

Lexical–semantic event-related potential effects in patients with left hemisphere lesions and aphasia, and patients with right hemisphere lesions without aphasia

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Summary

Lexical–semantic processing impairments in aphasic patients with left hemisphere lesions and non-aphasic patients with right hemisphere lesions were investigated by recording event-related brain potentials (ERPs) while subjects listened to auditorily presented word pairs. The word pairs consisted of unrelated words, or words that were related in meaning. The related words were either associatively related, e.g. 'bread–butter', or were members of the same semantic category without being associatively related, e.g. 'church–villa'. The latter relationships are assumed to be more distant than the former ones. The most relevant ERP component in this study is the N400. In elderly control subjects, the N400 amplitude to associatively and semantically related word targets is reduced relative to the N400 elicited by unrelated targets. Compared with this normal N400 effect, the different patient groups showed the following pattern of results: aphasic patients with only minor comprehension deficits (high comprehenders) showed N400 effects of a similar size as the control subjects. In aphasic patients with more severe

comprehension deficits (low comprehenders) a clear reduction in the N400 effects was obtained, both for the associative and the semantic word pairs. The patients with right hemisphere lesions showed a normal N400 effect for the associatively related targets, but a trend towards a reduced N400 effect for the semantically related word pairs. A dissociation between the N400 results in the word pair paradigm and P300 results in a classical tone oddball task indicated that the N400 effects were not an aspecific consequence of brain lesion, but were related to the nature of the language comprehension impairment. The conclusions drawn from the ERP results are that comprehension deficits in the aphasic patients are due to an impairment in integrating individual word meanings into an overall meaning representation. Right hemisphere patients are more specifically impaired in the processing of semantically more distant relationships, suggesting the involvement of the right hemisphere in semantically coarse coding.

Keywords: aphasia; lexical–semantic processing; right hemisphere semantics; event-related brain potentials; N400

Abbreviations: AAT = Aachen Aphasia Test; AL = left anterior temporal electrode; AR = right anterior temporal electrode; PL = left posterior temporal electrode; PR = right posterior temporal electrode; ERP = event-related brain potential; SOA = stimulus onset asynchrony

Introduction

Lexical-semantic impairments in aphasia

In this study, the presence and nature of lexical-semantic processing impairments in brain-damaged patients with Broca's aphasia, Wernicke's aphasia, or without aphasia, were investigated. Lexical-semantic deficits were tested by recording ERPs while subjects were engaged in listening to pairs of words that were either related or unrelated in meaning.

Impairments in the processing of word meaning have long been known to be one of the possible consequences of brain damage. Patients with Wernicke's aphasia, in particular, have been found to be severely impaired in lexical-semantic processing (e.g. Zurif *et al.*, 1974; Goodglass and Baker, 1976; Grober *et al.*, 1980). Evidence for a lexical-semantic deficit in these patients was mostly obtained by asking them for explicit judgements about the semantic aspects of the word input. Zurif *et al.* (1974), for instance, presented aphasic and control subjects with triplets of words and required them to select the two that best went together. The words varied along semantic dimensions such as human-nonhuman, ferocious-harmless, etc. The Wernicke's aphasics completely failed in grouping the words according to their shared semantic features. Results of this study and of other studies asking for explicit semantic judgements led to the claim that semantic deficits in Wernicke's aphasia resulted from a partial loss or disintegration of the representational structures for semantic information (e.g. Zurif *et al.*, 1974; Grober *et al.*, 1980).

In contrast to the Wernicke's aphasics, the performance of Broca's aphasics in the previously mentioned studies was close to normal. Their results, together with the clinical impression of fairly preserved language comprehension in most Broca's aphasics, led to the belief that their semantic lexicon was structurally largely unaffected.

This overall picture has been challenged by a number of recent word priming studies with aphasic patients (Milberg and Blumstein, 1981; Blumstein *et al.*, 1982; Milberg *et al.*, 1987; Friedman *et al.*, 1988; Katz, 1988; Chenery *et al.*, 1990; Prather *et al.*, 1992; Hagoort, 1993; Ostrin and Tyler, 1993). In these studies, subjects had to make a lexical decision, i.e. they had to decide as quickly as possible whether orthographically legal letter strings or phonotactically legal sound sequences were existing words or not. It has been firmly established that lexical decisions by neurologically unimpaired subjects are made faster and more accurately to words that are primed by a preceding word that is related in meaning, than to words preceded by an unrelated word context (Meyer and Schvaneveldt, 1971; for review, see Neely, 1991). These priming effects reflect, directly or indirectly, that lexical concepts in semantic memory are clustered according to some matrix of semantic similarity (cf. Collins and Loftus, 1975). A prerequisite, therefore, for obtaining priming effects is that the semantic lexicon is structurally largely unaffected.

The results of the word priming studies with aphasic patients deviated in two aspects from the standard picture on

semantic deficits in Wernicke's and Broca's aphasia. First, despite significantly longer response latencies, Wernicke's aphasics consistently showed the same pattern of results as the normal control subjects, i.e. both the control subjects and the Wernicke patients needed less time to recognize the target as a word when it was preceded by an associatively related word (Blumstein *et al.*, 1982; Milberg *et al.*, 1987; Friedman *et al.*, 1988; Hagoort, 1993). Secondly, surprisingly, Broca's aphasics had a less stable pattern of performance. Some investigators reported no priming effects in these patients (Milberg and Blumstein, 1981; Milberg *et al.*, 1987). In other studies, however, Broca patients showed the expected priming effect (Blumstein *et al.*, 1982; Katz, 1988; Hagoort, 1993; Ostrin and Tyler, 1993).

Two general conclusions have been drawn from these results. First, for many aphasic patients lexical-semantic deficits are not due to a loss of 'the integrity of the stored lexical knowledge base' (Milberg *et al.*, 1987, p. 139), but rather relate to a problem in the processing operations on lexical-semantic information. Thus, Wernicke's aphasics seem to be able to retrieve word meaning automatically, but fail in further exploiting this information when they have to elaborate on aspects of the retrieved word meanings (cf. Graf and Mandler, 1984; Hagoort, 1993). The second conclusion that has been drawn, is that Broca's aphasics might suffer from an impairment in the automatic routines to access lexical-semantic information (Milberg *et al.*, 1987).

Two criticisms have been raised against claims based on the results of these priming studies. The first criticism concerns the conclusion that semantic deficits in Wernicke's aphasics are not a consequence of structural impairments of the semantic lexicon. The second criticism focuses on the claim that Broca's aphasics are impaired in automatic lexical access.

Apart from the Friedman *et al.* (1988) study, all priming studies in which Wernicke patients showed priming effects used primes and targets that were not only semantically related, but were also strong associates. It has been suggested that in these cases priming effects are not necessarily a result of semantic relatedness, but could be due to connections between the word form representations (Fischler, 1977; Lupker, 1984; Moss, 1991; Shelton and Martin, 1992). Therefore, these results are thought to be inconclusive with respect to the nature of lexical-semantic deficits in aphasia. To meet this criticism, we used purely semantic, non-associatively related word pairs, in addition to word pairs that were strong associates.

Concerning the second criticism, Milberg *et al.* (1987) concluded for the Broca's aphasics from the absence of a priming effect in these patients that they 'have a processing deficit in automatically accessing lexical representations of words' (p. 138). However, both the empirical and the theoretical basis of the claim for an automatic access deficit in Broca's aphasics is actually rather weak. So far, the majority of priming studies have found largely normal priming results in patients with Broca's aphasia (Blumstein *et al.*, 1982; Katz,

1988; Milberg *et al.*, 1988; Hagoort, 1993; Ostrin and Tyler, 1993). In two studies only, were normal priming effects not obtained (Milberg and Blumstein, 1981; Milberg *et al.*, 1987).

The theoretical weakness of the claim resides in the implicit assumption that word priming studies only or mainly tap automatic processing of lexical information, including word meaning. As has been argued elsewhere (Hagoort, 1993), there is convincing evidence (Neely, 1977, 1991; Balota and Chumbley, 1984; de Groot, 1984; Seidenberg *et al.*, 1984; de Groot *et al.*, 1986; Neely and Keefe, 1989; Neely *et al.*, 1989; Keefe and Neely, 1990) that priming effects can be attributed to both automatic and more controlled priming mechanisms, such as expectancy induced priming and semantic matching (Neely, 1991). A number of factors determine whether automatic or controlled priming mechanisms are the main contributors to the overall priming effect. One of these factors is the stimulus onset asynchrony (SOA) between prime and target. Automatic priming is mainly tapped at short SOAs, whereas controlled priming mechanisms contribute largely to priming effects observed at long SOAs (e.g. Neely, 1977, 1991; de Groot, 1984). In the studies in which no priming effects were observed in the Broca's aphasics (Milberg and Blumstein, 1981; Milberg *et al.*, 1987), investigators used relatively long intervals between the onsets of the primes and the targets. Hagoort (1993) varied the interval between primes and targets, and observed basically normal priming results at short intervals but no priming at long intervals in a group of Broca's aphasics and a group of Wernicke's aphasics. Therefore, it cannot be safely concluded that the absence of a priming effect in the studies of Milberg and colleagues (Milberg and Blumstein, 1981; Milberg *et al.*, 1987) is due to an impairment in automatic lexical processing. Overall, the results of the reaction time priming studies with aphasic patients suggest that a more likely functional locus of reduced or absent priming effects is at the post-lexical level of semantic matching of primes and targets.

Other factors potentially influencing the priming results are the task requirements. These might induce strategic factors that are not normally (i.e. during ordinary language comprehension) involved in lexical processing (cf. C. M. Brown, P. Hagoort and D. Chwilla, unpublished results; Chwilla *et al.*, 1995). In this study we tried to avoid non-mandatory, task-induced strategic influences as much as possible, by requiring subjects to perform only the natural task, which in this case is listening to auditorily presented words.

