

Short- and Long-Delay Intracranial ERP Repetition Effects Dissociate Memory Systems in the Human Brain

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Abstract

■ Prior exposure to a stimulus can facilitate the performance to subsequent presentations of that stimulus. ERP studies have shown that this facilitation is associated with the modulation of two components (N400 and P600). Investigation of the time course of both behavioral and ERP repetition effects have led to the assumption that it is subserved by the combination of at least two mechanisms operating at different time-points: a short-delay semantic activation and a long-lasting episodic mechanism. The present experiment recorded intracranial ERPs from various structures during a continuous recognition

memory task to investigate the respective contribution of the different brain regions to short- and long-delay ERP repetition effects. The results are in good agreement with both the classical neuropsychological literature and the more recent data obtained with functional imagery techniques. They provide electrophysiological evidence of multiple anatomic-functional memory systems in the human brain: a short-term semantic activation system and a long-term episodic memory system, with interface structures that coordinate the functioning of these two systems. ■

INTRODUCTION

On a variety of tasks, performance is improved when a stimulus has been previously encountered in the list (Clarke & Morton, 1983; Forbach, Stanners, & Hochhaus, 1974; Scarborough, Cortese, & Scarborough, 1977; Winick & Daniels, 1970). In a typical paradigm, this “repetition effect” is manifest in the fact that stimulus response latency is shorter and the error rate is lower with the repeated presentation of the stimulus than with its initial presentation. The repetition effect lies at the interface between reading and memory, as reflected in the debate over whether the beneficial effects of item repetition are due to the persistent activation of an abstract representation in a semantic memory (Morton, 1969) or to the retrieval of a specific episodic memory trace (Jacoby, 1983). However, it is becoming increasingly clear that the repetition effect cannot be fully explained by either semantic or episodic mechanisms alone (Feustel, Shiffrin, & Salasoo, 1983).

Short- versus Long-Delay Repetition Effects, Semantic versus Episodic Processing

Accordingly, a number of studies have attempted to examine the relative contribution of each mechanism by

looking at the time-course of the repetition effect. Short-delay repetition produces a marked decline in word classification time. This phenomenon occurs in a wide variety of tasks using various types of stimuli (e.g., words, nonwords, or nonverbal stimuli such as faces) and is independent of the conscious recall of the priming stimulus (Bentin & Moscovitch, 1988; Dannenbring & Briand, 1982; Forster & Davis, 1984; Humphreys, Besner, & Quinlan, 1988; Monsell, 1985; Ratcliff, Hockley, & McKoon, 1985; Scarborough et al., 1977). These data suggest that the short-delay repetition effect may be viewed as the consequence of a short-lasting change in the accessibility of the representation of the stimulus, which might be either semantic or episodic. On the other hand, long-delay repetition, although resulting in a smaller response facilitation than short-delay repetition, does not decrease with increasing interitem delays (Monsell, 1985; Ratcliff et al., 1985). Moreover, the amount of facilitation produced by long-delayed repetition can be affected by task-related parameters (Bentin & Moscovitch, 1988; Hockley, 1982) and, at least within the context of repetition priming paradigms, appears to depend upon explicit awareness of the occurrence and identity of the prime (Humphreys et al., 1988; Oliphant, 1983). This effect is also observed in tasks using nonwords or nonverbal stimuli (faces) when subjects are

familiarized with the stimuli prior to testing, and when repetition is assessed under conditions that require access to the trace formed during familiarization (Bentin & Moscovitch, 1988). Such data suggest that the long-delay repetition effect depends on the availability of a preexisting episodic representation of the stimulus in memory.

From the above considerations, it appears likely that the repetition effect represents the contribution of a number of processes operating at different time-points following stimulus presentation. Forster and Davis (1984) have proposed that the repetition effect involves at least two separate components. The short-term component produces a large facilitation that affects only immediate or short-delay repetition. Thus, Forster and Davis (1984) argue that the short-delay repetition effect represents an automatic consequence of repeated access of the same semantic representation of an item. Moreover, Monsell (1985) suggests that the large amount of facilitation produced by a short-delayed repetition is the result of the concomitant activation of the semantic associates of the items (e.g., semantic priming). The long-term process produces less response facilitation but shows little decay over long delays in repetition. Forster and Davis (1984) argue that the semantic activation of a word's representation persists for a short period of time so as to allow interpretation of the word, and then decays so that the lexical system is not overloaded by the concurrent activation of many entries. These authors therefore propose that the stable long-term component of the repetition effect cannot be semantic in origin but rather reflects the reaccessing of the episodic memory trace that was established in relation to the context-specific presentation of the item and is enhanced by subsequent presentation of the same item. A similar, but less dissociative position has been adopted by Ratcliff et al. (1985), who imply that the short- and long-term components overlap, so the short-delay repetition effect receives the contribution of both episodic and semantic factors, whereas long-delay repetition effect primarily reflects episodic processing. This latter view can better account for the strong immediate repetition effects with nonwords and nonverbal stimuli.

Event-Related Potential (ERP) Correlates of the Repetition Effect

The repetition effect has been extensively explored with ERPs recorded in a wide variety of tasks involving semantic priming, lexical decision, and implicit or explicit recognition and using various type of stimuli such as words, nonwords, pictures, and faces (Barrett and Rugg, 1989; Begleiter, Porjesz, & Wang, 1995; Bentin & McCarthy, 1989; Bentin, McCarthy, & Wood, 1985; Bentin & Peled, 1990; Friedman, 1990; Holcomb, 1993; Karayanidis, Andrews, Ward, & McConaghy, 1991; Kazmerski & Friedman, 1997; Neville, Kutas, Chesney, & Schmidt, 1986; Noldy, Stelmack, & Campbell, 1990; Rugg, 1985; Rugg, 1987;

Rugg & Doyle, 1994; Rugg & Nagy, 1987; Rugg & Nagy, 1989; Smith, 1993; Smith and Halgren, 1987; Van Petten, Kutas, Kluender, Mitchiner, & McIsaac, 1991). The basic finding is that waveforms elicited by the first presentation of a stimulus are relatively less positive than those elicited by the second presentation of the same item. The divergence between the waveforms starts at about 300 msec and lasts until about 600 msec from the stimulus onset. This "ERP repetition effect" reflects the modulation of at least two underlying components, namely, the N400 (attenuated by repetition) and the P600 (enhanced by repetition).

The timing and psychological correlates of the N400 are consistent with its representing a period of associative activation, leading to the formation or the access to the representation of items in memory (Halgren, 1990; Halgren and Smith, 1987). The amplitude of this component is influenced by the overall amount of activation that is available for a representation as a result of a prior exposure (Karayanidis et al., 1991). The relationship linking the P600 to memory processes is less clear. It is classically assumed that this component is equivalent to the well-known P300 or P3 but has long latency due to the complexity of the preceding cognitive processing (Halgren, 1990; Kutas, McCarthy, & Donchin, 1977; Van Petten et al., 1991). Theories concerning the cognitive correlates of these late positive components includes stimulus categorization (Desmedt, 1981), context updating (Donchin & Coles, 1988), contextual closure, and template matching (Verleger, 1988). At this point, it should be emphasized that the cognitive processes underlying both the N400 and P600 components are so widely defined that it is difficult to identify the different ERP components with specific processes such as semantic activation or access to episodic traces. Rather, modulation of these ERP components (i.e., the ERP repetition effect) may reflect the interaction of a variety of different information sources that all contribute to item recognition (Karayanidis et al., 1991).

There is considerable evidence to support this assertion. The fact that the ERP repetition effect is elicited for semantically primed words (Bentin et al., 1985; Holcomb, 1993; Rugg, 1985) and is more pronounced for words than for nonwords (Rugg, 1987; Rugg & Nagy, 1987) implies a contribution of semantic processes. On the other hand, the influence of episodic memory is indicated by the observation that the ERP repetition effect persists over repetition lags from 0 to 19 (Bentin & Peled, 1990; Friedman, 1990; Rugg & Nagy, 1989), is related to the conscious recollection (e.g., "context retrieval") of a memory trace (Smith, 1993), and is obtained with nonverbal stimuli such as faces (Barrett & Rugg, 1989; Begleiter et al., 1995; Bentin & McCarthy, 1989; Smith & Halgren, 1987). As in behavioral studies, some investigators have attempted to examine the relative contribution of each mechanism by examining the time-course of the ERP repetition effect (Bentin & Peled,

1990; Karayanidis et al., 1991; Nagy & Rugg, 1989). Interestingly, Karayanidis et al. (1991) noted that in all these studies, the ERP repetition effect for delayed repetition shows a tendency to lie between those obtained for the first presentation and immediate or short-delay repetition, at least at Pz. This observation is consistent with the view of Ratcliff et al. (1985) that some processes (i.e., semantic activation) affecting the short-delay repetition are not operative at long delay. Therefore, it could be argued that the short-delay ERP repetition effect is influenced by both short-term semantic and episodic factors, whereas the long-delay ERP repetition effect is primarily determined by a stable episodic process.

Intracranial ERP Investigation of the Repetition Effect

There is by now a growing body of data from direct intracranial ERP recordings in epileptic patients undergoing stereoencephalography showing that ERP components of similar morphology and latency and that are sensitive to the repetition of items can be recorded from various brain regions while patients are performing recognition memory tasks (Guillem, N'Kaoua, Rougier, & Claverie, 1995b; Grunwald, Elger, Lehnertz, Van Roost, & Heinze, 1995; Halgren, Baudena, Heit, Clarke, & Marinkovic, 1994a; Halgren, Baudena, Heit, Clarke, & Marinkovic, et al., 1994b; Halgren, Smith, & Stapleton, 1984; Heit, Smith, & Halgren, 1990; McCarthy & Wood, 1980; Puce, Andrewes, Berkovic, & Bladin, 1991; Seeck et al., 1993; Smith, Stapleton, & Halgren, 1986). These studies have demonstrated that a number of temporal, frontal, and parietal lobe structures contribute to the generation (e.g., large amplitude gradients and local polarity reversals) and modulation (e.g., ERP repetition effect) of these potentials. Therefore, depth-recorded N400 and P600 may provide valuable indices to investigate the relative contribution of each brain structure to the cognitive processes underlying the scalp-recorded ERP repetition effect (i.e., semantic and episodic processes).

