior occipitotemporal junction (Lu *et al*, 1991). Preliminary evidence suggests that this scalp P160 continues to be evoked by misarranged face fragments, but that the N220 is altered when face features (eyes, mouth, nose, etc) are no longer correctly placed with respect to each other (George *et al*, 1993). The possibility that face integration begins with the N220 component is consistent with the observation that this is the first scalp component to show clear effects of delayed face repetition (Marinkovic and Halgren, 1993).

The gross anatomical location of the large N130–P180–N240 generator in the fusiform g suggests that it may lie in an area homologous to the basal portion of area V4 in the monkey neocortex. This area has the largest number of connections of any visual area (39 identified connections with 21 visual areas: Felleman and VanEssen, 1991). While V4 occupies a position in the hierarchy of visual connections between V2 and inferotemporal cortex, it receives input directly from V1 and projects as far up the hierarchy as area TF/TH. Thus, the anatomy of V4 suggests that it plays a pivotal role in the visual-encoding of face-information and its widespread distribution to association areas.

This interpretation would be consistent with the observation that, although the N130–P180–N240 was largest, focal and polarity-inverting in the fusiform g, similar complexes could be recorded in many other areas. For example, clear large P180s were recorded in the supramarginal g, and (although recording opportunities were limited) in other posterior parietal sites. Other studies have found an N2–P3a–SW complex associated with the orientation of attention in these same sites to auditory stimuli (Halgren *et al*, submitted). Lesion and PET studies in humans have also implicated this area in the polymodal direction of attention (Mesulam, 1990), and this area may include areas in the posterior superior temporal sulcus considered in monkeys to be part of the dorsal visual pathway, concerned with local-

izing objects for movement (Ungerleider and Mishkin, 1982). Although V4 does project to such areas, its more robust connections are with the ventral visual pathway, projecting to the temporal lobe and concerned with object identification. Thus, N130–P180–N240 were systematically recorded in and around the posterior parahippocampal g (possibly area TF/TH), which has been found to be metabolically activated during face identification (Sergent *et al*, 1992). N220s could also be recorded in the hippocampus, where lesions produce deficits in recent declarative memory for faces (Milner, 1971). The N240 was especially prominent in middle temporal g sites, which could correspond to the inferotemporal cortex of monkeys, or be generated in the immediately superior temporal sulcus. Both areas in primates have been found to contain units that specifically fire to faces (Desimone, 1991; Ojemann *et al*, 1992; Perrett *et al*, 1992; Rolls 1992). In monkeys, cells in inferotemporal cortex are seemingly more specifically sensitive to the identity of the individual (Baylis *et al*, 1987; Hasselmo *et al*, 1989), while cells in the superior temporal sulcus are more sensitive to the direction of gaze (Harries and Perret, 1991).

These data suggest the following hypothetical information-processing stages in the fusiform g: N130, the arrival of local contour and color information (corresponding to the 'primitive sketch' of Marr (1982)); P180, the extraction of face specific characteristics (corresponding to the 'structural encoding' stage of the psychological theory of Bruce (1988); and N240, the integration of these characteristics into a spatial arrangement. In this schema, the fusiform g would receive information from lower-level visual cortices (V1 and V2) during the N130, and would project face-specific encoding to widespread cortical areas during the P180 (including facial characteristics especially useful for the direction of attention), and the N240 (including integrated faces especially useful for individual identification, declarative memory, and emotional judgements).

Clearly, the face-encoding function proposed to occur during the N130–P180–N240 is prior not only to face-identification, but also to other face-processing functions. This would predict that lesions of the fusiform g and surrounding areas would produce a more general deficit than just in the identification of familiar faces. In fact, many prosopagnosics also are deficient at judging facial expression and/or gender, suggesting a more general and fundamental deficit in face-processing (Bruyer, 1991). Thus, declarative face identification could use the same face-encoding processes in the fusiform g as do discrimination of other face properties such as gender and emotion, with the relatively greater deficit in face identification being due to its need for greater precision in face-encoding.

The same formulation would account for preserved implicit (*eg* autonomic) face recognition in prosopagnosics (Damasio *et al*, 1990) by supposing that such implicit recognition depends on imprecise face-encoding outside of the fusiform g. The possible location of this encoding would be in lateral occipito-temporal cortex where indeed, a smaller N130–P180–N240 may be recorded, and which probably belongs to the same cytoarchitectonic area as the posterior fusiform site where the N130–P180–N240 is maximal.

Widespread N310–N430–P630

Following the N130–P180–N240, faces evoke a series of potentials termed N310–N430–P630. Except in the fusiform g these potentials are also evoked by words, and will be discussed below. However, it is interesting to note that like the N130–P180–N240, the N310–N430–P630 are also consistently maximal in mediobasal (hippocampal and amygdala formations) rather than lateral sites. This distinction between lateral and basal streams within the ventral visual stream itself has recently been made on anatomical and behavioral grounds in monkeys (Martin-Elkins and Horel, 1992). That is, although V4 in monkeys is both basal and lateral, the forward projections from V4 tend to remain within the lateral or basal streams. The critical area where cooling produces delayed match to sample deficits is in the anterior basal stream (George *et al*, 1989), between the rhinal and middle temporal sulci (mainly TE1, termed 'AITv' by Felleman and VanEssen (1991) but also including perirhinal cortex a36). This area gets its input from area TF (in the posterior parahippocampal g), and TF gets its input from basal V4. Cooling of TF also gives large DMS deficits whereas cooling of more dorsal areas does not. The correspondence between this basal pathway and the regions where large EPs were evoked to faces is striking, with the P170 recorded in posterior fusiform g (ventral V4?), the N240-N310 in posterior parahippocampal g (TF?), and the N310–N430–P630 in anterior parahippocampal and periamygdaloid areas (AITv and a36?).