Language impairment after right hemisphere lesion

It is by now fairly well-established that the right hemisphere can play a role in some aspects of language comprehension (cf. Zaidel, 1985; Joannette *et al.*, 1990). Lexical-semantic processing is clearly one of these aspects (e.g. Heesch and Jurgens, 1977; Gainotti *et al.*, 1981; Drews, 1987; Chiarello,

1988; Gazzaniga and Miller, 1989; Abernethy and Coney, 1990, 1993; Chiarello *et al.*, 1990, 1992; Rodell *et al.*, 1992; Beeman *et al.*, 1994). One kind of evidence for the involvement of the right hemisphere in lexical-semantic processing comes from patients with right hemisphere brain damage. These patients are reported to be impaired in retrieving or using lexical-semantic information (e.g. Gainotti *et al.*, 1981). Different and often not very well-articulated views, however, exist about the nature of the right hemisphere competence for lexical-semantic processing (cf. Joannette *et al.*, 1990). In general, the current evidence suggests that the left and right hemisphere might be differentially sensitive to specific types of semantic relationships (e.g. Drews, 1987; Chiarello *et al.*, 1990; Rodell *et al.*, 1992; Beeman *et al.*, 1994). A stronger right hemisphere effect for word pairs that were semantically but not associatively related has been observed (e.g. Chiarello *et al.*, 1990; Rodell *et al.*, 1992). Chiarello *et al.* (1990), for instance, observed a left visual field/right hemisphere advantage in the size of the priming effect for word pairs that were purely semantically related, but not for words that were also associatively related. These results are compatible with the claim of Beeman *et al.* (1994) that the left hemisphere is more effective in processing strongly related words, whereas the right hemisphere becomes more effective when the semantic distance between the words increases.

The present study enables a comparison of ERP effects to the processing of very strongly related, associative word pairs, and to the processing of more distantly, purely semantically related word pairs. The more distant meaning relationships between the semantically related word pairs, is demonstrated by the fact that the second word of the related pairs was never produced by subjects in an association test. Association tests usually elicit words that are closely related in meaning to the stimulus word. On the basis of the current evidence in the literature we should expect that the patients with right hemisphere lesions show more abnormal ERP effects for the semantically related word pairs than for the associatively related word pairs.

Event-related brain potentials and word priming

In this study, we recorded ERPs while subjects were listening to word pairs. Scalp-recorded ERPs reflect the summation of the synchronous post-synaptic activity of a large population of neurons. Event-related potentials differ from background EEG in that they reflect brain electrical activity time-locked to particular stimulus events. The time-locked average waveform typically includes a number of positive and negative peaks with a specific distribution over the scalp, usually referred to as components.

For the purposes of neurolinguistically oriented ERP research, the most informative ERP components belong to the class of the so-called 'endogenous' components. Endogenous components are relatively insensitive to variations in physical stimulus parameters (e.g. size, intensity), but highly responsive to the cognitive processing

consequences of the stimulus events. The modulations in amplitude or latency of an endogenous ERP component as a consequence of some experimental manipulation, usually form the basis for making inferences about the nature of the underlying cognitive processes.

Event-related potential recordings have at least two advantages when investigating language impairments in neurological patients (cf. Hagoort and Kutas, 1995). One is that reliable ERP effects can be obtained even in the absence of any additional task over and above the natural one of listening to speech or reading words and sentences. Especially for testing patients with severe comprehension deficits, the absence of an additional task might be beneficial. Moreover, the absence of an additional task also prevents its possible interference with the language processes that one wishes to investigate. The other advantageous aspect of ERPs is that they are tightly linked in time to the underlying language processing events. They are therefore believed to allow inferences not only about the types of linguistic information that patients are (in)sensitive to, but also about possible changes in the time course of retrieving and exploiting the relevant sources of information during language comprehension.

The most relevant ERP component for this study is the N400. The N400 was first reported by Kutas and Hillyard (1980). These authors observed the presence of a large negative deflection in the ERP waveform to a semantically anomalous word in a sentence context, e.g. the word 'dog' in the sentence 'I take coffee with cream and dog' elicits a large N400 component. The N400 elicited by an anomalous content word occurring at different positions within a sentence, usually (i.e. with healthy student subjects) peaks between 380 and 440 ms and is larger over posterior than over anterior regions of the scalp (Kutas and Hillyard, 1983). The difference in the amplitude of the N400 to the semantic anomaly and its control (e.g. the ERP to 'sugar' in 'I take coffee with cream and sugar') is referred to as the N400 effect. Since its first report, it has become clear that N400 effects can be obtained with a variety of paradigms and using a variety of language stimuli, by no means restricted to violations (for reviews, *see* Kutas and Van Petten, 1988, 1994; Hagoort and Kutas, 1995).

N400 effects are not only obtained in a sentence context, but can also be observed in response to content words that are preceded by only one other content word. The ERP to the second of a pair of words that are associatively or semantically related is characterized by a reduction in N400 amplitude relative to words that are preceded by an unrelated word (e.g. Bentin *et al.*, 1985; Rugg, 1985, 1987; Boddy, 1986; Kutas and Hillyard, 1989; Holcomb and Neville, 1990, 1991). This N400 semantic priming effect has been observed for both written and spoken words. For spoken words, the N400 effect appears to be earlier and more prolonged, as well as symmetric or slightly larger over the left than the right hemisphere (Holcomb and Neville, 1990). With respect to the processing nature of the N400 effect, there is recent evidence that both in a sentence and at the word-word level

it primarily reflects post-lexical processes that are involved in semantic integration (Rugg *et al.*, 1988; Brown and Hagoort, 1993; Hagoort *et al.*, 1993; Holcomb, 1993; Chwilla *et al.*, 1995; C. M. Brown, P. Hagoort and D. Chwilla, unpublished results).

The major goal of this study is to further determine the nature of lexical-semantic processing deficits in aphasic patients by assessing N400 priming effects in these subjects. We investigated N400 effects in these patients not only in relation to their aphasia syndrome (Broca's or Wernicke's aphasia), but also, independent of their syndrome classification, with respect to their scores on a comprehension subtest of a standardized aphasia test battery. This allows us to evaluate the influence of the severity of the comprehension deficit on the N400 priming effects.

To determine whether possibly abnormal N400 effects in the aphasic patients can be related in a meaningful way to their specific comprehension deficit, a number of additional recordings were done (*see* Hagoort and Kutas, 1995). First, a control group of neurologically unimpaired subjects was tested. These elderly controls were matched to the patients on age, education and handedness.

Secondly, in order to determine the linguistic specificity of possibly abnormal ERPs, we also tested the patients in a non-linguistic cognitive task. For this purpose we presented tone stimuli in a classical oddball paradigm. It is a standard observation in ERP research that in neurologically intact subjects the infrequently presented tones in such a paradigm elicit a large positive deflection in the ERP waveform (cf. Fabiani *et al.*, 1987). Very often this positivity reaches its maximal amplitude at ~300 ms after stimulation, and is therefore known as the P300. We tested whether or not possible changes in the N400 to word stimuli were correlated with the P300 elicited in the tone oddball paradigm. If, in patients, changes in N400 effects are exactly matched by changes in P300 effects, these changes might be indicative of a less specific consequence of brain damage or a less specific cognitive deficit than one would conclude from clear dissociations between the results for these two endogenous components.

Finally, in addition to the aphasic patients and the elderly controls, we tested a group of non-aphasic subjects with right hemisphere lesions. The testing of these patients served two purposes. The first purpose is to increase our understanding of the contribution of the right hemisphere to lexical-semantic processing. The second purpose is to obtain evidence on the specificity of N400 changes in the aphasics, by looking at patterns of associations and dissociations between the results of non-aphasic patients with right hemisphere lesions and aphasic patients with left hemisphere lesions.

Methods

Subjects

The subjects in this experiment were 20 aphasic patients, eight patients with right hemisphere lesions, and 12 elderly

controls. The elderly control subjects and the patients with right hemisphere lesions were paid for their participation. The testing procedures were approved by the ethical committee of the Nijmegen University Hospital. All healthy control subjects and all neurological patients gave informed consent, according to the declaration of Helsinki. All subject groups were approximately matched with respect to age and level of education. All elderly control subjects were right-handed according to an abridged version of the Oldfield Handedness Inventory (Oldfield, 1971). None of these subjects reported familial left handedness. The aphasic patients and the patients with right hemisphere lesions were also (premorbidly) right-handed. According to the responses on a second questionnaire, none of the elderly control subjects had any known neurological impairment or used neuroleptics. None of the control subjects reported hearing loss or memory problems.

All neurological patients were administered the standardized Dutch version of the Aachen Aphasia Test (AAT) (Graetz *et al.*, 1992). Time of administration was at least 6 months post-onset. Both presence and type of aphasia were diagnosed on the basis of the AAT results and on the basis of a transcribed sample of the patient's spontaneous speech. All patients with right hemisphere lesions were diagnosed as non-aphasic. Thirteen patients with left hemisphere lesions were diagnosed as Broca's aphasics, and seven patients with left hemisphere lesions were diagnosed as Wernicke's aphasics. According to their scores on the comprehension subtest of the AAT, aphasic patients had severe to mild comprehension deficits. In the comprehension subtest of the AAT, patients are required to match the linguistic input to one out of four pictures. The linguistic input consists of both single words and sentences, both written and spoken. Table 1 summarizes the relevant aspects of the individual patient history and AAT results. These include information on age, gender, lesion volume, performance on the AAT subtest on comprehension, and scores on the Token Test for all neurological patients. The Token Test is a valid measure of the general severity of the aphasia, independent of syndrome type (Orgass, 1986; Willmes, 1993). The general severity of the aphasia ranged from light to severe. The Token Test results also substantiate that none of the patients with right hemisphere lesions was aphasic (*see* Table 1).