The Present Experiment

There is by now a large body of evidence from classical neuropsychology (see McCarthy & Warrington, 1990, for a review) and the more recent data from functional imaging techniques (e.g., Grasby et al., 1993; Perani et al., 1993) showing that the semantic and episodic processes are subserved by different networks of interconnected brain structures. In view of the current interpretations concerning the repetition effect, it is likely that assessing the time-course of the ERP repetition effect recorded from different brain structures may also offer the possibility to evaluate the relative contribution of these structures to both kinds of processing, thus helping to dissociate multiple memory systems in the human brain.

Therefore, the purpose of the present study was to investigate the ERP repetition effect recorded from various brain regions. A continuous recognition memory task for pictures was used with repetition occurring with either a short (6 items) or a long (19 items) lag. According to the above data, the presence of an ERP repetition effect only at short lag would indicate that the structure from which those ERPs have been recorded is involved in the semantic activation. On the other hand, if both short- and long-delay ERP repetition effects are present, this would mean that the structure contributes to the long-lasting episodic processing of items.

The choice of the protocol design and stimuli used in this study may raise two issues. The first concerns the relevance of using pictures as stimuli to assess the contribution of semantic factors modulating the ERP repetition effect. The use of such kinds of stimuli was primarily done to take into account the fact that patients in whom epilepsy onset occurs at early ages often present difficulties in reading. However, a number of studies have shown that a semantic priming effect can be obtained for pictures as well as for words (Vanderwart, 1984; Warren & Morton, 1982) and that the encoding of both types of stimuli is affected in an analogous interactive manner by semantic relatedness (Kroll & Potter, 1983; Sperber, McCauley, Ragain, & Weil, 1979). These observations are consistent with models emphasizing that even if there are differences in picture and word processing, both are ultimately processed by the same semantic system (Nelson, Reed, & McEvoy, 1977; Potter, 1979; Seymour, 1976; Snodgrass, 1980). According to this view, the most parsimonious interpretation would be that a semantic (if not lexical) activation is actually involved in modulating the short-delay (ERP) repetition effect for pictures. The second issue concerns the relevance of using an interitem lag involving six intervening items to assess semantic activation, whereas numerous studies, mainly using lexical decision tasks, assume that such activation decays within a few hundred milliseconds and so it is present on immediate repetition and disappears completely if there are other intervening items. This was primarily done to take into account the distractibility of some patients by maintaining a difficulty level sufficient to ensure that the focus of patients' attention remains on performing the continuous task (i.e., an immediate repetition that could be perceived as very easy would have encouraged attentional switch). Indeed, there are data to suggest that shifts in attention may be more important than the delay in reducing the semantic activation (Kellogg, Newcombe, Kammer, & Schmidt, 1996; Nelson, McEvoy, Janczura, & Xu, 1993; see also Nelson, McKinney, Gee, & Janczura, 1998). Consistent with this view, there is increasing evidence that semantic activation or priming may last longer and span many intervening items (at least eight items) under conditions that enhance the spread of activation to related associates and attributes (Allen, Goldstein, Madden, & Mitchell,

1997; Becker, Moscovitch, Behrmann, & Joordens, 1997; Joordens & Becker, 1997; Kellogg et al., 1996). From these data, it appears that the duration of the semantic priming effect is in fact related to the amount of information (representations and attributes) activated in semantic networks as a function of the task demand. By this view the processing of pictures associating pictorial, semantic, and lexical representations is more likely to achieve a sufficient degree of activation than the processing of words in the context of a simple lexical decision task.

In any respect, the present study does not address the distinction between lexical and semantic processing but rather emphasizes the dissociation between short-lived "lexico-semantic" processes and long-lasting episodic mechanisms. Therefore, in the subsequent discussion, the term *semantic* should only be taken as a general term qualifying the set of processes that contribute specifically to the short-delay repetition effect.

RESULTS

Behavioral Measures

Behavioral measurements for both the R-6 and R-19 conditions, in the form of reaction times, scores (percent of correct responses), and corresponding d' statistics are presented in Table 1. Analyses of variance (ANOVAs) with repeated measures revealed that significant differences exist in reaction time, score and d' data, showing that the performance declines with the delay.

These results are consistent with previous behavioral studies of repetition effects showing that the behavioral facilitation was smaller for delayed than for immediate or short-delayed repetition (Bentin & Moscovitch, 1988; Feustel et al., 1983; Ratcliff et al., 1985). As noted in the Introduction, this suggests that some processes influencing short-delayed repetition are not operative after a long delay. According to this view, the data suggest that the continuous recognition procedure used in the present study may provide a suitable behavioral context for an ERP investigation of the involvement of the different brain structures in the cognitive processes underlying the short- and long-delayed repetition effects, respectively.

ERP Component Identification

Visual inspection of the recordings revealed that the most prominent feature common to all the waveforms obtained from the different structures is the presence of two long-latency ERP components identified on the basis of latency, typical polarity, and task correlates. The first was typically negative in polarity and peaked around 400 msec, so it was referred to as N400. The second component followed the N400 with a peak latency around 600 msec. This component was typically positive and was referred to as P600. As described in other studies, the posterior temporal cortex is only one structure in which the P600 was not reliable enough to be identified in each patient.

It should be noted that in some brain regions, other components (e.g., an early positive component at parietal sites and a negative slow wave within the frontal structures) described in previous studies were also identified in the current recordings. However, because the statistical analysis did not reveal any repetition effect for these components, only the results concerning N400 and P600 are presented in the subsequent sections.

Some recordings presented N400 and/or P600 components were the opposite of their normal polarity (e.g., some hippocampal and orbital recordings), and some were characterized by a large-amplitude component that overlapped markedly with the other components so that these were no longer identifiable (i.e., some cingulate recordings). These recordings were therefore not included in the analysis (see Guillem, N'Kaoua, Rougier, & Claverie, 1996a, 1996b).

In the other recordings, the amplitudes of the N400 and P600 components were quantified, in each structure and in each subject, by averaged voltage (with respect to the mean of the prestimulus baseline) over two time windows. The mean latency windows used for the different structures are specified in Table 2.

Global ERP Analysis

For the N400, the 8 (Structure) \times 2 (Hemisphere) \times 3 (Condition) ANOVA with repeated measures on the fac-

Table 1. Behavioral Data and Statistical Analysis (*SD* Are in Parentheses)

	Response		<i>F</i>	<i>df</i>	<i>p</i>
	<i>R-6</i>	<i>R-19</i>			
Reaction time (msec)	949.2 (178.8)	979.0 (194.8)	12.96	1.33	0.001
Scores (% correct)	93.89 (8.97)	90.47 (12.53)	9.01	1.34	0.005
d' statistics	1.81 (0.52)	1.65 (0.52)	5.44	1.34	0.02

Table 2. Mean Latency Windows for Component Identification in each Brain Structure

Structures	Latency windows (msec)	
	N400	P600
Hippocampus	325-510	510-745
Amygdala	365-540	540-775
Anterior temporal cortex	370-540	540-745
Anterior cingulate gyrus	325-510	510-745
Lateral frontal cortex	365-540	540-775
Orbito-frontal region	370-540	540-745
Parietal cortex	325-510	510-745
Posterior temporal cortex	370-540	

tor of task condition revealed the main effects of task condition ($F(2, 282) = 24.67; p = 0.0001; \epsilon = 0.97$), and structures ($F(7, 282) = 5.52; p = 0.0001; \epsilon = 0.97$), with a tendency for an interaction between factors ($F(14, 282) = 1.66; p = 0.06; \epsilon = 0.97$). These results suggest that for this component the structures responded differentially as a function of the interitem lag.

The 7 (Structure) \times 2 (Hemisphere) \times 3 (Condition) ANOVA with repeated measures on the factor of task condition performed on the P600 data revealed only a main effect of task condition ($F(2, 254) = 22.26; p = 0.0001; \epsilon = 0.94$). These results suggest that the P600 repetition effect is similar across structures.

ERPs Recorded from the Anterior Temporal Structures

Hippocampus

In 18 patients, data were obtained from 22 contacts located in the hippocampus. Representative hippocampal recordings and a schematic representation of the results are presented in Figure 1.

For the N400, the 2 (Hemisphere) \times 3 (Condition) ANOVA with repeated measures on the factor of task condition revealed a main effect of task condition ($F(2, 40) = 4.91; p = 0.01; \epsilon = 0.98$). There were no effects of site or interactions between factors. Partial 2 (Hemisphere) \times 2 (Condition) ANOVAs revealed that the effect of task condition was significant when comparing A versus R-6 and A versus R-19 conditions (Table 3). These results indicate that the number of intervening items did not affect the hippocampal N400 repetition effect.

The same comparisons made on the P600 data did not reveal any significant effects.

Amygdala

Recordings from the amygdala were obtained from 19 contacts in 13 patients. Figure 2 provides representative

ERPs obtained from this structure together with a schematic representation of the results.

For the N400, the 2 (Hemisphere) \times 3 (Condition) ANOVA with repeated measures on the factor of task condition revealed a main effect of task condition ($F(2, 34) = 7.10; p = 0.003; \epsilon = 0.94$). There were no effects of site or interactions between factors. Partial 2 (Hemisphere) \times 2 (Condition) ANOVAs revealed that the effect of task condition was significant when comparing A versus R-6 and A versus R-19 conditions (Table 3). These data revealed that the N400 repetition effect was present whatever the interitem lag.

The 2 (Hemisphere) \times 3 (Condition) ANOVA with repeated measures on the P600 data also showed a main effect of task condition ($F(2, 34) = 4.66; p = 0.02; \epsilon = 0.86$). There were no effects of site or interactions between factors. Partial 2 (Hemisphere) \times 2 (Condition) ANOVAs revealed that the effect of task condition was significant only when comparing A versus R-6 conditions (Table 3). These results are similar to those obtained for the N400 component.

Anterior Temporal Cortex

In 18 patients, recordings were obtained from a total of 34 contacts exploring the anterior temporal cortex. Representative recordings from this structure and a schematic representation of the results are presented in Figure 3.

For the N400, the 2 (Hemisphere) \times 3 (Condition) ANOVA with repeated measures on the factor of task condition revealed a main effect of task condition ($F(2, 64) = 5.97; p = 0.004; \epsilon = 0.97$). There were no effects of site or interactions between factors. Partial 2 (Hemisphere) \times 2 (Condition) ANOVAs revealed that the effect of task condition was significant when comparing A versus R-6 and A versus R-19 conditions (Table 3). These data revealed that the N400 repetition effect was present whatever the interitem lag.