The lateral and basal paths have also somewhat distinct projections to other cortical and limbic

areas. The basal path procedes from the lingual and fusiform g to the parahippocampal gyrus, areas TF/TH and thence to entorhinal and perirhinal cortices, and finally the hippocampus and amygdala (Herzog and VanHoesen, 1976; Amaral and Insausti, 1990; Suzuki and Amaral, 1990). The subiculum (output of the hippocampus), in turn, projects to the lateral orbitofrontal cortex, and the amygdala to the posterior orbitofrontal cortex (Barbas and De Olmos, 1990; Amaral *et al*, 1992; Morecraft *et al*, 1992). Thus, the prominent potentials in the orbitofrontal cortex reported elsewhere (Halgren *et al*, 1994) may be an extension of the same mediobasal route.

The lateral route procedes from the posterior inferior temporal g to the more anterior and lateral inferotemporal cortical regions in the inferior and middle temporal gyri (Baizer *et al*, 1991). This cortex projects to: area PGa (of Seltzer and Pandya, 1989), a multimodal area in the fundus of the superior temporal g; the inferior frontal g on the lateral side of the frontal lobe; and the supramarginal g (inferior parietal lobule) (Felleman and VanEssen, 1991; Morecraft *et al*, 1992). EPs seen in these later regions have been associated with orienting attention (Halgren *et al*, submitted).

It should be noted that alternative pathways exist that could allow activity to bypass a lesion in the successive stages of either pathway. For example, the (medial) posterior pHCG also projects widely to the lateral association areas, and conversely, the lateral inferotemporal cortex projects to the entorhinal ctx and thus enters the hippocampal/amygdalar stream (Van Hoesen, 1982; Amaral and Insausti, 1990; Amaral *et al*, 1992).

Possibly word-specific potentials

Responses that appeared to be specific to words were much less prominent in the current study than those apparently specific to faces. In general, possible word-specific responses appeared as positivities in the 200–300 ms range in lateral and basal occipitotemporal cortices, especially on the left. Such early positivities to words could also be observed in Wernicke's area, the left posterior superior temporal and supramarginal gyri. However, responses in this area were generally small and lacked specificity. Clear word-specific positivities were observed in one subject in lateral cortex lying between Wernicke's area and the occipital cortex, in the posterior superior temporal g area 37 (beneath the angular g). Lesion studies suggest that this area may be important in reading, perhaps translating the word from a visual code to a phonemic code that could then access semantic information in Wernicke's area (Geschwind, 1965; Benson, 1979). Bilateral metabolic activation has been observed somewhat more posteriorly during reading (Haxby *et al*, 1991). The same left 'infero-angular' area was metabolically activated in a lexical decision task, where its degree of metabolic activation was found to correlate with the size of the N400 evoked by the words (Nenov *et al*, 1991). From the fact that the N400 is evoked by pronounceable nonwords, but not by nonpronounceable nonwords (Smith and Halgren, 1987b), it was proposed that the metabolic activation represented a process of phonemic encoding antecedant to the N400 (Halgren, 1990a). This proposal would be supported by the current observation of word-specific activity in this area preceding the N430. The hypothesis of an antecedant process to the N400 lateralized to the left hemisphere is also consistent with the observation that in split-brain subjects, unilateral presentation of a word to the left but not the right hemisphere results in an N400 (Kutas *et al*, 1988).

The most commonly observed potentially word-specific activity was a P190–P220 recorded in the fusiform g, especially in the left hemisphere (areas 19 and/or 37). While lesions of the fusiform g do not produce clinically-detectable language deficits, electrical stimulation of the fusiform g produces language deficits indistinguishable from those produced by stimulation of Wernicke's area (Lüders *et al*, 1986, 1991; Burnstine *et al*, 1990). The fusiform P190–P220 to words may also be related to the finding by Petersen *et al* (1990) that the left ventral occipital cortex is metabolically activated to all orthographically regular words even if passively presented, although the center of this activation was posterior to that observed in the current study. Petersen *et al* suggested that this response was to wordform (Shallice, 1988). By analogy to the structural face-encoding function proposed for the (mainly) right fusiform P180, the (mainly) left fusiform P190–P220 may visually encode words for distribution both medially and laterally, leading directly to lexical access and contextual integration. Such a direct reading route that does not involve phonemic encoding has been inferred on the basis of experimental psychological findings (Seidenberg, 1985; Humphreys and Evett, 1985). These experiments suggest that direct reading is

limited to high frequency words in habitual readers. Thus, under this hypothesis the lack of obvious reading deficit after left fusiform g lesions would be due to the ability of phonemic reading to substitute for direct reading, and the aphasic effects of left fusiform stimulation would result from its connections with Wernicke's and other language areas. This hypothesis would predict that lexical frequency rather than pronounceability would influence the potentials recorded in the left fusiform g.