All lesions, except one, were due to cerebrovascular accidents. The lesion of one patient (Patient 13) was due to a bacterial meningitis. Figures 1, 2 and 3 give the CT/MRI lesion data of all the patients for whom adequate CT/MRI information was available. Lesions evident on a CT/MRI scan were transcribed onto corresponding CT/MRI templates by an experienced neurologist. These CT/MRI templates were read into a computer program that permitted reconstruction of the lateral perspective, determination of lesion volume, and the computation of the group-averaged lesions (Frey *et al.*, 1987; for detail, *see* Knight *et al.*, 1988). Figures 1, 2 and 3 show the average axial reconstructions and lateral views of

the Broca's aphasics, the Wernicke's aphasics and the patients with a right hemisphere lesion, respectively.

Although the lesions of both patients with a Broca's aphasia and patients with a Wernicke's aphasia cover a large area of the left hemisphere, Fig. 1 shows that the averaged lesion in the Broca's aphasics has its largest area of overlap in the left posterior frontal lobe with some temporal lobe involvement, whereas the averaged lesion of the Wernicke's aphasics (*see* Fig. 2) shows a more left posterior focus, largely restricted to the superior and middle temporal lobe with some parietal involvement. The averaged lesion of the patients with right hemisphere lesions (Fig. 3) shows a more diffuse image without a clearly focused area of overlap.

The mean age for the normal control subjects was 59.3 years (range 50–70 years), the mean age for the patients with right hemisphere lesions was 57.4 years (range 43–71 years); for the Broca's aphasics it was 54.4 (range 27–72 years), and for the Wernicke's aphasics it was 57.4 (range 45–67 years).

Materials

The stimuli consisted of two lists of auditorily presented Dutch word pairs. Each list contained 83 word pairs that were related in meaning, and an additional 83 unrelated pairs.

In line with the standard usage in the literature on word priming, we will refer to the first word as the prime, and to the second as the target. The lists differed with respect to the type of relationship between the words in the related pairs.

In the associative list, the related word pairs (e.g. 'bread–butter') consisted of strong associates. A pair was considered to be associatively related if the target word appeared as an associate of the prime in published Dutch word association norms (de Groot, 1980; Lauteslager *et al.*, 1986; de Groot and de Bil, 1987). All related target words, except four, appeared as the first associate in the norms. The targets had a mean association frequency of 45.9% (SD = 15.2). Targets in the related and unrelated condition were closely matched in lexical frequency. The frequencies were established on the basis of Dutch frequency norms for a corpus of 720 000 words (Uit Den Boogaart, 1975). Targets had a mean lemma frequency of 87.6 (SD = 134.9) in the related condition and 79.1 (SD = 149.8) in the unrelated condition. The mean duration of the auditory primes was 584 ms (SD = 99 ms). The targets had a mean duration of 562 ms [549 ms in the related condition (SD = 101 ms), and 574 ms in the unrelated condition (SD = 94)].

In the semantic list, all related word pairs were nouns that were semantically, but not associatively, related (e.g. 'church–villa'). As items for the semantic list we selected prototypical members of 31 semantic categories. Prototypicality ratings were derived from Vonk (1977) and from a short pre-test. Related word pairs were constructed by pairing two members of the same semantic category (e.g. 'church–villa'). The unrelated items were constructed by pairing members from

Table 1 Individual patient information for Broca's aphasics, Wernicke's aphasics, and non-aphasic patients with a right hemisphere lesion

Patient	Age (years)	Sex	Token Test*	Comprehension Score AAT†	Auditory compreh. score AAT	Lesion volume (cm ³)
01 Broca HC	40	M	17	94/120	45/60	59.60
02 Broca HC	49	M	31	92/120	44/60	66.40
03 Broca HC	60	F	18	104/120	49/60	—
04 Broca LC	37	F	31	85/120	49/60	112.10
05 Broca LC	68	M	34	65/120	37/60	72.90
06 Broca HC	71	F	7	108/120	52/60	127.10
07 Broca LC	42	M	41	65/120	33/60	219.05
08 Broca HC	53	M	13	98/120	49/60	49.55
09 Broca —	72	F	20	87/120	41/60	—
10 Broca HC	64	M	25	108/120	50/60	60.35
11 Broca LC	58	F	20	82/120	48/60	85.05
12 Broca LC	66	M	28	76/120	42/60	—
13 Broca —	27	M	24	93/120	47/60	141.85
14 Wernicke HC	45	F	21	99/120	48/60	64.65
15 Wernicke LC	51	M	43	66/120	37/60	67.20
16 Wernicke LC	65	M	45	—	39/60	123.65
17 Wernicke HC	52	M	30	95/120	48/60	110.90
18 Wernicke HC	60	M	33	87/120	45/60	25.40
19 Wernicke LC	67	M	44	84/120	40/60	88.25
20 Wernicke LC	62	M	47	84/120	42/60	26.90
21 Right hem.	71	F	0	120/120	60/60	—
22 Right hem.	58	M	0	118/120	60/60	41.10
23 Right hem.	50	F	4	96/120	45/60	—
24 Right hem.	56	M	1	117/120	57/60	99.65
25 Right hem.	59	M	3	106/120	54/60	75.05
26 Right hem.	66	F	2	103/120	48/60	43.45
27 Right hem.	43	M	0	114/120	56/60	95.60
28 Right hem.	56	M	1	110/120	56/60	43.25

The aphasic patients were clustered on the basis of their comprehension scores into high comprehenders (HC) and low comprehenders (LC). Ranges of severity are based on the norms of the Dutch version of the AAT. *Severity of disorder as indicated by the Token Test: no/very mild disorder (0–6); light (7–23); middle (24–40); severe (>40). †Severity of comprehension disorder as indicated by the AAT subtest comprehension (includes word and sentence comprehension in both auditory and visual modality): severe (1–66); middle (67–89); light (90–106); no/very mild disorder (107–120). In addition, the score on the auditory part of the comprehension subtest (both words and sentences) is specified.

different semantic categories (e.g. 'hand–cherry'). All primes of the word pairs that were constructed in this way were used in an association test. In this test, 20 subjects from the University of Nijmegen who were paid for their participation, were required to write down for every prime, the first three words that came to mind. One or more occurrences of the target word among the 60 responses to a prime, led to the removal of the word pair from the stimulus list. In this way we established that none of the remaining 83 semantically related word pairs were also associatively related.

The targets in both conditions were closely matched in lexical frequency. The 83 related targets had a mean lemma frequency of 40.5 (SD = 76.4). The mean lemma frequency of the unrelated targets was 33.7 (SD = 69.2). The primes had a mean duration of 593 ms (SD = 111 ms). On average the targets had a duration of 583 ms [586 ms in the related condition (SD = 105 ms), and 579 ms in the unrelated condition (SD = 111 ms)].

The 166 experimental items of each list were preceded by six start-up items. The experimental session began with a set of 48 practice items to familiarize the subjects with the

experimental situation. See the Appendix for the full set of the experimental items.

All words were spoken by a female speaker in a sound-attenuating booth and recorded on a digital audio tape. Subsequently, the stimuli were stored in a VAX 750 computer. A speech waveform editing system was used to construct the word pairs. A pulse for triggering the EEG sampling programme was placed 150 ms before prime onset. The pulse was inaudible to the subjects. The SOA between primes and targets was 1183 ms. The silent interval between primes and targets varied between 300 and 840 ms. Word pairs were separated by a 4-s silent interval. One digital audio test tape was constructed containing the practice set and both experimental lists.

In addition to the test tapes with word stimuli, a digital audio tape was constructed with tones. This tape contained 300 tones, 60 tones of 1 kHz and 240 tones of 2 kHz. The tones were presented in a random order with a frequency of 1 s⁻¹, and had a duration of 20 ms. A trigger pulse was placed 150 ms before the onset of each 1 kHz tone, and before the onset of 60 randomly chosen 2 kHz tones. The

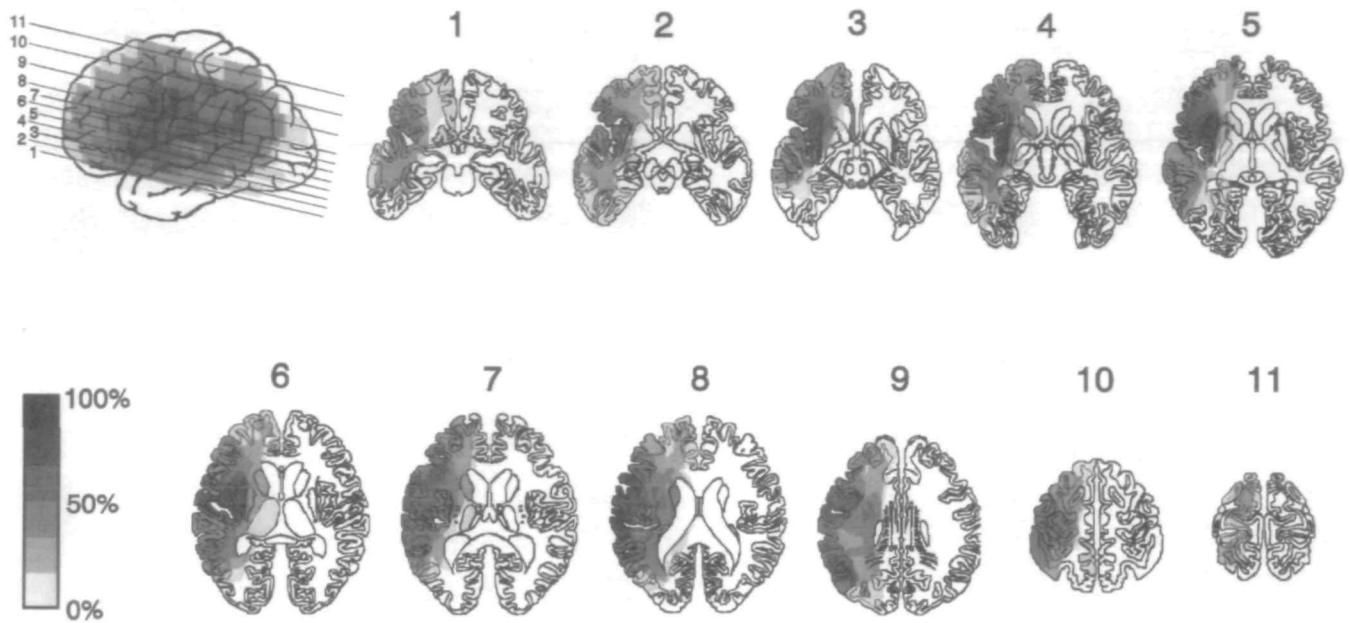


Fig. 1 Lesion extent of the Broca's aphasics. Lesions determined by available CT-scans or MRI-scans from individual patients were transcribed onto templates 0° to the canthomeatal line. These lesion data were then read into a reconstruction program. The digitized data were averaged to generate the group lesion densities. The 11 lines through the lateral reconstruction indicate the 11 axial sections. The shading scale indicates the percentage of patients with damage in the corresponding area. Lesions were averaged over 10 Broca's aphasics.