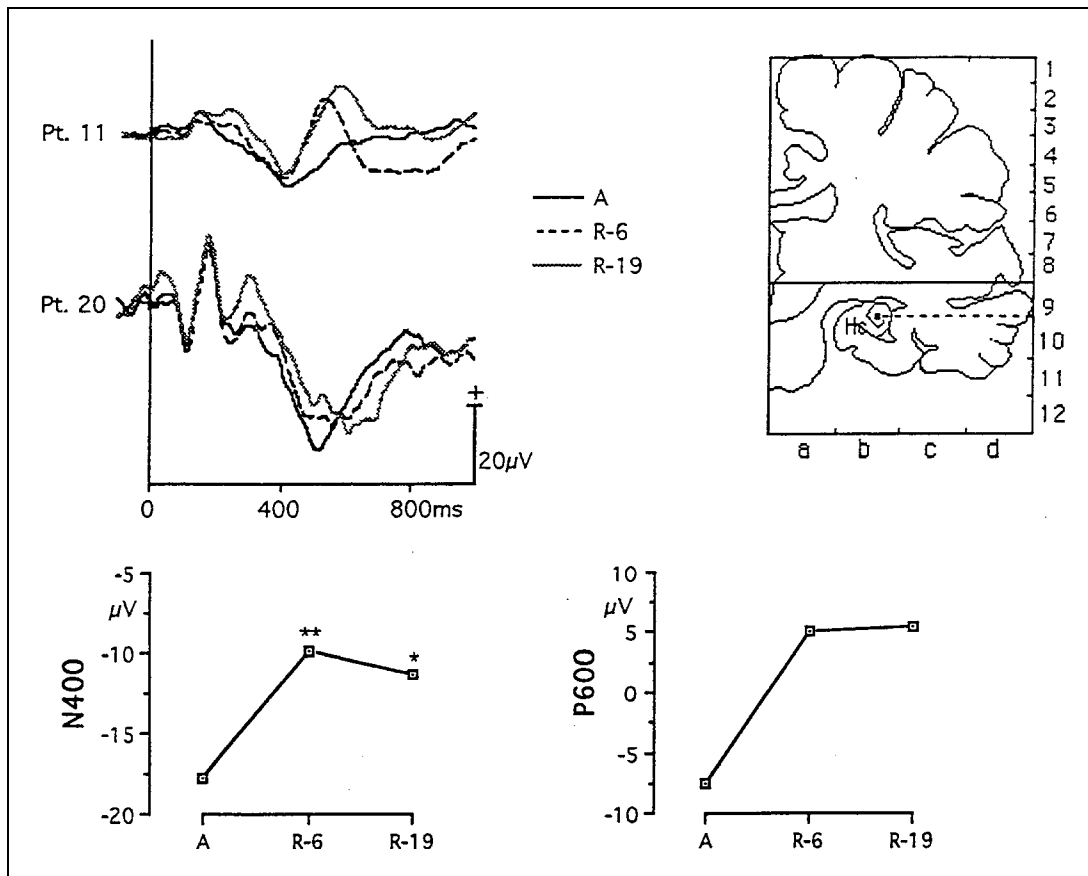


Figure 1. Representative ERPs recorded in the hippocampus (Hc) in the three task conditions (upper panel) and schematic representation of the time-course of the ERP repetition effect for N400 and P600 components (lower panel). The vertico-frontal brain slice shows the approximate electrode trajectories and contact location (a similar presentation has been adopted for the subsequent figures).

The 2 (Hemisphere) \times 3 (Condition) ANOVA with repeated measures on the P600 data also showed a main effect of task condition ($F(2, 64) = 5.41; p = 0.01; \epsilon = 0.87$). There were no effects of site or interactions between factors. Partial 2 (Hemisphere) \times 2 (Condition) ANOVAs revealed that the effect of task condition was significant when comparing A versus R-6 and A versus R-19 conditions (Table 3). These results indicate that the number of intervening items did not affect the P600 repetition effect.

ERPs Recorded from the Anterior Brain Areas

Anterior Cingulate Gyrus

In 13 patients, recordings were obtained from a total of 18 contacts exploring the anterior cingulate gyrus. Representative cingulate recordings and a schematic representation of the results are presented in Figure 4.

For the N400, the 2 (Hemisphere) \times 3 (Condition) ANOVA with repeated measures on the factor of task condition did not reveal any significant effects.

The 2 (Hemisphere) \times 3 (Condition) ANOVA with repeated measures on the P600 data showed a main effect of task condition ($F(2, 32) = 4.16; p = 0.04; \epsilon =$

0.63). There were no effects of site or interactions between factors. Partial 2 (Hemisphere) \times 2 (Condition) ANOVAs revealed that the effect of task condition was significant only when comparing A versus R-6 conditions (Table 4). These data revealed that the P600 repetition effect was present only in the R-6 condition.

Lateral Frontal Cortex

Recordings were obtained in 11 patients from 17 contacts located in the lateral frontal cortex. Figure 5 provides representative ERPs obtained from this structure together with a schematic representation of the results.

For the N400, the 2 (Hemisphere) \times 3 (Condition) ANOVA with repeated measures on the factor of task condition revealed a main effect of task condition ($F(2, 32) = 3.43; p = 0.04; \epsilon = 0.97$). There were no effects of site or interactions between factors. Tests for simple effect revealed that the effect of task condition was significant only when comparing A versus R-6 and conditions (Table 4). These data revealed that the N400 repetition effect was present only in the R-6 condition.

The 2 (Hemisphere) \times 3 (Condition) ANOVA with repeated measures on the P600 data showed a main

Table 3. Mean Amplitudes (μV ; SD) and Statistical Analysis for ERP Components Recorded from the Anterior Temporal Lobe Structures

Structure	Response			A/R-6			A/R-19		
	A	R-6	R-19	F	df	p	F	df	p
Hippocampus ($n = 22$)									
N400	-17.82 (12.28)	-9.82 (16.82)	-11.30 (21.01)	10.44	1.20	0.004	5.06	1.20	0.03
P600	-7.53 (12.90)	5.15 (20.72)	5.41 (21.93)	2.77	1.20	n.s.	3.70	1.20	n.s.
Amygdala ($n = 19$)									
N400	-33.95 (21.31)	-21.25 (17.71)	-26.30 (21.24)	11.34	1.17	0.004	6.44	1.17	0.02
P600	-5.35 (18.27)	4.85 (14.93)	-0.66 (18.18)	6.56	1.17	0.02	2.49	1.17	n.s.
Anterior temporal cortex ($n = 34$)									
N400	-16.39 (17.89)	-8.45 (22.70)	-9.13 (17.37)	11.88	1.32	0.002	7.73	1.32	0.009
P600	0.74 (13.69)	7.46 (19.74)	8.88 (15.91)	4.62	1.32	0.04	10.97	1.32	0.002

effect of task condition ($F(2, 32) = 5.19$; $p = 0.02$; $\epsilon = 0.78$). There were no effects of site or interactions between factors. Partial 2 (Hemisphere) \times 2 (Condition) ANOVAs revealed that the effect of task condition was significant only when comparing A versus R-6 conditions (Table 4). These results are similar to those obtained for the N400 component.

Orbito-Frontal Region

In eight patients, recordings were obtained from a total of 13 contacts exploring the orbito-frontal region. Representative recordings from this brain region and a schematic representation of the results are presented in Figure 6.

For the N400, the 2 (Hemisphere) \times 3 (Condition) ANOVA with repeated measures on the factor of task condition revealed a main effect of task condition ($F(2, 22) = 6.76$; $p = 0.01$; $\epsilon = 0.66$). There were no effects of site or interactions between factors. Partial 2 (Hemisphere) \times 2 (Condition) ANOVAs revealed that the effect of task condition was significant when comparing A versus R-6 and A versus R-19 conditions (Table 4). These data revealed that the N400 repetition effect was present whatever the interitem lag.

The 2 (Hemisphere) \times 3 (Condition) ANOVA with repeated measures on the P600 data also showed a main effect of task condition ($F(2, 22) = 19.18$; $p = 0.0001$; $\epsilon = 0.68$). There were no effects of site or interactions between factors. Partial 2 (Hemisphere) \times 2 (Condition) ANOVAs revealed that the effect of task condition was

significant when comparing A versus R-6 and A versus R-19 conditions (Table 4). These results indicate that the number of intervening items did not affect the P600 repetition effect.

ERPs Recorded from the Posterior Brain Areas

Parietal Cortex

Recordings were obtained in four patients from 12 contacts located in the parietal cortex. Figure 7 provides representative ERPs obtained from this area together with a schematic representation of the results.

For the N400, the 2 (Hemisphere) \times 3 (Condition) ANOVA with repeated measures on the factor of task condition revealed a main effect of task condition ($F(2, 20) = 3.49$; $p = 0.05$; $\epsilon = 0.62$). There were no effects of site or interactions between factors. Partial 2 (Hemisphere) \times 2 (Condition) ANOVAs revealed that the effect of task condition was significant only when comparing A versus R-6 conditions (Table 5). These data revealed that the N400 repetition effect was present only in the R-6 condition.

The same comparisons made on the P600 data did not reveal any significant effects.

Posterior Temporal Cortex

Recordings were obtained in 5 patients from 15 contacts located in the posterior part of the right temporal cortex. Figure 8 provides representative ERPs obtained from

Figure 2. Representative ERPs recorded in the amygdala (Am) in the three task conditions and schematic representation of the time-course of the ERP repetition effect for N400 and P600 components.