Cognitive stages common to faces and words

Following the earlier sensory, word- and face-specific components, three prominent potentials were recorded in the depth that seem to correspond to the classical cognitive components: 1) N310 (or N3), with a latency of 250–360 ms in the depth; 2) N430 (or N4 or N400), with a latency of 350–500 ms in the depth, depending on structure, patient and task; and 3) P630 (or late positive component, LPC, or P3b), with a latency of 500–750 ms in the depth. Additional components corresponding to the previously described late slow wave (at around 800–1000 ms) were also observed.

Scalp studies have found that the N4 is the most prominent component related to semantic variables and evoked by words and faces (Halgren, 1990a). Previous depth recordings have demonstrated N4 generation in the hippocampal formation, as well as large N4s in the amygdala, but without precisely localizing the generators within these regions (McCarthy and Wood, 1984, 1985; Smith *et al*, 1986). Furthermore, the lack of significant change after unilateral temporal lobectomy implies that extratemporal N4 generators also exist (Smith and Halgren, 1989).

Following the N4, a P3b is usually recorded with a widespread scalp topography and no clear modality specificity (Vaughan, 1987; Amaral *et al*, 1992). Human intracranial recordings have demonstrated a very large P3 generator localized to the hippocampal formation (Halgren *et al*, 1980, 1983, 1986; Stapleton and Halgren, 1987; McCarthy *et al*, 1989; Heit *et al*, 1990). However, the P3 evoked by rare tones is not significantly affected by unilateral anterior temporal lobectomy (ATL) which includes most of the hippocampal formation (Wood *et al*, 1982; Stapleton *et al*, 1985; Johnson, 1988). Possible candidates for P3 generators outside the hippocampus suggested by intracranial recordings include the frontal lobe (Wood and McCarthy, 1985; Smith *et al*, 1990) and posterior cingulate g (Ojemann and Lettich, 1983). However, the waveforms in these areas resemble that of the P3a rather than P3b. Extracerebral mapping of evoked magnetic fields correlated with the scalp P3 in simple classification tasks have yielded mixed results, indicating an apparent endogenous magnetic field generator in either the 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 plus thalamus (Rogers *et al*, 1991). Recently, the best fitting dipole during the LPC in a verbal short-term memory task was found to be in the MTL (Starr *et al*, 1991). However, the validity of fitting a single dipole to any component later than 100 ms should be severely questioned by the multiple complex generating structures demonstrated by the current study. Scalp recordings in patients with unilateral pathology localized with CT suggest that the temporo-parietal junction is essential for P3b generation (Knight *et al*, 1989; Knight, 1990). Animal models have implicated cholinergic synapses in humans (Meador *et al*, 1988) and noradrenergic synapses in monkeys (Pineda *et al*, 1989) in modulation of the P3.

In the current study, the N310–N430–P630 had a very widespread distribution, being recorded in virtually all structures that were well-sampled with the depth electrodes: lingual g, fusiform g, lateral occipito-temporal cortex, hippocampal formation, amygdala, temporal pole, middle and superior temporal g, supramarginal g, and posterior cingulate g. Not all components were equally represented in all areas, with the P630 being largely absent from the supramarginal and posterior cingulate gyri, and the N310 being rare in the fusiform and superior temporal gyri. In general, the largest and most reliable N310–N430–P630s were recorded in the hippocampal, amygdala and temporal-pole regions, and the possible generating structures within these regions is discussed below. However, generation of the N430 in particular appears to be rather widespread, with polarity-inversions having been recorded in lingual g, fusiform g, lateral occipito-temporal cortex, middle and superior temporal g, hippocampal formation, and supramarginal g.

Generation of the N310–N430–P630 in medial temporal structures

Hippocampal formation. The largest potentials in the hippocampal formation are the N3, N4 and

P3b. Although the N3 and N4 were not always clearly distinguishable, in some patients their voltage topographies were found to be clearly different, and they could invert or change amplitude between leads independently, strongly implying that these are indeed separate components, and not simply the same potential but at different latencies in different patients. Local polarity inversions and very steep voltage gradients strongly imply local generation, as does the fact that the N3/N4/P3b were larger amplitude within the hippocampal formation than in surrounding structures that were sampled by more medial and lateral, or by more superior and inferior, leads on the same electrodes. The N3/N4/P3 were found to be large both left and right, anteriorly and posteriorly, with no apparent difference in the locations within the hippocampus where they were positive as opposed to negative. A generator of the N3/N4 within the hippocampus proper (*ie* within Ammon's Horn), is suggested by the fact that they were most often maximal in the lateral hippocampal leads adjacent to the ventricle.

Amygdala. Although large potentials were consistently recorded in the amygdala, they are unlikely to be generated within the amygdala itself because of its cellular arrangement. Amygdala neuronal cell bodies are arranged fairly diffusely and generally have a stellate morphology, sending their dendrites in all directions (McDonald, 1992). Consequently, synaptic currents generated by amygdalar afferents are unlikely to summate spatially, and thus are unlikely to generate a field-potential recordable at the macro level. Nonetheless, the large amplitude and steep voltage gradients sometimes observed in amygdala recordings suggest that the generator of these potentials lies close to the amygdala.