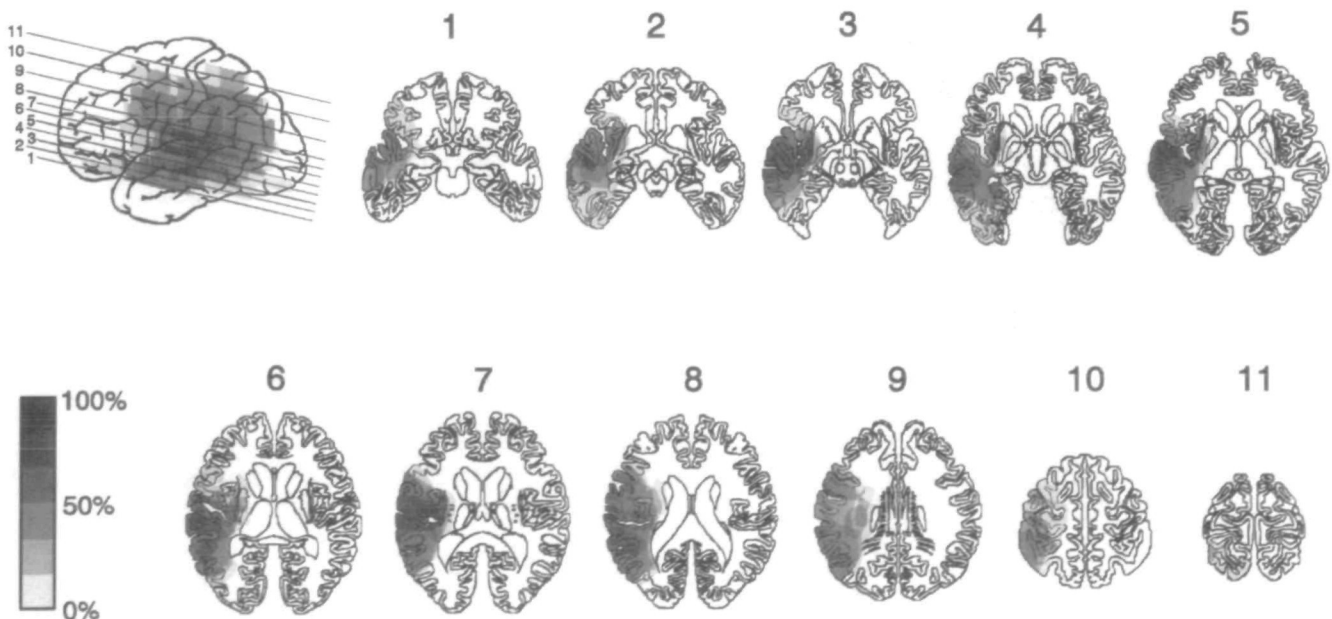


Fig. 2 Lesion extent of the Wernicke's aphasics ($n = 7$). For details *see* Fig. 1 legend.

300 experimental tones were preceded by a practice set of 50 tones (10 tones of 1 kHz, and 40 tones of 2 kHz), to familiarize the subjects with the stimuli and the task.

Procedure

The subjects were tested individually in a dimly illuminated sound-attenuating booth, seated in a comfortable reclining

chair (apart from five patients who had to be tested in their wheelchairs). They were instructed to move as little as possible, and to keep their eyes fixated on a marker on the wall at eye level. For the word stimuli, subjects were asked to listen attentively to the words. No additional task demands were imposed. All stimuli were presented via a DAT-recorder (SONY 300ES). The subjects listened to the stimuli via a closed-ear Sennheiser HMD-224 headphone.

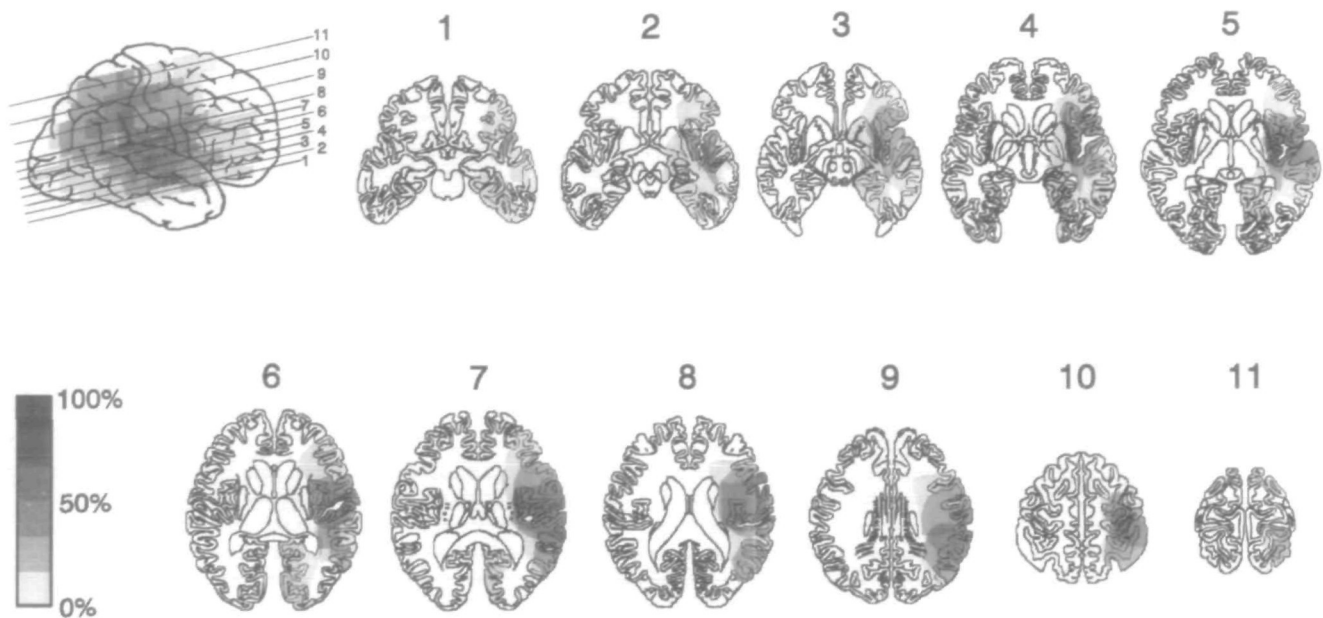


Fig. 3 Lesion extent of the patients with a right hemisphere lesion for whom adequate CT/MRI information was available ($n = 6$). For details see Fig. 1 legend.

The elderly controls were tested in one session, a total of 35 min of stimulation. The order of presentation of the two word lists was counterbalanced across subjects. The patients were tested in two separate sessions. Each session started with the practice list to familiarize the subjects with the stimulation situation and to train them to fixate their eyes during word presentation and to blink between trials. If necessary, the practice list was repeated. The experimental lists were interrupted at least four times for a short break. The order of the associative and semantic list session was counterbalanced as much as possible for the three patient groups.

At the end of a session, the subjects were interviewed about the salient features of the word stimuli. This was done to test whether they had noticed the semantic relationships between words.

The ERPs to the tones in the oddball paradigm were recorded in a separate session. Subjects were asked to count the low tones silently, and to give a running total at the end of the session. Patients who were unable to count, were assessed in the practice session for their ability to discriminate between the 1 and 2 kHz tones, by asking them to raise their index finger upon the occurrence of a low tone. All patients showed good discrimination performance.

EEG recording

EEG activity was recorded using an Electrocap with seven scalp tin electrodes, each referred to the left mastoid. Three electrodes were placed according to the International 10–20 system (Jasper, 1958) at frontal, central and parietal sites. Symmetrical (left and right) anterior temporal electrodes (AL

and AR, respectively) were placed halfway between F7 and T3, and F8 and T4 sites, respectively. Symmetrical posterior temporal electrodes (PL, PR) were placed lateral (by 30% of the interaural distance) and 13% posterior to the vertex. Vertical eye movements and blinks were monitored via a supra- to sub-orbital bipolar montage. A right to left canthal bipolar montage was used to monitor for horizontal eye-movements. Activity over the right mastoid bone was recorded on an additional channel to determine if there were differential contributions of the experimental variables to the two presumably neutral mastoid sites. No such differential effects were observed in any of the data.

The EEG and electrooculography recordings were amplified with Nihon Kohden AB-601G bio-electric amplifiers, using a Hi-Cut of 30 Hz and a time constant of 8 s. Impedances were kept below 5 k Ω . The EEG and EOG were digitized on-line with a sampling frequency of 200 Hz. Sampling started 150 ms before the presentation of the prime, and in the oddball task 150 ms before the sampled tones. Sampling for the word stimuli continued for a period of 3 s, and 850 ms for the tone stimuli. The experimental trials were stored along with condition codes for off-line averaging and data analysis.