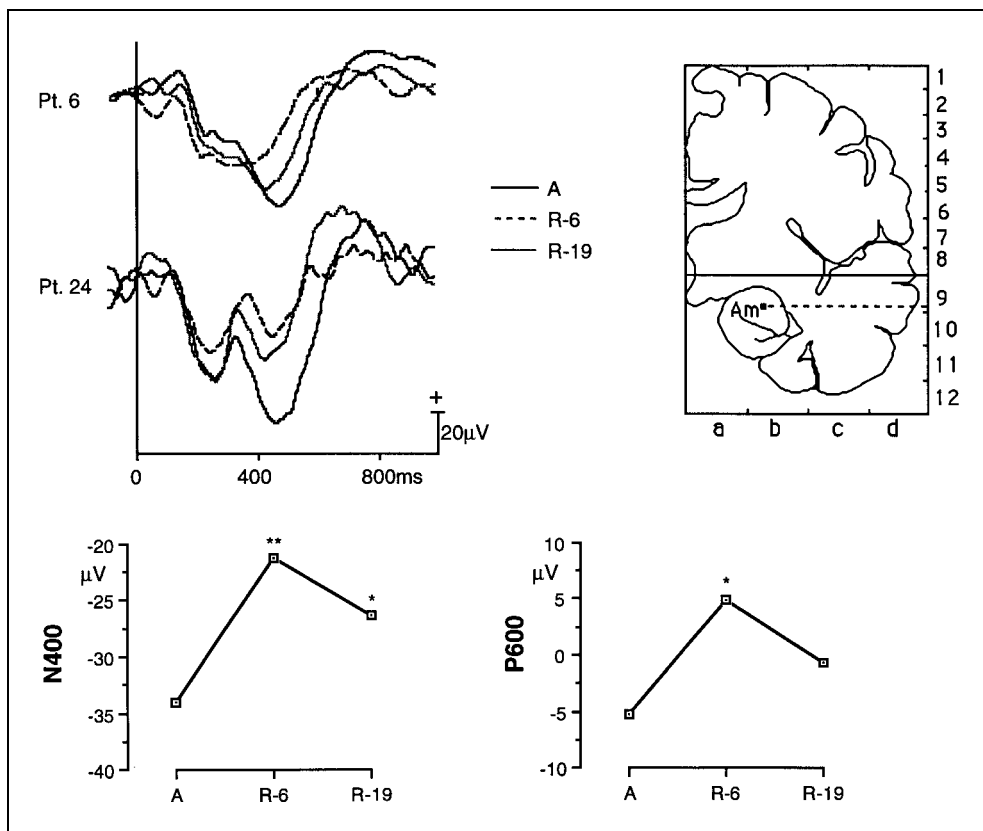


Figure 3. Representative ERPs recorded in the anterior temporal cortex (middle temporal gyrus, gTm) in the three task conditions and schematic representation of the time-course of the ERP repetition effect for N400 and P600 components.

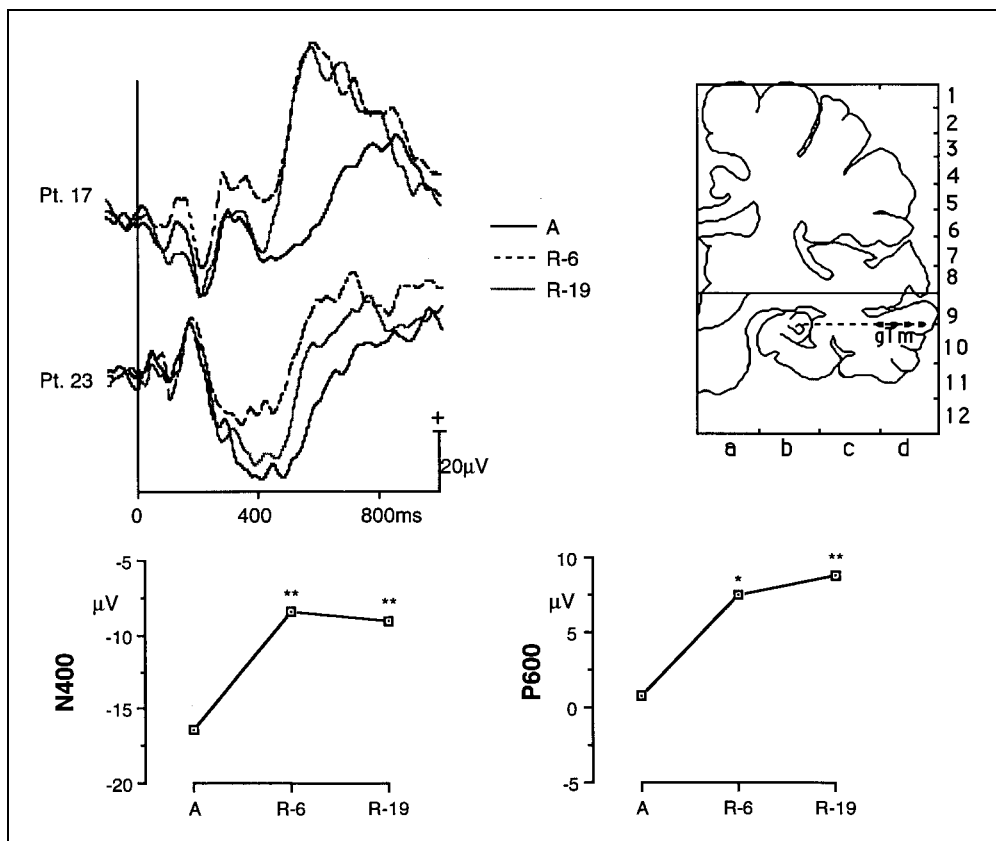
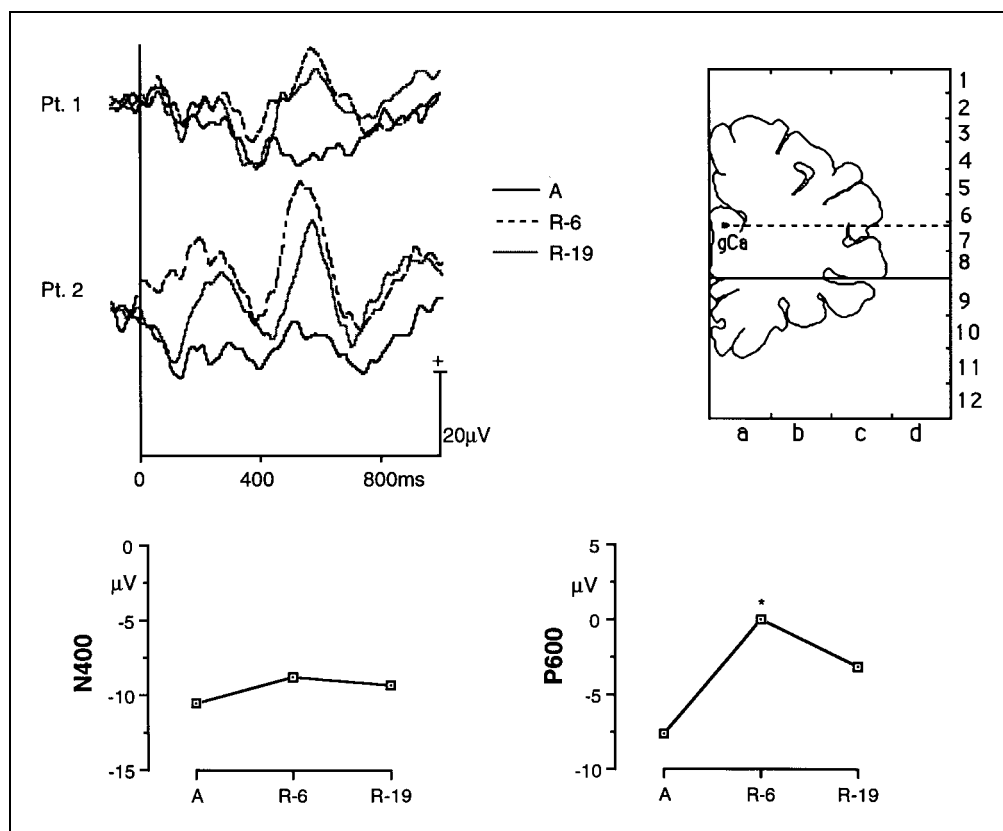


Figure 4. Representative ERPs recorded in the anterior cingulate gyrus (gCa) in the three task conditions and schematic representation of the time-course of the ERP repetition effect for N400 and P600 components.



this cortical area together with a schematic representation of the results.

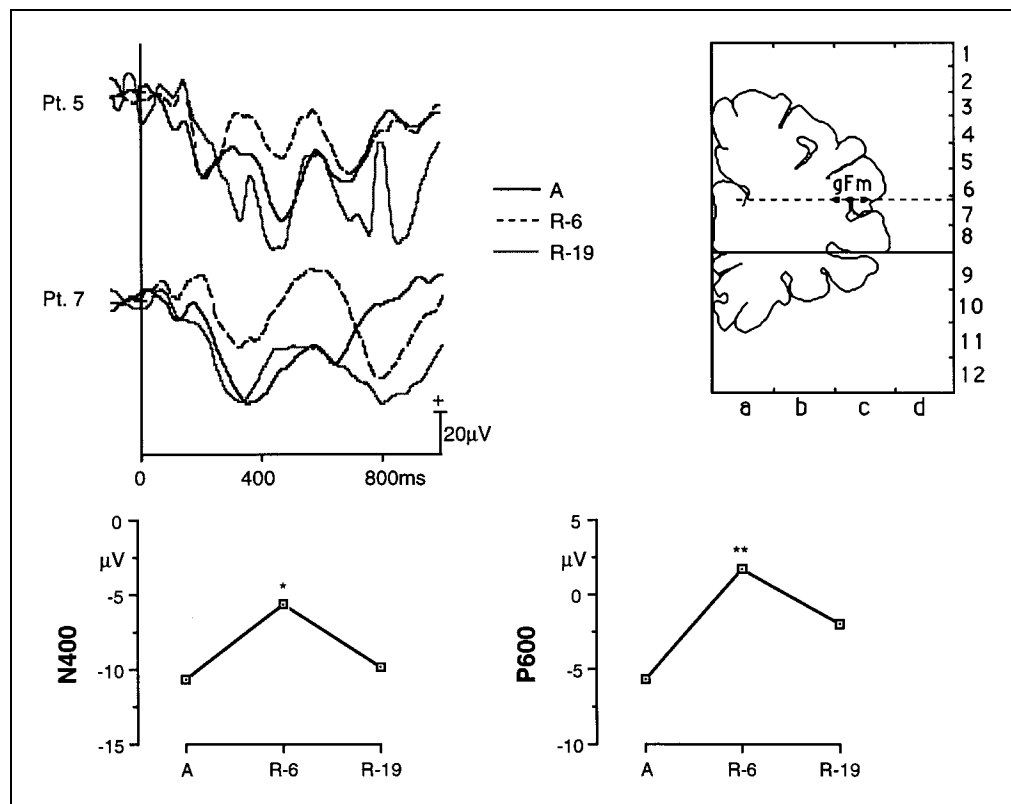
Because all recording were obtained from the right hemisphere, only a simple ANOVA with repeated measures on the factor of task condition was performed on

the N400 data. This analysis revealed a main effect of task condition ($F(2, 28) = 5.61; p = 0.02; \epsilon = 0.57$). There were no effects of site or interactions between factors. Tests for simple effect revealed that the effect of task condition was significant only when comparing A versus R-6