In saggital views of the brain about 27 mm from the midline, the anterior hippocampus is seen to lie immediately posterior to the amygdala (Talairach *et al*, 1967). Anterior hippocampal electrodes in our patients were placed 10 to 17 mm posterior to the amygdala electrodes. Since the hippocampus has an ideal cellular arrangement for local generation of field-potentials, and has been found to generate large responses in these tasks, it is the most obvious candidate for generation of the field potentials recorded in the amygdala. However, when this hypothesis was tested, the amygdala response was larger in about as many cases as the hippocampal response was larger. Although the hypothesis of hippocampal generation would predict that the hippocampal potentials would be larger, some variation would be expected due to the precise location of the recording electrode contacts with respect to the generating neuronal fields. This variation however cannot explain the fact that some of the largest amygdala potentials were found in patients in whom no endogenous potentials could be observed with simultaneous multilead hippocampal recordings. Presumably, the total lack of hippocampal potentials in these patients is due to local sclerosis (*cf* Squires *et al*, 1983; Wood *et al*, 1988; Puce *et al*, 1989). Hippocampal sclerosis is the most common pathology encountered in temporal lobes removed to cure seizure disorders (Brown, 1973). In these series, as well as in autopsy specimens from subjects with temporal lobe epilepsy, this sclerosis has been found to extend to the amygdala in only about half of the cases when it has been observed in the hippocampus (Margerison and Corsellis, 1966). Thus, it seems likely that the patients with no hippocampal endogenous potentials to words and/or faces, but with large amygdala potentials suffered from pathology that affected the hippocampus but not the amygdala.

In any case, it is clear from these four cases that hippocampal potentials are not necessary for large amygdala endogenous responses, and thus the hippocampus is highly unlikely to be the origin of the amygdala potentials. Furthermore, the largest potentials in the amygdala area were found medially, as was the steepest voltage gradient in a lead that may have penetrated the periamygdaloid cortex into the cisterna ambiens. These observations are thus consistent with a generator in the rhinal cortex that covers the medial and basal surfaces of the amygdala like a shell. It should be clear that regardless of whether the amygdala itself is a generator of the potentials recorded within its limits, it is strongly interconnected with the hippocampus and with rhinal cortex, and thus is undoubtedly involved in the neural processing indexed by these potentials (Amaral *et al*, 1992).

Temporal pole. The N310–N430–P630 recorded within the temporal pole were also consistently large and focal, strongly implying that they were generated locally or in nearby structures. One possibility is the medial cortex, in or near areas 28 (entorhinal cortex), 35 (perirhinal cortex) and 36 (between the rhinal and anterior medial temporal sulci in monkeys, according to Amaral *et al* (1987)).

The possibility of a rhinal cortex generator is consistent with various evidence. First, in primates, most rhinal cortex is in the most anterior portion of the temporal lobe, in the cortex medial, anterior and inferior to the amygdala, and with a smaller band extending back in the parahippocampal g and immediately adjacent fusiform g (Talairach *et al*, 1967; Van Hoesen and Pandya, 1975; Duvernoy 1988; Amaral and Insausti, 1990; Amaral *et al*, 1992). Thus, potentials generated in rhinal cortex would be recorded not only in the temporal pole, but also in the amygdala and parahippocampal gyrus, explaining the similarity of the potentials recorded in these three regions. Furthermore, it would explain why large potentials are commonly recorded in the amygdala despite the fact that the amygdala is unlikely to generate large field potentials itself (see above). Finally, a parahippocampal g N460/P620 generator has already been inferred from the very large and clearly polarity-inverting potentials to words demonstrated in this region by Smith *et al* (1986).

A rhinal generator is consistent with the local topography of the temporal pole potentials, usually being largest medially. However, this topography is also consistent with several other local as well as more distant possible generating structures. For example, most of temporal pole cortex is area 38, a region which has been implicated in individuation of complex stimuli (see below). Another possible generator within the temporal pole could lie in the depths of the most anterior part of the superior temporal sulcus, inasmuch as inversions of similar potentials have also been noted in more posterior parts of this sulcus.

Nearby structures outside the temporal pole could also generate potentials with the observed topography, for example the amygdala, about 15 mm from the temporal pole recording contacts. However, as noted above the amygdala's cellular arrangement is inappropriate for spatial summation of synaptic activity into large field-potentials. Furthermore, in most subjects where both the temporal pole and amygdala were recorded and displayed similar waveforms, the temporal pole potentials were larger than those recorded in the amygdala. Conceivably, both the amygdala and temporal pole potentials could be generated in the anterior hippocampus, which is about 20 mm posterior to the temporal pole electrodes, and which is known to generate very large and polarity-inverting late potentials (this paper, and Smith *et al*, 1986). However, in some cases reported here large temporal pole potentials were observed despite an absence of field potentials in a presumed sclerotic anterior hippocampus.

If the rhinal cortex is not a generator for the potentials recorded in the temporal pole, then the most likely nearby generator appears to be the orbitofrontal cortex. A recent study (Halgren *et al*, 1994) obtained clear evidence for local generation of large N4/P3b components in the orbitofrontal cortex: 1) large amplitude potentials, in absolute terms as well as in comparison to superior and posterior neighbouring structures; and 2) steep voltage gradients including common polarity-inversions. The coordinates of the maximal responses suggested a generator in area 11, in the orbital part of the middle frontal g, slightly anterior to the sulcus separating it from the inferior frontal g.

The orbital cortex lies in close proximity dorsally and medially to the temporal pole. Very often, orbitofrontal leads record potentials to words and faces that have a similar waveform to those observed in the temporal pole, but with substantially larger amplitudes and clear polarity inversions. Furthermore, the sole 'temporal pole' contact recording inverted potentials was rather medial and superior, and thus may very well have actually been in the orbitofrontal cortex. This possibility is supported by the observation that an inversion of the same potentials with similar waveforms but somewhat larger amplitudes were observed in the same patient in leads at the same distance to midline but 26 mm anterior and unquestionably lying in the orbitofrontal cortex. On the other hand, in the three other patients with simultaneous orbital and temporal pole recordings, the potentials were larger in the temporal pole.