Results

First we will discuss the N400 effects for the two lists of word pairs. Then we will discuss the P300 effects in the tone oddball task. In a final result section, we present individual subject comparisons between the ERP measurements.

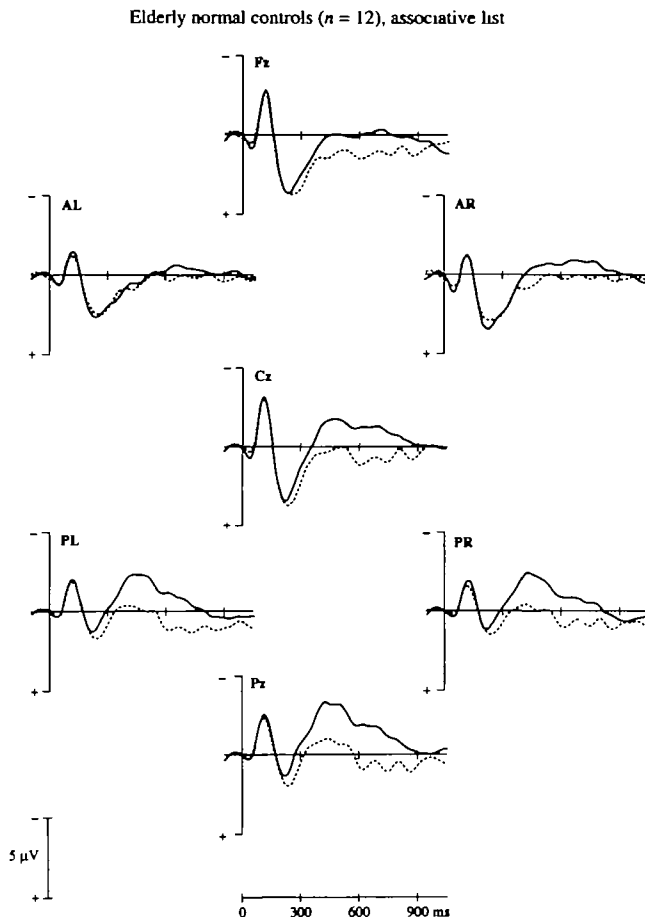


Fig. 4 Grand average ERPs for the elderly normal controls ($n = 12$) to the unrelated targets (continuous line) and the related targets (dotted line) in the associative list.

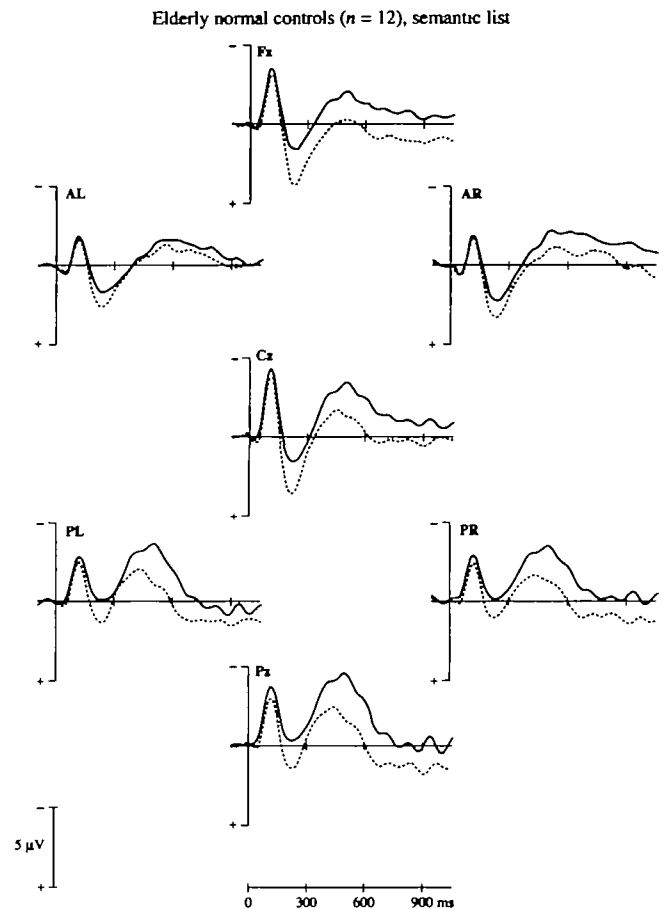


Fig. 5 Grand average ERPs for the elderly normal controls ($n = 12$) to the unrelated targets (continuous line) and the related targets (dotted line) in the semantic list.

Analysis of N400 effects

Prior to off-line averaging, all single trial waveforms were screened for electrode drifting, amplifier blocking and other artifacts. Trials containing such artifacts were rejected. For subjects with a substantial number of blinks, single trials were corrected via a procedure described by Gratton *et al.* (1983). This correction procedure estimates and removes the contribution of eye blinks from the ERP recorded at each electrode site. For the time-locked latency windows (for analyses, *see below*), the overall rejection rate was 23% for the elderly controls, 32% for the aphasic patients, and 35% for the patients with right hemisphere lesions.

Average waveforms were computed by subject over the related and unrelated target words (i.e. the second words of the pairs) in the associative and the semantic list. Statistical analyses on the N400 effects were performed on the basis of the mean amplitudes in the latency range of 400–750 ms post target. This latency range was determined on the basis of a visual inspection of the waveforms (*see Figs 4–11*), and is certainly later than the latency range of N400 effects usually observed for young student subjects, but fits with earlier reports on the longer latency of N400 effects in elderly subjects (Harbin *et al.*, 1984; Gunter *et al.*, 1992). Calculations

of the mean amplitudes were done separately for each of the seven electrodes, relative to a 100 ms pre-target baseline. Since the N400 effects show a clear posterior distribution, only the values for the centroparietal electrode sites were entered into the statistical analyses. The mean amplitude values were entered into a repeated measures ANOVA for each subject group separately. In the analyses, Subjects, Relatedness (related, unrelated), Type of Relationship (associative, semantic), and Electrode Site (Cz, Pz, PL, PR) were completely crossed. In addition, ANOVAs were performed in which the patient data were compared with the data of the normal controls. These analyses had Group of Subjects (normal controls, patient group) as the additional between-subject factor. To compensate for inhomogeneous variances and covariances across treatment levels, the Greenhouse–Geisser correction was applied when evaluating effects with more than one degree of freedom in the numerator (Greenhouse and Geisser, 1959; *see Winer*, 1971). The adjusted degrees of freedom and P values will be presented.

Given that lesion consequences on volume conduction are not easy to quantify, one has to be very careful in assigning a cognitive–functional interpretation to subtle differences in the scalp distributions of the ERP effects between the different

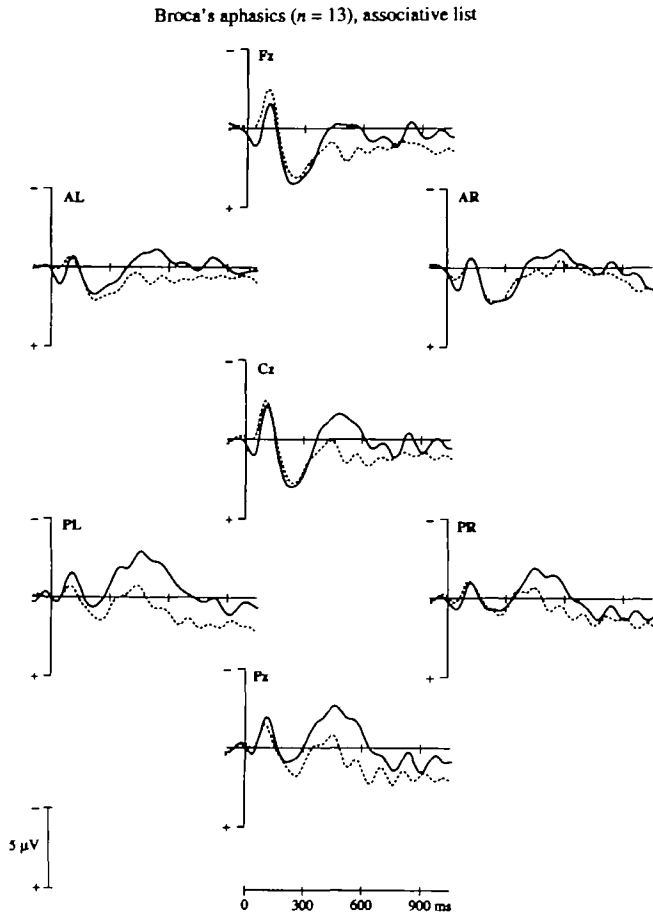


Fig. 6 Grand average ERPs for the Broca's aphasics ($n = 13$) to the unrelated targets (continuous line) and the related targets (dotted line) in the associative list.

subject groups. Although we will describe the distributional aspects of the effects, as a result of this difficulty of quantifying lesion consequences on scalp topography, we will not attach any substantial functional significance to distributional differences between subject groups.

Normal controls

Figure 4 shows the average waveforms to related and unrelated target words in the associative list for the group of 12 normal controls. Figure 5 shows the average waveforms for the semantic list in the same group of subjects.