Table 4. Mean Amplitudes (μV ; SD) and Statistical Analysis for ERP Components Recorded from the Anterior Frontal Lobe Structures

Structure	Response			A/R-6			A/R-19		
	A	R-6	R-19	F	df	p	F	df	p
Anterior cingulate gyrus ($n = 18$)									
N400	-10.58 (12.95)	-8.84 (11.09)	-9.30 (12.93)	0.45	1.16	n.s.	0.65	1.16	n.s.
P600	-7.64 (13.92)	-0.01 (13.32)	-3.17 (12.75)	4.93	1.16	0.04	3.73	1.16	n.s.
Lateral frontal cortex ($n = 17$)									
N400	-10.66 (8.93)	-5.63 (9.70)	-9.83 (13.71)	7.18	1.15	0.02	0.15	1.15	n.s.
P600	-5.64 (10.29)	1.71 (14.25)	-1.94 (20.28)	14.88	1.15	0.001	1.48	1.15	n.s.
Orbito-frontal region ($n = 13$)									
N400	-13.44 (18.50)	-8.99 (20.09)	-2.69 (19.76)	5.14	1.11	0.04	10.04	1.11	0.009
P600	-7.12 (16.91)	4.32 (20.53)	5.37 (30.15)	22.00	1.11	0.0007	21.98	1.11	0.0007

Figure 5. Representative ERPs recorded in the dorsolateral prefrontal cortex (middle frontal gyrus, gFm) in the three task conditions and schematic representation of the time-course of the ERP repetition effect for N400 and P600 components.



conditions (Table 5). These data revealed that the N400 repetition effect was present only in the R-6 condition.

DISCUSSION

Intracranial ERPs: General Comments

Recordings from the whole brain region explored in the present study displayed two major long-latency depth ERP components (e.g., N400 and P600) that have been previously described in studies designed to investigate the intracranial topography and the local generation of memory ERP components (Guillem et al., 1995b; Halgren et al., 1994a, 1994b). These components were of comparable morphology and latency to those recorded on the scalp during recognition memory tasks that evoke the well-documented ERP repetition effect (see Introduction).

The most reliable data derived from the recordings was that the N400 amplitude is sensitive to the repetition of items (e.g., “N400 repetition effect”) in almost all the structures explored. Moreover, the interaction noted in the global analysis shows that differences in the time-course of the ERP repetition effects (on either the N400 or P600 component) exists across the different structures explored. This result demonstrates that the structures explored in the present study contribute differently to the semantic and episodic processes that underlie ERP repetition effects elicited on the scalp.

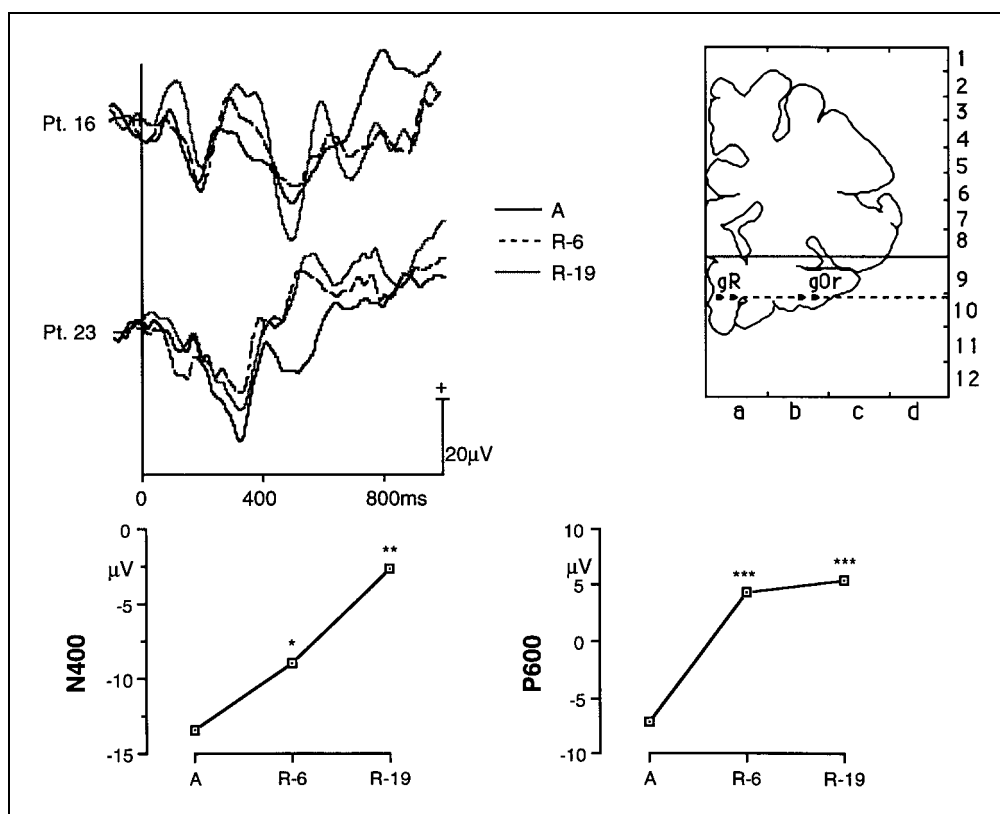
By contrast, the absence of structure by lag interaction

on the P600 amplitude suggests that the “P600 repetition effect” is similar across structures. Although the psychological construct underlying the P600 modulation remains unclear (see Introduction), this finding suggests that the P600 reflects some mechanisms that are common to both the semantic and episodic processing of items. Moreover, it should be emphasized that the P600 repetition effect was not consistently observed in all the structures explored, except in the anterior cingulate gyrus. A large amplitude P600 that is sensitive to the repetition of items characterizes ERPs recorded from this structure. This is consistent with previous results showing that the anterior cingulate gyrus contributes primarily to the generation and modulation of such positive components (P3a: Baudena, Halgren, Heit, & Clarke, 1995; P600: Guillem et al., 1995b; or F-P600: Guillem, N’Kaoua, Rougier, & Claverie, 1996a). Therefore, it is likely that the cingulate gyrus is an important anatomical component that subserves an interface role between semantic and episodic systems (see below).

Intracranial ERPs and Neuropsychological Data: Differential Contribution of Brain Structures to Memory Functioning

The following sections investigate to what extent the respective role of the different brain regions as assessed by means of intracranial ERPs fit the more classical data from the neuropsychological literature. Thus, for conven-

Figure 6. Representative ERPs recorded in the orbito-frontal region (gyrus rectus, gR, and orbital gyrus, gOr) in the three task conditions and schematic representation of the time-course of the ERP repetition effect for N400 and P600 components.



ience, the brain structures have been grouped according to the three main functional brain areas: anterior temporal lobe (e.g., amygdala, hippocampus, and anterior temporal cortex), posterior cortices (e.g., parietal cortex and posterior temporal lobe), and frontal lobe (e.g., anterior cingulate gyrus, lateral frontal cortex, and orbital region).

Anterior Temporal Lobe Structures

ERPs obtained from the anterior temporal lobe structures present a significant repetition effect at both short and long lags. In the current theoretical context, this pattern of activity is expected for structures that are involved in the reaccessing of episodic memory traces.

The involvement of the anterior temporal lobe in episodic memory is broadly supported by the classical data from neuropsychology. Numerous studies have emphasized that lesions to the anterior temporal area produce a profound deficit in various tasks requiring the learning and recall of new events (i.e., anterograde amnesia; see Smith, 1989, for a review). On the other hand, some experiments have shown that although a left temporal lobectomy produces impairments on recall and recognition of words, the patients nonetheless showed the normal pattern of deriving benefit from semantic encoding (Rains, 1987; Wilkins & Moscovitch, 1978). This finding suggested to the authors that the observed semantic deficits are mild compared to the deficits in episodic memory. These behavioral observations led to

the conclusion that the anterior temporal lobe contributes primarily to the acquisition and retrieval of episodic information. The present results are therefore in complete agreement with this assumption.

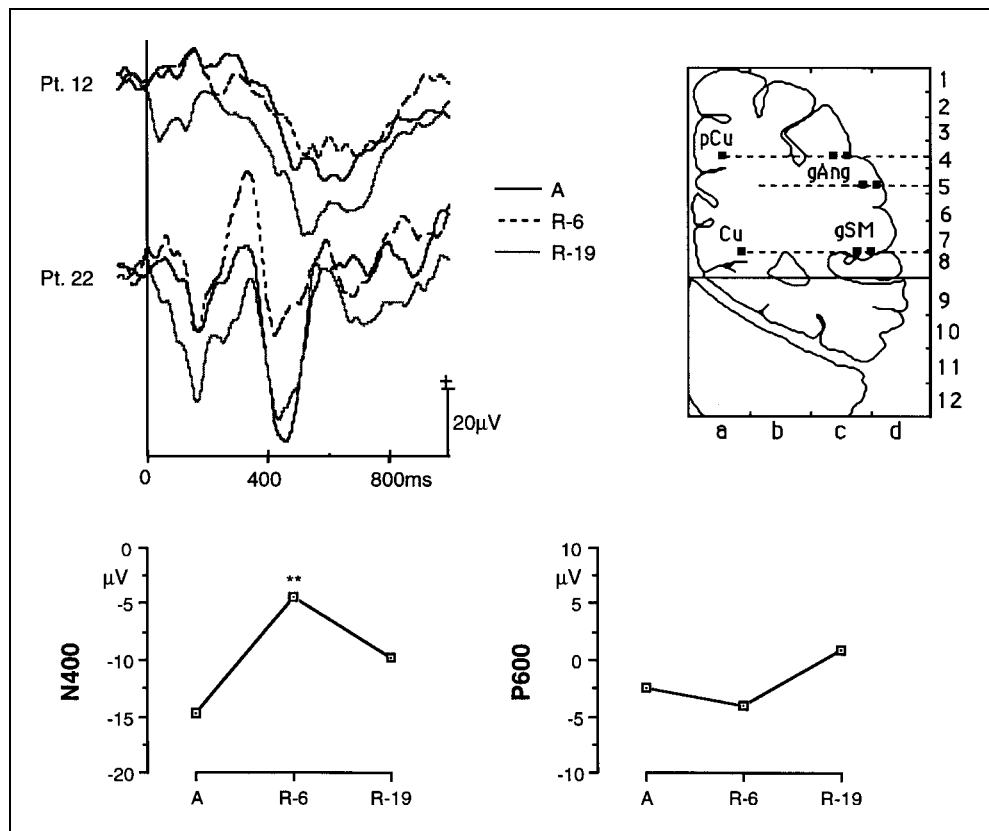
Also consistent with this view is the observation that the ERP repetition effect recorded from the amygdala and anterior temporal cortex shows a little decline over repetition lags from 6 to 19. Such time-related modifications that could arise from changes in the strength of the memory traces are thought to contribute to the recency judgment (Guillem et al., 1996b; Hinrichs, 1970). This kind of contextual (i.e., temporal) indexation is characteristic of episodic memory traces being established in relation to the context-specific attributes of the items.