In conclusion, the current study confirms earlier results indicating that the N4 and P3b to words are generated in the medial temporal lobe (McCarthy and Wood, 1984, 1985; Smith *et al*, 1986). Furthermore, this study extends this finding to faces, and suggests that the most likely generator of the late potentials recorded in the temporal pole may be the rhinal cortex (an extension of the parahippocampal g generator already identified). An orbitofrontal cortex contribution may also be possible, and given the dense anatomical interconnections of the orbital and rhinal cortices (Barbas and De Olmos, 1990; Amaral *et al*, 1992; Morecraft *et al*, 1992), generation in both structures could be expected.

Functional significance

Cognitive correlates of the N310–N450–P600

The cognitive processes embodied by the N4–P3b have been very extensively studied in scalp recordings from normal subjects (reviews: Kutas, 1988; Kutas and Van Petten, 1988; Halgren, 1990a, 1994). Less attention has been paid specifically to the N310, in part because it is often difficult to distinguish from overlapping potentials at the scalp. The N310 in the depth may be a type of scalp 'processing negativity'. These potentials have been associated with the extraction of features and matching of them to an internal template (Ritter *et al*, 1984). They require complex stimuli such as letters or words and are observed when these stimuli change unpredictably from trial to trial and when stimulus identification is important for task performance (Lovrich *et al*, 1986). The discovery of large N310s in both lateral and medial temporal lobe sites is consistent with the observation that this potential (as evoked by words) declines over the temporal scalp after lesions of the underlying regions, with greater bilateral effects after right-hemisphere lesions (Smith and Halgren, 1988). This area on the right has also been implicated in high-level visual processing in PET (Petersen *et al*, 1990; Haxby *et al*, 1991; Wise *et al*, 1991), stimulation (Fried *et al*, 1982), lesion (Kimura, 1963) and unit-recording (Ojemann *et al*, 1992) studies in humans.

The cognitive task correlates, timing, and anatomical extent of the N4 suggests that it embodies the global integration of the stimulus with the current cognitive context, in order to neurally-encode the event. This hypothesis is supported by the following experimental findings: 1) the N4 is only evoked by stimuli (in any modality) that are potentially meaningful within a broad semantic system, such as words or faces, *ie* precisely those stimuli which need to be integrated with the context to determine their meaning (Halgren, 1990a) (the N2b may play an analogous role for simple sensory stimuli: Pritchard *et al* (1988)); 2) a large number of conditions modulate N4 amplitude to a given stimulus (*eg* sentence context, previous presentation of a semantic associate, truth of the completed event, presence of the stimulus in primary or recent memory), with the size of the N4 being decreased when this information facilitates integration of the N4 with the context (Halgren and Smith, 1987; Kutas and Van Petten, 1988); 3) the modulating stimuli may be in a different modality (*eg* auditory *versus* visual), or in a different knowledge domain (*eg* words *versus* faces), suggesting that the modulated network has access to all of these types of information and/or encodes information at a level deeper than modality or knowledge domain (Barret and Rugg, 1990; Domalski *et al*, 1991; Nigam *et al*, 1992); 4) hippocampal formation and amygdala unit-firing during the N4 shows specificity both for the stimulus (*ie* particular word or face), as well as for the context in which it is presented (Heit *et al*, 1988); 5) the N4 is the first EP component to clearly show these sensitivities to meaningfulness, specificity and context, and is the last to occur before the response must be specified (Halgren, 1990a); 6) the global integration of an event is considered to be the essence of controlled or conscious processing, and the N2/N4/P3b have been associated with such processes *via* self-report and latency (see Halgren, 1994 for review); and 7) the extensive anatomical distribution of putative N4 generators in most or all supramodal association cortex areas provides a sufficiently broad neural substrate to encode all of the knowledge domains that contribute to an encoded event (demonstrated in this paper and in Halgren *et al*, 1994). Again, the brainstem is intimately involved in the triggering of the N4, inasmuch as it is still evoked bilaterally after presentation of words to only the left hemisphere in patients with complete section of the forebrain commissures (Kutas *et al*, 1988).

The P3b follows the N4 in these pardigms, and tends to be modulated by the same conditions that modulate the N4, but in the opposite direction. For example, the P3b is larger when integration is facilitated by repetition (Halgren and Smith, 1987). The P3b had a peak latency of about 620 ms, about equal to the average reaction time in this task. Thus, the P3b begins at about the same time that the response decision is made, leading to the suggestion that the P3b represents cognitive closure (Desmedt, 1981). Within the medial temporal lobe, the P3b has the same topography as the typical slow wave following interictal spikes (Altafullah *et al*, 1986). Since this slow wave is generated by synaptic inhibition, the P3b may be also, and unit-recordings tend to support this hypothesis (Heit *et al*, 1990). Based on neural network modelling studies, we have suggested that the P3b represents the second phase of the same cognitive contextual integration process as the N4 (Read *et al*, 1993). The first (N4) phase would provide relative excitation to facilitate the spread of information from its sensory and memory entry-points into the cogni-

tive network, and the second (P3b) phase would embody recurrent inhibition acting to prevent this spread from recruiting spurious elements (or even becoming explosive and evoking epileptiform activity), and ultimately reducing activity in recurrent excitatory networks to permit the evolution of new networks.