Both Figs 4 and 5 show sizeable N1 and P2 components following the onset of the spoken target words. These components are followed by a broad negative deflection with a clear posterior, but symmetrical distribution. This negative deflection is very similar in topography to previously observed N400s to spoken words (Holcomb and Neville, 1990). The N400 is substantially larger to unrelated than to related target words. This relatedness effect holds for both lists, as is substantiated by the ANOVA on the mean amplitude in the 400–750 ms range post-target. The analysis yielded a significant effect of Relatedness [$F(1,11) = 25.07$, $MSe =$

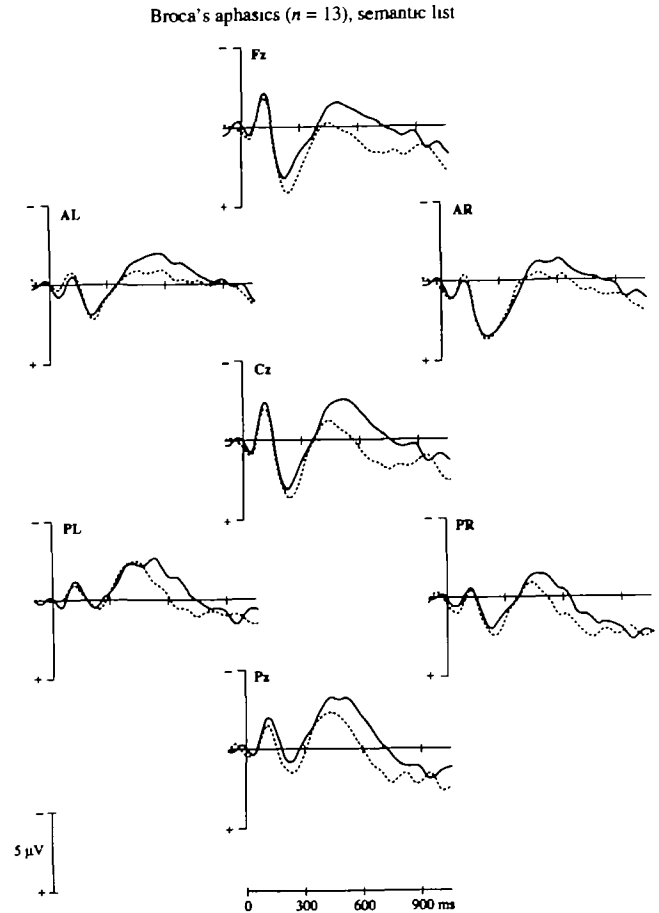


Fig. 7 Grand average ERPs for the Broca's aphasics ($n = 13$) to the unrelated targets (continuous line) and the related targets (dotted line) in the semantic list.

7.40, $P = 0.0004$), but no interaction between Type of Relationship and Relatedness ($F < 1$). The size of the N400 effects is not statistically different for the associative ($-2.01 \mu\text{V}$) and the semantic ($-1.92 \mu\text{V}$) list.

In addition to the N400 effects, the amplitude of the P2 is larger in the related than in the unrelated target waveforms. This P2 effect is larger for the semantic list than for the associative list. The P2 amplitude is not known to be sensitive to aspects of the semantic relationship between words. Moreover, the possibility that the P2 effect is due to an overlapping, differential N400 for related and unrelated targets, cannot be easily discarded. We will therefore focus our discussion of the results mainly on the N400, as the functionally most relevant component for this study.

Aphasic patients

Figures 6 and 7 present the average waveforms for the group of 13 Broca's aphasics. On the whole, the waveforms for these patients are not very different from the ones of the elderly controls. Just as for the normal controls, the waveforms of the Broca's aphasics show clear N1 and P2

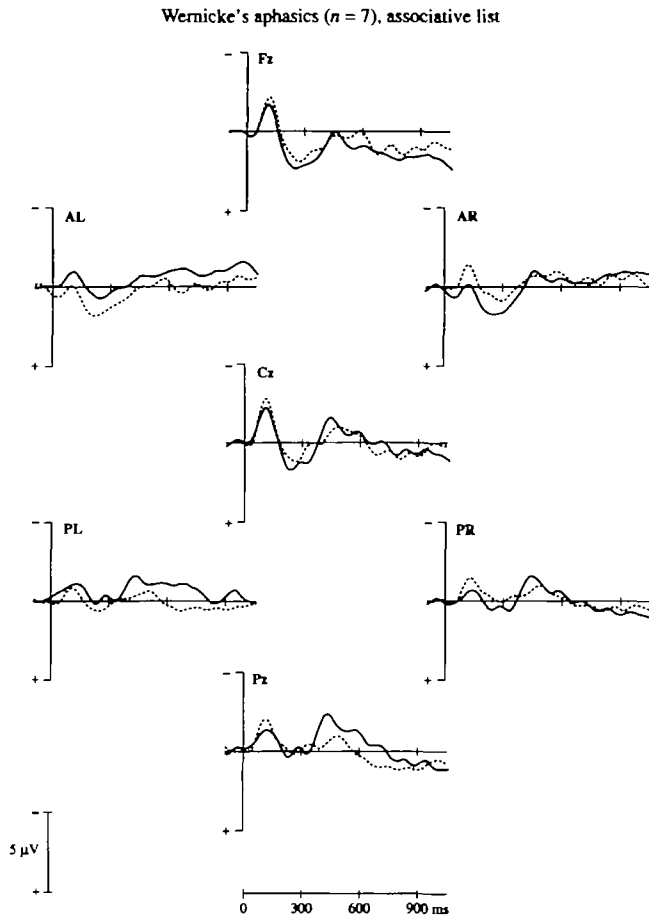


Fig. 8 Grand average ERPs for the Wernicke's aphasics ($n = 7$) to the unrelated targets (continuous line) and the related targets (dotted line) in the associative list.

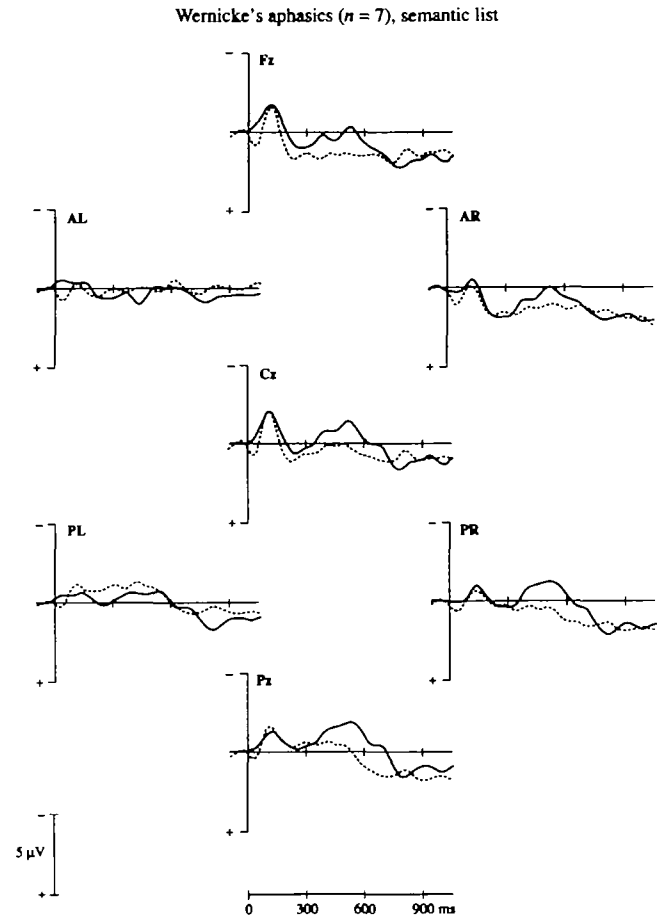


Fig. 9 Grand average ERPs for the Wernicke's aphasics ($n = 7$) to the unrelated targets (continuous line) and the related targets (dotted line) in the semantic list.

components, albeit that the N1 is slightly reduced in amplitude relative to the control subjects.

The N400 is also clearly present in the waveforms, and shows the usual centroparietal maximum. In the associative list but not in the semantic list, it is slightly larger over the left posterior electrode (PL) site than over the right posterior electrode (PR) site. Most importantly, the N400 amplitude is larger for the unrelated than for the related target words. This N400 effect is found to be statistically reliable in an ANOVA, which obtained a significant effect of Relatedness [$F(1,12) = 26.70$, $MSe = 4.99$, $P = 0.0002$]. However, no significant Type of Relationship by Relatedness interaction was found ($F < 1$). The size of the N400 effect was not statistically different for the associatively related word pairs ($-1.79 \mu\text{V}$) and the semantically related pairs ($-1.41 \mu\text{V}$). An ANOVA with Group of Subjects (normal controls, Broca's aphasics) as between-subject factor neither obtained a significant Group of Subjects by Relatedness interaction ($F < 1$), nor a significant third order interaction between Group of Subjects, Relatedness and Type of Relationship ($F < 1$).

The average waveforms of the seven Wernicke's aphasics are presented in Figs 8 and 9. Both N1 and P2 components

are reduced in the Wernicke's aphasics relative to the control subjects. The N400 is also clearly reduced, but has retained its centroparietal distribution. The N400 seems to be slightly larger over the right hemisphere than over the left hemisphere, especially in the semantic list (see Fig. 8). Overall, an N400 effect is still present. The ANOVA on the mean amplitude in the 400–750 ms latency range yielded a significant effect of Relatedness [$F(1,6) = 6.15$, $MSe = 3.27$, $P = 0.048$], but no interaction between Type of Relationship and Relatedness due to effects of similar size in the associative list ($-0.78 \mu\text{V}$) and the semantic list ($-0.92 \mu\text{V}$). However, a significant three-way interaction between Type of Relationship, Relatedness and Electrode Site was obtained. This interaction is mainly caused by the asymmetrical N400 effect in the semantic list, in which electrode PR showed a clear N400 effect but electrode PL did not (see Fig. 9). The ANOVA with Group of Subjects (normal controls, Wernicke's aphasics) as the between-subject factor, resulted in a marginally significant interaction between Group of Subjects and Relatedness [$F(1,17) = 3.72$, $MSe = 5.94$, $P = 0.07$]. The size of the N400 effect in the Wernicke's aphasics was reduced relative to the normal controls. However, no significant Group of Subjects by Type of Relationship by Relatedness interaction