Posterior Cortical Areas

Recordings from the posterior areas of the cortex revealed marked differences from the above structures, in that the ERP repetition effect is significant only in the short-lag condition. This could reflect the contribution of these brain regions to the semantic processing of items.

The precise anatomical correlates of impaired semantic memory are poorly defined. Findings in patients with semantic memory impairment produced by herpes simplex encephalitis (Warrington & Shallice, 1984) or progressive cerebral degeneration (McCarthy & Warrington,

Figure 7. Representative ERPs recorded in the parietal cortex (cuneus, Cu; precuneus, pCu; angular gyrus, gAng; supra marginal gyrus, gSM) in the three task conditions and schematic representation of the time-course of the ERP repetition effect for N400 and P600 components.



1988) concur to suggest an important role for the temporo-parietal association cortex. Studies of language disorders provide some support for this view in that some functions, such as word retrieval, comprehension, reading, and writing, are mediated by lexical and/or semantic processing. Such deficits have been widely documented in patients with focal lesions in various regions of the left hemisphere. However, a significantly higher incidence of these impairments has been found for lesions affecting the posterior areas explored in the present study, that is, the superior part of the posterior

lobe (Wernicke's area), the angular gyrus, and supramarginal gyrus (see McCarthy & Warrington, 1990, for a review). These observations therefore make the present ERP data highly consistent with the neuropsychological literature.

Frontal Lobe Structures

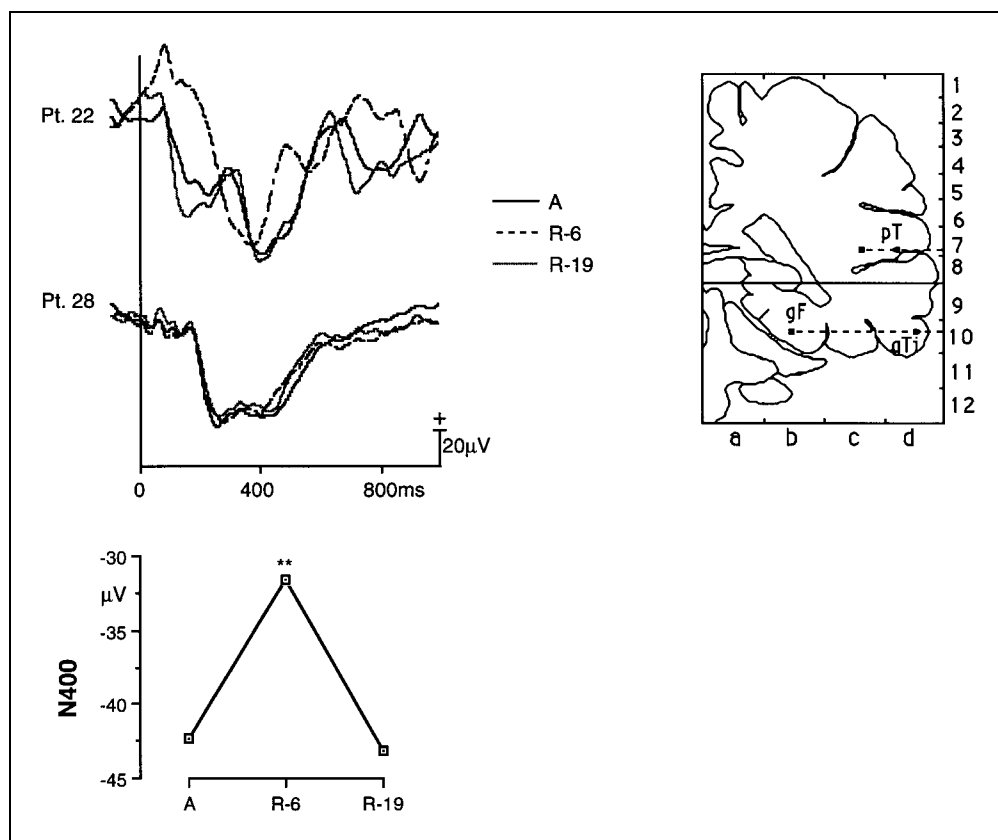
The results obtained from the frontal lobe are in good agreement with anatomical and neuropsychological data showing the functional heterogeneity of this broadly

Table 5. Mean Amplitudes (μV ; SD) and Statistical Analysis for ERP Components Recorded from the Posterior Structures

Structure	Response			A/R-6			A/R-19		
	A	R-6	R-19	F	df	p	F	df	p
Parietal cortex ($n = 12$)									
N400	-14.82 (13.10)	-4.46 (13.19)	-9.83 (13.71)	20.40	1.10	0.001	1.81	1.10	n.s.
P600	-2.53 (15.17)	-4.10 (14.81)	0.91 (22.56)	0.16	1.10	n.s.	1.17	1.10	n.s.
Posterior temporal cortex ($n = 15$) ^a									
N400	-42.40 (33.42)	-31.62 (36.62)	-43.11 (36.53)	7.92	1.14	0.01	0.13	1.14	n.s.

^a No reliable P600 component was recorded in the posterior temporal cortex.

Figure 8. Representative ERPs recorded in the posterior temporal cortex (fusiform gyrus, gF; planum temporal, pT; inferior temporal gyrus, gTi) in the three task conditions and schematic representation of the time-course of the ERP repetition effect for the N400 components.



defined brain region. The differences observed in the time-course of the ERP repetition effect across frontal lobe structures are consistent with the classical distinction made between the dorsolateral and orbito-frontal regions (Fuster, 1980; Petrides, 1989).

Recordings from the lateral frontal cortex (N400) and anterior cingulate gyrus (P600) showed a significant ERP repetition effect only in the short-lag condition, suggesting their involvement in the semantic processing rather than in the episodic memory system. This view is consistent with the observation that although patients with frontal lobe lesions have disturbances in sequencing and organizing information in memory, they do not develop a full-blown amnesic syndrome (Mayes & Meudel, 1983; Milner, 1964; Stuss & Benson, 1986). However, the pathological involvement of the frontal lobe produces a variety of language abnormalities in grammar and speech production (i.e., Broca's aphasia) or verbal fluency and constructing complex propositions (i.e., dynamic aphasia) (see McCarthy & Warrington, 1990, for a review). Although poorly documented, severe deficits, such as decreased spontaneous speech, have also been described in association with bilateral anterior cingulate lesions (see Devinsky, Morrell, & Vogt, 1995, for a review). Therefore, together with the present ERP results, the deficits observed with lesions to the anterior frontal structures suggest they contribute to organizing and

controlling the activation of information within a semantic memory system.

In contrast to the data from the above structures, ERPs recorded from the orbito-frontal region display a long-lasting repetition effect, thus indicating its contribution to the episodic processing of items. This view is supported by neuroanatomical data indicating that the orbito-frontal region is an important component of a limbo-thalamic system, which also includes the medial temporal lobe structures (Pandya & Barnes, 1987) that are involved in episodic memory (see above). This assumption seems difficult to reconcile with the observation that patients who had undergone a psychosurgical procedure confined to the orbito-frontal region could learn new information in an apparently normal manner (Stuss et al., 1982). These patients were, however, significantly impaired on memory tests featuring interference or distracting stimuli. This suggested to the authors that although not producing major memory impairments, orbito-frontal lesions affect memory functioning by disrupting the ability to handle interference. The present data show that orbito-frontal recordings are characterized by the presence of an ERP repetition effect that persists over repetition lags (i.e., intervening items) and are also consistent with the view that this brain region contributes to the maintenance of information in the face of interference. Therefore, the orbito-

frontal region appears to play a directive, controlling role that influences the successful retrieval of information from episodic memory.

Intracranial ERPs and Functional Neuroimaging Data: Functional Neuroanatomy of Memory Systems in the Human Brain

The results presented above have revealed associations between specific components of memory function (i.e., semantic/episodic processing) and the specific time-course of the intracranial ERP repetition effect recorded from various cerebral regions. These data are in agreement with the classical results of clinical and neuropsychological studies, providing electrophysiological evidence for a distinction between two distinct anatomo-functional systems in the human brain.

Recent advances in brain imaging techniques (such as positron emission tomography, or PET) provide an alternative approach for studying the anatomo-functional correlates of cognitive functions, by means of the quantitative measurement of regional cerebral blood flow (rCBF) and metabolism (see Pahl, 1990, and Petit, 1992, for reviews). Thus, the aim of the subsequent section is to point to the similarities between the present intracranial ERP and the results of brain imaging studies with regard to the anatomo-functional correlates of the two components of memory processing explored in this study.

A Short-Term-Activated Semantic System

The present study has identified a first group of structures, including widespread areas within the posterior temporo-parietal regions as well as the dorsolateral prefrontal cortex and the anterior cingulate gyrus. The activity of these brain regions is characterized by a short-lived ERP repetition effect, suggesting that they constitute a large network of interconnected cerebral structures that represent the anatomic substrate of the semantic processing of items. This assumption is consistent with the classical view that the semantic representations are not well localized but rather depend on the activation of semantic feature fragments, and connections between them (Allport, 1985; Damasio, 1989; Wernicke, 1874).