Widespread integration during the N450

Thus, the cognitive task correlates and timing of the N4 imply that it embodies contextual integration. The results reported here suggest that the N4 is generated in widespread areas. The disparate functions of these areas can be inferred from the effects of lesions and cognitive activation studies with PET. Briefly, this evidence suggests the following functions for probable N4 generating structures: lingual g, primitive visual sketch; fusiform g, face (right) or word (left) structural encoding; lateral occipito-temporal cortex, intermediate visual analysis; middle and superior temporal g and supramarginal g, long-term object and semantic memory; hippocampal formation and rhinal cortex, recent declarative memory; and amygdala region, emotional evaluation. This implies that the contextual integration process embodied by the N4 is a correspondingly widespread process, uniting structures with very disparate functional roles.

This process would result in the evolution of a widespread cortical-subcortical network optimally encoding the event, through excitatory feedforward and feedback connections, focused by local surround inhibition. The disparate perceptual, mnestic and emotional aspects of the event are thus 'bound' in a distributed mutually excitatory recurrent network. Singer (1993) has hypothesized that this binding process occurs through a synchronizing 40 Hz rhythm. Simulation studies suggest that the maximal communication time between disparate elements being integrated through this mechanism is about one-third of the period of the rhythm (25 ms/3 = 8.3 ms: Schuster and Wagner, 1990; König and Schillen, 1991). This would correspond to a distance of 7.2 cm (assuming a myelinated axon diameter of 1 μ : Patton, 1982). Although all of the numbers used in this calculation are approximate, this argument nonetheless suggests that: 1) there is sufficient time within even a high-frequency (gamma-band) cycle for the far-flung structures where the N4 is generated to communicate amongst each other; and 2) multiple high frequency cycles (approximately eight) may occur within a single N4. The utility of multiple cycles for the successive refinement of the encoding neural network has been suggested by simulation studies (Read *et al*, 1993).

It is theoretically possible that the N4 embodies a process that, while widespread, does not indicate interaction between the structures where it is recorded, but rather a simultaneous but non-interactive state. Arguing against this interpretation is the fact that these areas are interconnected anatomically. Furthermore, as noted above the duration of the N4 (about 200 ms) is substantially longer than the probable time necessary to communicate information between even distant areas. Finally, the cognitive correlates of the N4 are consistent with its embodying just such a binding/integrating process, which would imply a communication between the participating structures.

Top-down influences on sensory association areas

Clearly, communication from lower-level to higher-level structures in the visual processing stream is strongly implied from the very existence of evoked potentials in the higher-level areas (this study), and similarly from unit activity in homologous areas of monkeys that depend on visual features of the stimulus. Similarly, in humans, unit responses in the hippocampus and amygdala specific to particular words or faces occur during the N4, implying passage through all the hierarchical levels in the bottom-up direction (Heit *et al*, 1988).

Evidence that communication is effective in the opposite (downstream) direction is found in the finding reported here that the N4s in the lowest-level structures recorded (lingual and fusiform g) were significantly decreased to repeated words and faces. Since repetition was after a delay of an average of 1 min, with numerous intervening stimuli, behavioral recognition would be expected to depend on recent declarative memory functions where the hippocampal formation plays an essential role, and this is supported by the deficits found on similar tests after hippocampal lesions (Milner and Teuber, 1968). More specifically, in the identical word recognition task, left (but not right) anterior temporal lobectomy abolishes the repetition-induced decrement in the scalp N4 (Smith and Halgren, 1989). This strongly implies that in the intact brain, information modulating the N4 to repeated stimuli passes from the anterior (probably medial) tem-

poral lobe to other N4 generating sites, presumably including the fusiform and lingual gyri.

This study found that in general, once a structure was activated, it continued to be activated. That is, if a structure showed evidence for generation of a given EP component then it would usually show evidence for generation of later components also. The posterobasal inferotemporal cortex was activated during the P180, N240 and N430 stages of information-processing suggesting that it participates not only in initial feature detection, but also in the integration of these features, identification of the resulting whole, and relation of that whole to the current cognitive context. In this case, the feedback connections to the ITC may help tune its perceptual networks during the N240 in the light of emotional and mnestic information. Conversely, the forward connections of the ITC would allow the final contextual integration of the stimulus during the N480 to have access to more strictly perceptual networks (Damasio, 1988).

Note that by suggesting a feedback from higher order structures to the stage of structural encoding (in the fusiform g), the data reported here diverge from the psychological model suggested by Bruce and Young (Bruce, 1988). It is proposed here that structural encoding occurs during the stage specific to faces, the P180; and that these encoded features are integrated into faces during the N240. By the P180, many structures are involved in processing the face, and they cannot be assumed to be engaged in structural processing – including the amygdala, the supramarginal g, the hippocampus, etc. It is clear from the fact that the N430 in the lingual and fusiform g are modulated by repetition in recent declarative memory that the top-down route from hippocampal formation to these areas is functional at least at this latency. The suggestion then is that even if one takes the most restrictive anatomo-physiological embodiment of the structural encoding stage, the lingual-fusiform g P180, the current data indicate that top-down influences from multiple structures are likely.