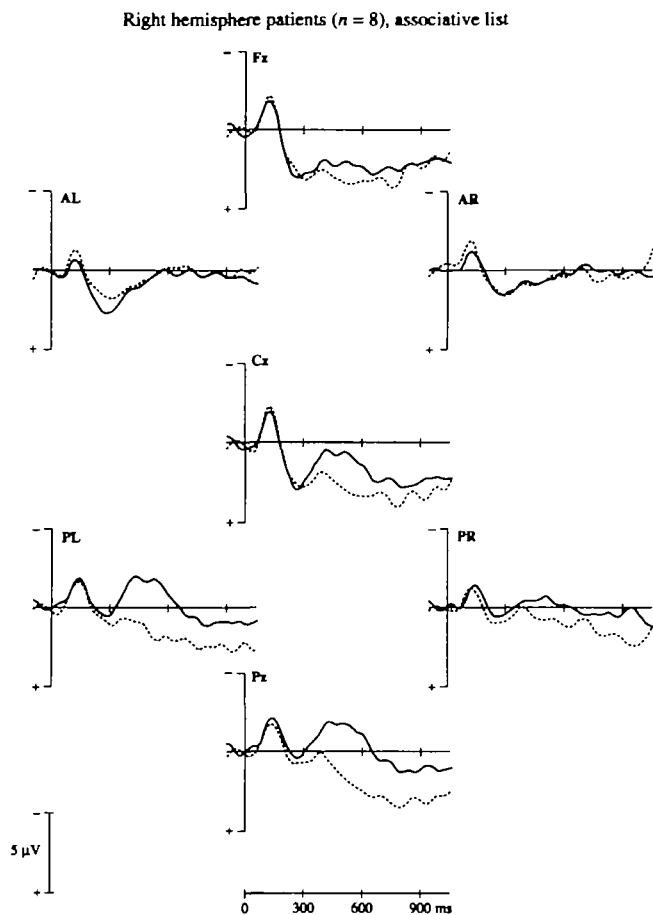


Fig. 10 Grand average ERPs for the patients with a right hemisphere lesion ($n = 8$) to the unrelated targets (continuous line) and the related targets (dotted line) in the associative list.

was observed ($F < 1$), indicating that the reduction held equally for the associatively and semantically related word pairs.

High versus low comprehenders

The classification of aphasic patients into syndrome categories is biased by deficit symptoms in language production. In addition, the legitimacy of categorizing patients by syndromes is an issue of dispute among neurolinguistic researchers (cf. Caramazza, 1984, 1986; Caplan, 1988; Shallice, 1988; Bates *et al.*, 1991). We therefore decided to group the aphasic patients in a way that was more directly related to the severity of their individual language comprehension deficit, i.e. the 20 aphasic patients were divided into a group of high and a group of low comprehenders on the basis of their language comprehension scores on the Aachen Aphasia Test. A median split of the comprehension scores determined for each individual aphasic patient in which group he or she belonged. Two patients were excluded from this analysis. One patient (Table 1, Patient 13) was excluded because his age and aetiology deviated from that of the other patients, thereby potentially compromising a straightforward comparison of

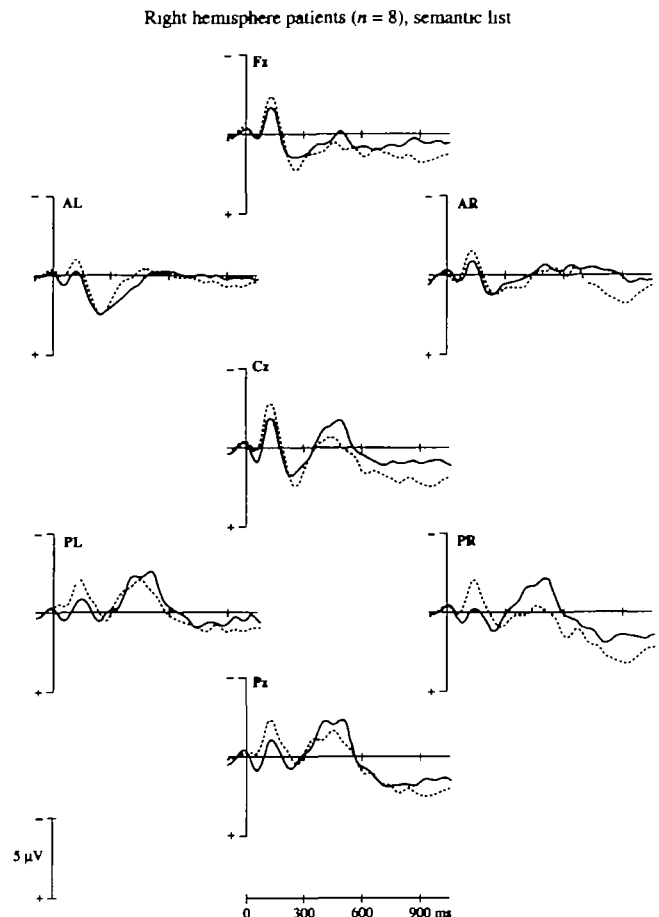


Fig. 11 Grand average ERPs for the patients with a right hemisphere lesion ($n = 8$) to the unrelated targets (continuous line) and the related targets (dotted line) in the semantic list.

the N400 effects in the high and low comprehenders. In order to get two groups of equal size, we excluded the oldest of two patients with a tie at the median score (Table 1, Patient 9). The resulting group of nine high comprehenders had a mean score of 98.3 (SD = 7.2) on the comprehension subtest of the AAT, the group of nine low comprehenders had a mean score of 71.9 (SD = 14.7) (*see* Table 1 for individual subject information).

The ANOVA on the mean amplitudes of these 18 aphasic patients with Group of Subjects (high comprehenders, low comprehenders) as the additional factor yielded a significant effect of Relatedness [$F(1,16) = 49.05$, $MSe = 2.57$, $P < 0.0001$]. In addition, a significant Group of Subjects by Relatedness interaction was obtained [$F(1,16) = 9.07$, $MSe = 2.57$, $P = 0.008$]. Both subject groups showed a significant N400 effect (high comprehenders, $F(1,8) = 48.69$, $MSe = 2.65$, $P = 0.0001$; low comprehenders, $F(1,8) = 8.21$, $MSe = 2.49$, $P = 0.021$), but the N400 effect was substantially larger in the high comprehenders ($-1.89 \mu V$) than in the low comprehenders ($-0.75 \mu V$). This was equally true for the associatively related targets (high comprehenders, $-2.18 \mu V$; low comprehenders, $-0.86 \mu V$) and for the semantically

related targets (high comprehenders, $-1.60 \mu\text{V}$; low comprehenders, $-0.65 \mu\text{V}$).

Two ANOVAs comparing the data of the high and low comprehenders against the normal controls resulted in a significant interaction between Group of Subjects and Relatedness for the low comprehenders [$F(1,19) = 5.67$, $\text{MSe} = 5.33$, $P = 0.028$], but not for the high comprehenders ($F < 1$). In neither case was there a significant three-way interaction between Group of Subjects, Type of Relationship, and Relatedness (both $F_s < 1$).

Together, these analyses indicate that the low comprehenders showed a reduction in N400 effect compared with both normal controls and high comprehenders, whereas these latter two groups did not differ.

Patients with a right hemisphere lesion

Figures 10 and 11 present the averaged waveforms for the group of eight non-aphasic patients with right hemisphere lesions. Relative to the elderly controls, these patients also show a reduction in the amplitude of the N1, which is quite comparable in size to that of the aphasic patients. For unclear reasons, in the semantic list the N1 seems to be reduced in the unrelated compared with the related condition, mainly over the posterior sites. However, most importantly, N400s with the characteristic centroparietal distribution are also observed in the patients with right hemisphere lesions.

In contrast to the elderly controls and the aphasic patients, however, the effects for the associative and semantic list seem to be different in the patients with right hemisphere lesions. In the associative list (Fig. 10) a clear N400 effect with a centroparietal distribution is obtained, larger over the PL site than over its right posterior homologue. In contrast, in the semantic list (Fig. 11) the N400 effect is much smaller than the effect in the associative list, especially for the posterior electrode sites. In addition, the N400 effect is larger for electrode PR than for electrode PL.

The ANOVA on the mean amplitudes of the eight patients with a right hemisphere lesion resulted in a marginally significant main effect of Relatedness [$F(1,7) = 4.51$, $\text{MSe} = 13.82$, $P = 0.07$]. Although the Type of Relationship by Relatedness interaction failed to reach significance [$F(1,7) = 3.42$, $\text{MSe} = 3.88$, $P = 0.11$], there was a substantial difference in the size of the N400 effect for the associative list ($-2.04 \mu\text{V}$) and the semantic list ($-0.75 \mu\text{V}$). Note that for the associative list, the N400 effect is of equal size to that of the normal controls. However, the effect for the semantic list seems to deviate from the pattern of the normal control group.

The suggestion of a difference in effects for associatively related and semantically related word pairs was supported by the results of separate ANOVAs for the associative and the semantic list, which yielded a marginally significant effect for the associatively related word pairs [$F(1,7) = 4.85$, $\text{MSe} = 13.73$, $P = 0.063$]. However, no significant effect

was obtained for the semantically related word pairs [$F(1,7) = 2.28$, $\text{MSe} = 3.97$, $P = 0.17$].

An additional ANOVA with Group of Subjects (normal controls, patients with right hemisphere lesions) as between-subject factor did not yield a significant Group of Subjects by Relatedness interaction ($F < 1$).

In summary, the data suggest that the patients with right hemisphere lesions are closer to the normals for the associative N400 effects than for the semantic N400 effects. Partly as a result of a lack of statistical power due to a limited number of patients, this difference between the associative and the semantic N400 effects is only weakly supported by the statistical analyses.

Analysis of P300 effects

Artifact rejection and correction procedures were identical to the ones for the target word ERPs. The overall rejection rate was 13% for the elderly controls, 14% for the aphasic patients and 14% for the patients with right hemisphere lesions.