Remarkably congruent results from PET studies have shown widespread cerebral activation within posterior and frontal areas on a variety of verbal tasks (Blaxton et al., 1996; Démonet et al., 1992; Démonet, Price, Wise, & Frackowiak, 1994; Frith, Friston, Liddle, & Frackowiak, 1991; Howard et al., 1992; Petersen, Fox, Posner, Mintun, & Raichle, 1988; 1990; Wagner, Desmond, Demb, Glover, & Gabrieli, 1998; Wise et al., 1991). Activation of the parietal areas (inferior parietal lobule and angular gyrus) and lateral (mainly Wernicke's area) and medial parts

(fusiform gyrus) of the posterior temporal lobe have been shown to be associated with lexical and/or semantic processing. The prefrontal cortex (mainly Broca's area) and anterior cingulate gyrus appear to be more concerned during tasks involving attention and the selection of verbal information.

Posner and Snyder (1975) have suggested that there are two distinct processes underlying retrieval of semantic information. The first process is an "automatic spreading activation" that is elicited by stimuli. On the basis of PET data, Frith et al. (1991) have suggested that the activation of the posterior cortex could reflect this process. Interestingly, the amount of spreading activation that is necessary to access the representation of items in memory is also believed to influence the N400 amplitude (Halgren, 1990; see Introduction). The present results showing a N400 repetition effect within the posterior brain structures therefore provide strong support for this interpretation. Even more consistent with this view is the correlation found between the amplitude of the scalp N400 and the metabolic activation of parietal areas assessed by combined ERP/PET measurements (Nenov et al., 1991).

The second process suggested by Posner and Snyder (1975) is a "strategic control" that has much in common with the "supervisory attentional system" of Shallice (1988) and the "central executive" component of working memory described by Baddeley (1986) that are thought to be subserved by the frontal lobe. PET studies have provided data suggesting that activation of the temporal neocortex is influenced by an inhibitory modulation from the prefrontal structures (Frith et al., 1991). The P600 component is believed to represent neuronal inhibition (Halgren, 1990; Heit et al., 1990). Therefore, the observation that the P600 recorded from the anterior cingulate gyrus is of a large amplitude and overlaps markedly with the N400 recorded from the temporal lobe (see Table 2) provides support for this view. It is tempting to suggest that the prefrontal cortex may achieve strategic control through the inhibitory mechanisms lying within the anterior cingulate gyrus, a structure that is strongly connected with the temporal cortical areas (this hypothesis will be detailed below).

A Long-Term-Activated Episodic System

The second group of structures defined on the basis of the present data includes the medial temporal structures (hippocampus and amygdala) and other areas such as the anterior temporal cortex and orbito-frontal region that are strongly interconnected with the limbic structures. The main characteristic of these brain structures is the presence of a long-lasting ERP repetition effect, suggesting that these structures constitute the anatomic basis of the episodic memory system.

Some PET studies have investigated the specific meta-

bolic impairments associated with episodic memory deficits in patients with global amnesia of different etiologies (Fazio et al., 1992; Perani et al., 1993). The results are consistent with those of neuropsychological studies, showing metabolic depression in a number of limbic or associated structures such as the hippocampus, cingulate gyrus, thalamus, and frontal basal cortex. The observed metabolic impairments did not necessarily correspond to alterations in structural anatomy as assessed by magnetic resonance imaging (MRI), thus providing evidence that all these interconnected structures contribute to the same functional network that underlies the episodic component of memory processing.

More interesting are the results of an activation study of rCBF measurements during subspan and supraspan tasks in normal volunteers (Grasby et al., 1993). The results provided evidence that some structures, such as the superior temporal cortex, presented rCBF differences between tasks that indicates their temporary activation (see above), whereas others presented rCBF increases with respect to the resting state, but not between subspan and supraspan tasks, thus indicating a more durable activation. Such sustained activation concerned mainly the thalamus, amygdala, hippocampus, parahippocampal gyrus, and temporal gyrus. It is of note that ERPs recorded within some of these structures are also characterized by a long-lasting repetition effect. Therefore, both PET and ERP data converge to the assumption that these structures are engaged immediately after the presentation of an item (subspan/short-lag effects) and also have the capacity to maintain their activation over time (supraspan/long-lag effects). This view is consistent with a role of limbic structures (mainly the hippocampus) in activating durably a specific matrix of neurons distributed within the neocortical areas that correspond to the representation of information (Damasio, 1989; Halgren, 1984; Teyler & DiScenna, 1986). This provides support for theoretical conceptions emphasizing that episodic memory is embedded in and supported by semantic memory, its role being to activate a specific pattern of information distributed within a semantic network corresponding to the specific event to be encoded or retrieved (Squire, 1992; Tulving, 1987).

An Interface between Semantic and Episodic Systems

A point at which the PET data of Grasby et al. (1993) appear not to fit those obtained with ERP recordings is the sustained activation of the anterior cingulate gyrus. This result is, however, consistent with the present observation that although not significant, the cingulate N400 shows a tendency for a long-lasting repetition effect (see Figure 4). Together with the fact that the cingulate gyrus is strongly connected to the prefrontal, orbito-frontal cortices, and thalamus (Baleydier & Mauguière, 1980), these observations suggest that it may

be a key component in the control of memory processes, lying at the interface between semantic and episodic systems.

Gabriel (1990) proposed a model in which the cingulate gyrus functions as a “gating system” that mediates performance of conditioned response in go/no-go tasks. The purpose of such a mechanism is to coordinate the activity of input and output systems. A further extension of this model to more elaborate memory processing would assume that the role of the cingulate cortex is to coordinate the semantic and episodic processes that lead to the activation of representation of an item. Guillem (1996) has hypothesized that the anterior part of the cingulate gyrus contributes to semantic-to-episodic control processes. In a short-delay condition, repeated stimuli that are compatible with an already activated representation generate a “match condition,” the consequence of which is an inhibition of activation mechanisms in the episodic system (e.g., temporal lobe structures). This increased inhibition could be reflected in the increased P600 amplitude (Halgren, 1990; Heit et al., 1990). On the other hand, in a long-delay condition, the representation of items is no longer active in the semantic system, so repeated stimuli generate a “non-match condition,” thus releasing the inhibition on the episodic system as reflected in the decreased P600 amplitude. Gabriel (1990) has provided arguments for a complementary episodic-to-semantic control system involving long-lasting inhibition within the posterior cingulate gyrus.

This view may not be as speculative as it appears. An interpretation of the P600 as reflecting the functioning of a “gating system” fits the classical interpretation of late positive components (e.g., P3a, P3b; P600) in terms of template matching (Verleger, 1988; see also Chao, Nielsen-Bohlman, & Knight, 1995). Even more consistent with the present hypothesis is the observation that an early latency and enhanced positivity elicited in short-delay repetition have a frontal scalp distribution, whereas the positivity associated with long delay repetition is more prominent at posterior sites (Chao et al., 1995; Nielsen-Bohlman & Knight, 1994).

CONCLUSION

The present findings, together with the neuropsychological and functional brain imaging data, support the view that partially independent anatomical networks of interconnected cerebral structures subservise the semantic and episodic components of memory.

Attempting to assess the respective role of each structure within these networks by equating cognitive processes with the modulation of neural activities remains largely a matter of speculation. There is, however, convergent behavioral, functional, and neurophysiological evidence to support the view that some anatomical

components are dedicated to specific processing operations. Furthermore, functional neuroimaging and ERP techniques provide arguments linking the differential contribution of brain structures to cognitive processes with excitatory and inhibitory neurophysiological mechanisms. This is indeed a basic tenet of cognitive neurosciences that fundamental processes can be described in anatomical and physiological terms.

METHODS

Patients

Recordings were obtained from 35 patients admitted for investigation of chronic epilepsy that had proved resistant to trials of all appropriate medications. They underwent presurgical evaluation for eventual surgical therapy consisting of neurological, neuropsychological, neuroradiological (MRI), and cerebral blood-flow (HMPAO-SPECT and Xe-CT), as well as EEG monitoring with stereotactically implanted depth electrodes (SEEG). In all cases, decisions as to the number and placement of electrodes were made strictly on clinical grounds without regard to the present report. In all cases, cognitive recordings were made only after fully informed consent was obtained from the patient.

Explored Brain Structures and Recording Sites

ERPs were recorded from various brain regions. Some of these regions corresponded to anatomically well-defined structures (e.g., amygdala, hippocampus, and anterior cingulate gyrus), whereas others corresponded to more broadly defined areas encompassing different neocortical regions: the anterior temporal cortex (e.g., middle temporal gyrus surrounding the amygdala and the hip-

pocampus), the posterior temporal cortex (e.g., posterior parts of the superior and inferior temporal gyrus), the lateral frontal cortex (e.g., middle and inferior frontal gyri), the orbital region (e.g., orbital gyrus and gyrus rectus), and the parietal cortex (e.g., superior and inferior parietal lobules). This grouping was made according to the specific involvement of the different structures in memory processing suggested by neuropsychological data, and their respective ERP characteristics reported in previous studies (Guillem et al., 1995b). The approximate locations of the recording sites are plotted on the standardized views presented in Figure 9.

Because only 12 channels of ERP data could be recorded at any given session (see below), it was not possible to collect ERP from all the contacts (15 to 84 contacts per patients). Therefore, recordings were preferentially collected from the most medial and/or lateral contacts located in structures involved in generating and modulating memory-ERP components (Guillem et al., 1995b). In addition, recordings from the medial temporal lobe (amygdala and hippocampus) were selected to take into account the observations that ERPs obtained from these structures are differently affected as a function of the location and extent of the epileptogenic zone (Guillem, N'Kaoua, Rougier, & Claverie, 1994; Guillem et al., 1995a). The clinical details of the 35 patients and the location of their respective recording sites are listed in Table 6.