Integration of emotion and cognition

Given that the predominant generators of the later cognitive evoked potentials are mainly in medial temporal limbic structures, any top-down influences during these EP components are likely to include emotion-related information (Halgren and Marinkovic, 1993). In particular, the prominent amygdala activity beginning 120 ms post-stimulus onset would permit input from the amygdala to help shape the content of the encoded experience (Halgren, 1992). Thus, the emotional evaluation of events occurs synchronously with their cognitive evaluation, prior to any conclusion having been obtained from that processing (*cf* Plutchik, 1980; Panksepp, 1982; Le Doux, 1987; Ohman, 1987). Conceivably, this would allow the limbic system to contribute to the myriad 'defense mechanisms' (repression, denial, undoing, projection, displacement, etc) that may distort or eliminate the conscious experience of an emotionally-significant event (Brenner, 1974). When sensory input is absent (*eg* during dreams), event integration would be dominated by limbic input, possibly resulting in emotionally-eloquent hallucinations (Halgren and Chauvel, 1993; Bancaud *et al*, 1994).

Integration of the declarative memory system

Bilateral lesions of the hippocampal formation produce a profound amnesia for recent events (Squire, 1992; Halgren 1994), and unilateral lesions produce a milder deficit somewhat specific for verbal (*eg* words) or non-verbal (*eg* faces) material (Kolb and Whishaw, 1985; Jones-Gotman, 1987). Amnesics often have hypometabolism in the hippocampus and related structures (Fazio *et al*, 1992; Heiss *et al*, 1992), and the hippocampal formation may be metabolically activated when memory recall or formation is required (Nenov *et al*, 1991; Squire *et al*, 1992; Nenov *et al*, submitted). Another candidate N4/P3b generating structure, the entorhinal/perirhinal cortex, has also been implicated in recent declarative memory by lesion (Murray, 1992), cooling (George *et al*, 1989), and unit-recording (Miller *et al*, 1993) studies in monkeys.

The current study demonstrated large effects of face or word repetition on several EP components, and in several areas including the hippocampus and rhinal cortex. Repetition effects on EPs to words have also been observed in several previous scalp (Sanquist *et al*, 1980; Johnson *et al*, 1985; Fabiani *et al*, 1986; Neville *et al*, 1986; Rugg and Nagy, 1989; Domalski *et al*, 1991; Smith and Guster, 1993) and depth (Smith *et al*, 1986; Puce *et al*, 1991) studies (reviewed in Halgren, 1994; Kutas, 1988; Rugg and Doyle, 1993).

At the scalp, significant word repetition effects have been observed on components peaking at

about 220, 400, and 550 ms. The effect at 220 is the least replicated, but seems to involve a positive peak, maximal over the frontal lobe, and is mainly observed at zero inter-stimulus lag (Paller *et al*, 1987; Rugg, 1987; Nagy and Rugg, 1989; Van Petten *et al*, 1991; Smith, 1993). It is possible that the decreased N240 observed in this study to repeated words in lateral occipitotemporal, and posterior cingulate cortices may contribute to this effect.

The major effect on repetition is a decrease in the N4 and increase in the P3b. Some have suggested that both effects are the result of a single superimposed positivity (Rugg, 1987). This explanation is less likely for tasks where the decreased N4 has different task correlates than the increased P3 (Van Petten *et al*, 1991; Paller and Kutas, 1992). However, these task effects could be explained as manipulating the onset and duration of a single superimposed positivity rather than demonstrating distinct generators. Unambiguous demonstration of distinct effects was provided by previous depth studies which demonstrated that the repetition effect could occur in medial temporal lobe sites where only one or the other of these two components was recorded (Smith *et al*, 1986). The current study extends this finding to brain areas outside the MTL, and suggests that the repetition effect may extend to several components: N240, N310, N430, and P630.

Scalp studies have clearly differentiated the repetition effect from those of probability, targetness, or confidence (Smith and Halgren, 1987b; Rugg and Nagy, 1989; Paller and Kutas, 1992; Rugg and Doyle, 1993; Smith and Guster, 1993). However, it remains highly controversial whether the repetition effect represents implicit (procedural or priming) memory (Johnson *et al*, 1985; Rugg and Nagy, 1989; Rugg and Doyle, 1992), explicit (declarative recollective) memory (Wood *et al*, 1980; Van Petten *et al*, 1991; Paller and Kutas, 1992; Halgren, 1994) or both (Bentin and Peled, 1992). The current finding that the repetition effects occur in sensory association cortex, and at relatively early latencies during components typically asociated with high-level sensory feature processing or template-matching, supports the possibility that some repetition effects may reflect implicit memory processes.

The most prominent repetition effects, however, are clearly in those medial temporal structures associated by lesion and PET studies with declarative memory, and in components (N4-P3b) associated with controlled integrative processing. This is consistent with scalp studies showing that the repetition effect is strongly correlated with the subjective sense of recollection (Smith, 1993); that it is maintained with cross-modal repetition (Domalski *et al*, 1991); and that it can be dissociated from fluency by brain lesions (Smith and Halgren, 1989).

However, the current study does not support a near division between early implicit memory repetition effects in sensory association cortex *versus* late explicit memory effects in the medial temporal lobe, because the basal occipitotemporal cortex sites showed very clear word repetition effects at N4 and P3b latencies. This may explain the finding of Paller and Kutas (1992) that priming effects were late, at about 450 ms latency, and located over the posterior scalp.