Depth Electrodes and ERP Recordings

Each patient was implanted with three to seven multi-contact electrodes of 5 or 12 contacts each. Electrodes approached their targets from the lateral skull surface and were placed in accordance with the clinical mani-

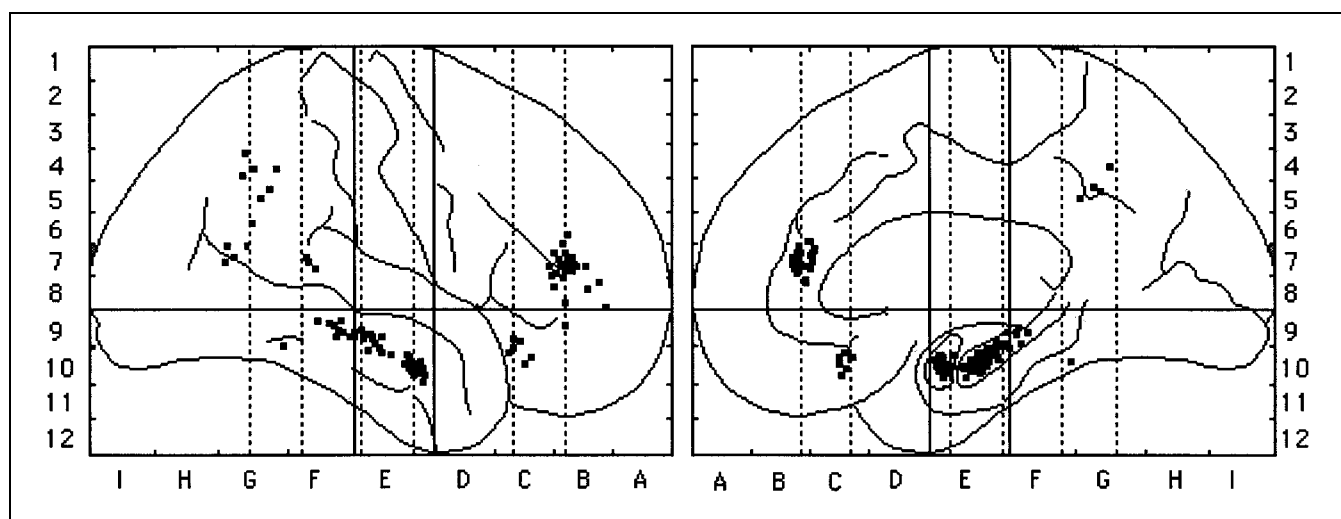


Figure 9. Distribution on lateral (left) and medial (right) sagittal views of the approximate location of intracranial probes projected on the standardized coordinate system of Talairach and Szikla (1967). Vertical and horizontal lines pass through the anterior and posterior commissures. Vertical dotted lines correspond to the vertico-frontal brain slices presented in the subsequent figures.

Table 6. Patient Characteristics

Pt. no.	Sex	Age	Handedness ^a	Seizure focus	Recording sites								Surgery	
					Hc	Am	aTc	aCg	lFc	oFc	s/iPc	pTc		
1	M	29	R	R	FT	-	R+L	-	R+L	-	-	-	-	RT
2	F	32	R	R	T	R+L	L	-	R	-	-	-	-	RT
3	F	35	R	R+L	T	R+L	-	-	-	-	-	-	-	RT
4	M	35	R	R	T	-	L	R+L	-	-	-	-	-	RT
5	M	28	R	R	F	-	-	-	-	R+L	-	-	-	RF
6	M	24	R	L	T	R+L	R+L	-	-	-	-	-	-	LT
7	F	12	R	R	FT	-	-	-	R	R	R	-	-	-
8	M	26	L	R	T	R+L	-	-	R	R	-	-	-	RT
9	M	18	R	R	T	R+L	-	R+L	-	-	-	-	-	-
10	F	22	R	R+L	T	R+L	-	-	R	-	-	-	-	-
11	F	26	R	L	T	R+L	R+L	-	-	-	-	-	-	LT
12	F	37	R	R	TP	-	-	-	-	-	-	L	-	RT
13	F	24	R	R	P	-	-	-	-	-	-	R	-	RT
14	F	23	R	R	T	R+L	R	-	-	-	R	-	-	RT
15	F	22	R	R+L	F	-	-	-	R+L	R	L	-	-	-
16	M	23	R	R+L	T	-	-	R+L	R+L	R+L	L	-	-	-
17	F	23	R	R+L	T	R+L	-	R+L	-	-	-	-	-	-
18	M	28	R	R+L	F	-	-	-	R	R+L	-	-	-	LF
19	M	35	R	L	TPO	-	L	R+L	-	-	-	-	-	-
20	M	36	R	L	T	R+L	R+L	R+L	-	-	-	-	-	LT
21	F	32	R	R+L	TPO	R+L	L	R+L	-	-	-	R+L	-	RT
22	F	20	R	R	T	-	-	-	-	-	-	R	R	RT
23	M	36	R	R+L	T	R+L	-	R+L	-	-	R	-	R	-
24	M	23	R	R+L	FT	-	R+L	R+L	R	R+L	-	-	-	-
25	M	30	R	R	T	R	R	R+L	-	-	R	-	-	RT
26	F	41	R	R+L	FT	-	-	R+L	R	R+L	-	-	-	RT
27	M	31	R	R+L	T	R+L	-	R+L	R+L	R+L	-	-	-	-
28	F	27	R	R	T	R+L	R+L	R+L	-	-	-	-	R	RT
29	M	24	R	R+L	T	R+L	-	R+L	-	-	R	-	-	LT
30	M	42	R	R+L	FT	-	-	-	R	R	-	-	-	-
31	M	29	R	R+L	T	R+L	-	R+L	R+L	R+L	-	-	-	RT
32	M	24	R	R	T	R+L	R	R+L	-	-	-	-	R	RT
33	M	23	R	R	T	-	-	R+L	-	-	-	-	R	RT
34	M	14	R	R	F	-	-	-	-	-	R+L	-	-	RF
35	M	40	R	R+L	T	-	-	-	-	-	-	-	-	RT

^a Harris test of lateral dominance (1961).

R: right; L: left; F: frontal; P: parietal; T: temporal

festations, scalp-EEG activity, and pathology revealed by brain imaging (Figure 9).

The electrode implantation procedure was adapted from that of Talairach and Bancaud (1965). Electrode placement was guided by neuroradiological workup done under stereotactic conditions using stereoscopic teleradiography. Brain structures were located in relation to veins, arteries, and ventricles and by projection of anterior and posterior commissure landmarks in the Talairach atlas (Talairach and Szikla, 1967). Depth electrodes (Cormedica) were of epoxyite-insulated stainless steel with a 1.5-mm diameter.

Recordings were all monopolar, referenced to linked earlobes, with a ground electrode on the forehead. SEEG signals were amplified and filtered (bandpass 0.03 to 100 Hz) using 12 ERP preamplifiers (U3-ALPHA ECEM) and recorded on a TEAC RD-200T data recorder. Waveforms were digitized off-line with an interpoint time of 2 msec (500 Hz) for trial epochs starting 100 msec before and ending 1948 msec after stimulus onset, and averages were computed separately for each stimulus type on a microcomputer (using LabVIEW 2, National Instruments, 1991). All sequences that were artifacted by epileptogenic activity (20 to 30% of the trials) or corresponded to false responses (less than 10% in average; see Table 1) were rejected from the averages.

Recognition Memory Task

The stimuli were 240 verbalizable pictures (white line drawings on black background) of common objects taken from the memory battery scale of Signoret and Whiteley (1979).

The pictures were randomized and placed in the stimulus series in sequential order. There were three blocks of slides (80 per blocks). In each block, 40 pictures were presented and reappeared subsequently in the sequence with 6 or 19 items intervening between the first and second presentations of the picture. Therefore, across the three blocks, there were 120 novel and 120 repeated stimuli.

The stimuli were presented on slides by using a tachistoscope (Kodak SA-V-2050: 1000lm for 24/36-mm slide) driven by a microcomputer (Apple MacIntosh II.Ci). Each picture subtended a visual angle of approximately 5° for the item and 10° for the horizontal dimension of the frame. The duration of stimulus exposure was 1 sec and the interstimulus interval varied from 3 to 5 sec. A relatively lengthy stimulus presentation time was adopted so that patients could perform the task in the postictal state (see Andrewes, Puce, & Bladin, 1990, and Puce et al., 1991).

Subjects made speeded-choice reaction time responses by pressing a response button as soon as a picture was identified as repeated. Subjects were instructed that items presented in one block were different from those of other blocks and that an item would

never be presented more than twice within a given block. Prior to each experimental session, a practice block of trials was administered to ensure that subjects understood the task and could respond appropriately. For the practice block, stimuli that did not appear in the experimental series were used.

ERP Analysis

ERPs corresponding to the first presentation of an item (A) and to the correct recognition of repeated pictures after 6 (R-6) or 19 (R-19) intervening items were analyzed by computer-aided visual inspection to identify the ERP components in each structure (see Results).

ERP component amplitudes were analyzed using ANOVAs (SuperANOVA, Abacus Concepts, Inc., 1989) with repeated measures on the factor of task conditions (A, R-6, R-19; i.e., condition). Multiple-factor ANOVAs with repeated measures were carried out with the Greenhouse-Geisser correction. In these cases, original degrees of freedom and corrected probability levels are reported along with the correction factor (ϵ).

To compare changes in component amplitudes across subjects, the data from recording sites where ERP components were opposite to their normal polarity were excluded from the analysis. To demonstrate that ERP components recorded from the various structures respond differentially as a function of interitem lag, a global (Structure) \times (Hemisphere) \times (Condition) ANOVA was performed. For each structure the lag effect was assessed by an analysis comparing ERP component amplitude according to the task conditions and the side of the recording site (left versus right; i.e., hemisphere). These (Hemisphere) \times (Conditions) ANOVAs were followed by post hoc comparisons performed to assess the ERP repetition effect in both lag conditions. Moreover, to evaluate the eventual ERP alterations consecutive to epileptogenicity, ANOVAs comparing ERP amplitudes according to the task conditions and the side of the main seizure focus were also performed. These analysis showed results that were similar to former ones, with no effect of the seizure focus or interactions between factors (see Results). Therefore, only the results of the (Hemisphere) \times (Condition) ANOVAs are presented in the Results section.

Behavioral Measures

For each patient, choice reaction time and percentage of correct responses were collected for R-6 and R-19 conditions, and signal detection indices of sensitivity (d') were computed from the percentage measures. These data were compared using one-factor ANOVAs with repeated measures.

Acknowledgments

This research was supported by INSERM. N°90CN27.

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