This point can be made much more emphatically for faces. Although they have been much less studied than words, repetition effects have also been observed to faces at the scalp (Bentin and Moscovitch, 1988; Barrett *et al*, 1988; Smith and Halgren, 1987a). The dominant effect is again a decreased N4 and increased P3b. Occasionally, a small repetition effect at the scalp can be seen at about 170 ms (Marinkovic and Halgren, 1993). The current study showed that not only did clear repetition effects to faces occur in the fusiform g. N4, the differential posterior hippocampal formation responses to repeated faces may occur as early as 130 ms after stimulus onset, and are quite clear 240 ms after onset. This implies that declarative memory circuits are engaged in processing very early, simultaneously with the later stages of form processing and very probably before conscious perception. Thus, declarative memory may participate in early stages of perceptual, as well as later stages of cognitive integration.

Clearly, extensive studies will be required to definitively assign these repetition effects in different structures at different latencies to the implicit *versus* declarative memory systems. What the current study establishes is that these effects are widespread in both time and space, and are unlikely to reflect a single process. Furthermore, their anatomical extension – simultaneously including the hippocampal formation, amygdaloid region and visual as well as supramodal association cortices – strongly supports models of declarative memory which posit an interaction between these structures during the formation and

retrieval of recent declarative memories (Marr, 1971; Halgren, 1984; Squire *et al*, 1984; Teyler and Di Scenna, 1986).

Unity of the semantic store

The telencephalic regions involved in emotional and memory encoding, and in final contextual integration of complex meaningful material, seem to usually be non-specific, that is, seem to be used for integration of both words and faces. Although early components gave some evidence for specificity for faces *versus* words, components after 240 ms were evoked by both in most areas. It must be noted that a small difference in amplitude related to an interaction of laterality (dominant/non dominant) and material (words/faces) would have been difficult to demonstrate in this study given that the electrodes were in most cases implanted unilaterally, and even with bilateral implantations, there is often unilateral epileptiform pathology that confounds interpretation. In fact, a previous study with bilaterally symmetrical implantations into the MTL demonstrated that although the N4 to words was present bilaterally, it was significantly larger in the dominant MTL (Smith *et al*, 1986). This is consistent with the conclusion of spit-brain and lesions that word recognition is only partially lateralized to the dominant hemisphere, and face recognition to the nondominant, with either hemisphere possessing some capacity to process both types of stimuli (Hecaen, 1981; Ellis, 1983; Zaidel, 1989; Perrett *et al*, 1988; Damasio *et al*, 1990).

In the past several years, case studies demonstrating remarkably specific deficits in semantic memory for particular categories of objects have been reported (Warrington and McCarthy, 1987). These findings have been taken as arguing against an overall semantic store, and rather for multiple stores, each of which being specific for a particular category of object or modality of apprehension (McCarthy and Warrington, 1988). In contrast, the current results suggest that the semantic store may be largely unitary, except for relatively small regions that are specific (in this study, for words or faces). For example, the EPs evoked by words or faces appear to often be specific at earlier latencies and/or in particular structures (*eg* the P180 in the right fusiform g for faces), and usually non-specific (*ie* evoked by words and faces) at longer latencies in multiple cortical and limbic areas. Cognitive studies suggest that it is during these longer latencies that semantic interpretation takes place. The fact that the lesions which produce category-specific deficits for faces are centered in this same right fusiform area suggests that such lesions do not destroy the entire semantic system for faces but an entry-point to that system. That is, fusiform lesions would prevent both the specific encoding of faces, and the distribution of this information to widespread association and limbic areas where its semantic significance would be probed. More generally, category-specific semantic deficits would be produced by lesions in critical structures (where material-specific EPs are found) by preventing access by stimuli in that category to the more widespread nonspecific semantic network. In some cases, the material-specific EP may embody processing that is a necessary antecedant process for evoking the N4. In such cases the proposed mechanism predicts that material-specific semantic deficits would be accompanied by an anatomically-widespread but material-specific absence of the N4.

In short, the widespread and overlapping structures activated by faces and words in the current study suggest that specific deficits could only be produced by lesions to specific antecedent structures allowing faces or words to enter the distributed network for higher processing. Furthermore, the overlap between structures evoked by words *versus* faces exposes a limitation of using a 'subtraction' methodology for finding brain areas activated by a particular task in comparison to another very similar task (commonly used in PET studies). Clearly, such methodology would fail to reveal the widespread areas shown by this study to be involved in two tasks using very different material.

Conclusion

Assuming that cognitive processing is reflected in locally-recorded field-potentials, then the current study demonstrates that face- and word-processing in the human brain is not through a strictly sequential activation of successive cortical and limbic areas, nor through a completely parallel simultaneous undifferentiated activation of all structures. Rather, processing appears to proceed through distinct stages, overlapping but of increasing post-stimulus peak latencies, and

with distinct generators and cognitive functions. These stages can be conceptualized as representing: 1) focal sensory processing; 2) localized specific word or face structural encoding; and 3) widespread semantic contextual integration.

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Note added in proof

Recently, Allison *et al* [Allison T, Ginter H, McCarthy G, Nobre AN, Puce A, Luby M, McCarthy K, Spencer DD (1993) Electrophysiological studies of face recognition in human extrastriate cortex. *Soc Neurosci* (Abstracts) 19, 976] reported recording a negative potential at about 200 ms from the surface of basal occipitotemporal cortex. This potential appears to be identical (except inverted) to the P180 evoked in the fusiform g in the current study.

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