Average waveforms were computed by subject over the 60 rare tones (oddballs) and 60 randomly selected frequent tones (standards). Statistical analyses on P300 effects were performed on the mean amplitudes in the latency range of 250–500 ms after tone onset. Mean amplitudes were computed relative to a 150 ms pre-stimulus baseline. The resulting values were entered into a repeated measures ANOVA for each subject group separately. In the analyses, Subjects, Probability (standards, oddballs) and Electrode Site (Cz, Pz, PL, PR) were completely crossed. In addition, ANOVAs were performed in which the patient data were compared with the data of the normal controls. These analyses had Group of Subjects (normal controls, patient group) as the additional between-subject factor.

Normal controls

For different reasons, only nine of the 12 normal control subjects were available for participation in the tone oddball task. Figure 12 shows the averaged waveforms of these nine subjects for the standard and oddball tones. The figure shows clearly that the oddball tones elicited a substantially larger P300 than the standard tones. For the centroparietal electrode sites, the sizeable effect of $7.29 \mu\text{V}$ was statistically significant [$F(1,8) = 88.41$, $\text{MSe} = 10.81$, $P < 0.0001$].

Aphasic patients

We were unable to collect ERPs to the tone oddball task for two of the 20 aphasic patients. The averaged waveforms for the remaining 12 Broca's aphasics and six Wernicke's aphasics are presented in Figs 13 and 14, respectively. Five aphasic patients (three Broca's and two Wernicke's aphasics) were unable to count, but could discriminate between high and low tones.

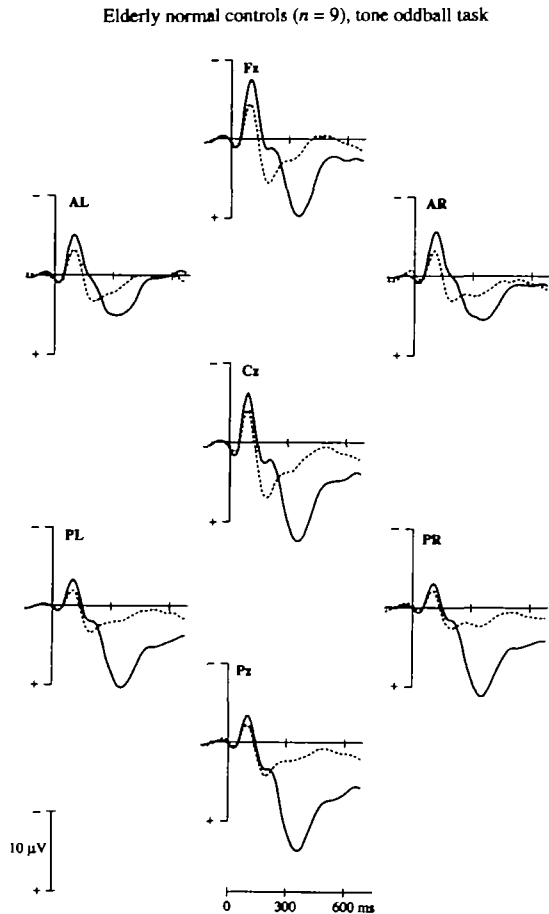


Fig. 12 Grand average ERPs for the elderly normal controls ($n = 9$) to the rare oddball tones (continuous line) and the frequent standard tones (dotted line) in the oddball paradigm.

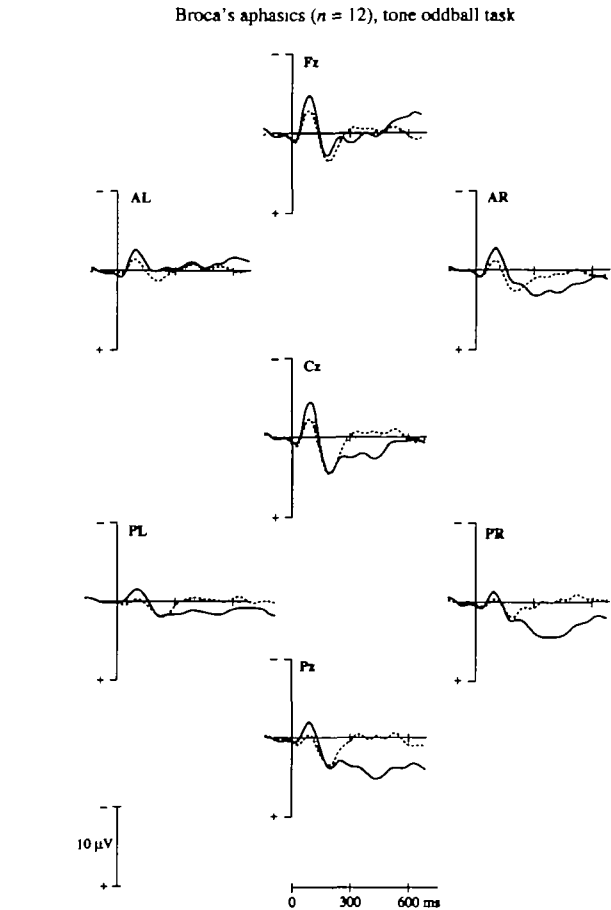


Fig. 13 Grand average ERPs for the Broca's aphasics ($n = 12$) to the rare oddball tones (continuous line) and the frequent standard tones (dotted line) in the oddball paradigm.

Figures 13 and 14 demonstrate clearly that both patient groups show an oddball effect, but the effect is less peaked and of a smaller size than in the normal controls. Moreover, this P300 effect is larger over the right hemisphere than over the left hemisphere. Between the two patient groups no difference is observed in the size of the oddball effect over the centroparietal electrode sites in the 250–500 ms latency range ($3.02 \mu\text{V}$ for the Broca's aphasics; $2.97 \mu\text{V}$ for the Wernicke's aphasics). The ANOVA resulted in a significant oddball effect for the Broca's aphasics [$F(1,11) = 6.50$, $MSe = 33.7$, $P = 0.027$], and a marginally significant effect for the Wernicke's aphasics [$F(1,5) = 5.14$, $MSe = 20.65$, $P = 0.073$]. Statistical comparisons between the data of the patient groups and the normal controls resulted in a significant Group of Subjects by Probability interaction for both the ANOVA including the data of the Broca's aphasics [$F(1,19) = 7.77$, $MSe = 24.06$, $P = 0.012$], and the analysis including the data of the Wernicke's aphasics [$F(1,13) = 9.18$, $MSe = 14.59$, $P = 0.0097$]. Both patient groups showed a reduced P300 oddball effect relative to the normal controls.

Just as for the N400 results, we did an additional analysis of the data on the basis of dividing patients into a group of high and a group of low comprehenders. The same two

patients who were excluded in the N400 analysis on high and low comprehenders, were also excluded here. Moreover, one patient had only completed a reduced version of the tone oddball, and was excluded for this reason. To have an equal number of patients in the groups of high and low comprehenders, one other patient was selected at random and excluded. Fourteen patients remained, seven high comprehenders and seven low comprehenders. An ANOVA on the mean amplitudes with Group of Patients (high versus low comprehenders) as additional factor, resulted in a significant oddball effect [$F(1,12) = 18.11$, $MSe = 19.59$, $P = 0.0011$]. In addition, a significant interaction between Group of Patients and Probability was observed [$F(1,12) = 5.11$, $MSe = 19.59$, $P = 0.043$], indicating that the oddball effect was reliably larger for the high comprehenders ($5.45 \mu\text{V}$) than for the low comprehenders ($1.67 \mu\text{V}$). Comparing the P300 effects in high and low comprehenders with the normal controls resulted in a significant interaction between Group of Subjects and Probability for the analysis including the data of the low comprehenders [$F(1,14) = 14.93$, $MSe = 16.63$, $P = 0.002$]. In contrast, the oddball effect for the high comprehenders did not differ significantly from that of the normal controls [$F(1,14) = 2.12$, $MSe = 12.51$, $P = 0.17$].

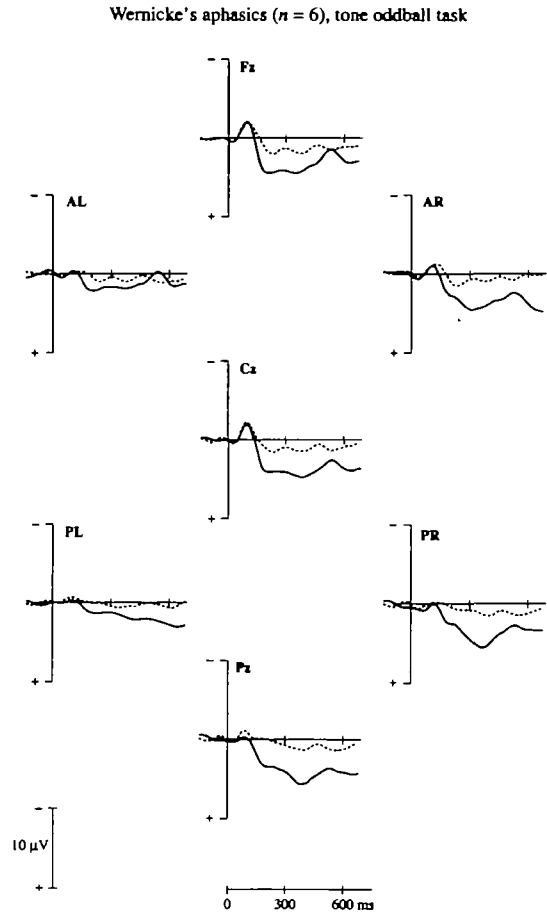


Fig. 14 Grand average ERPs for the Wernicke's aphasics ($n = 6$) to the rare oddball tones (continuous line) and the frequent standard tones (dotted line) in the oddball paradigm.

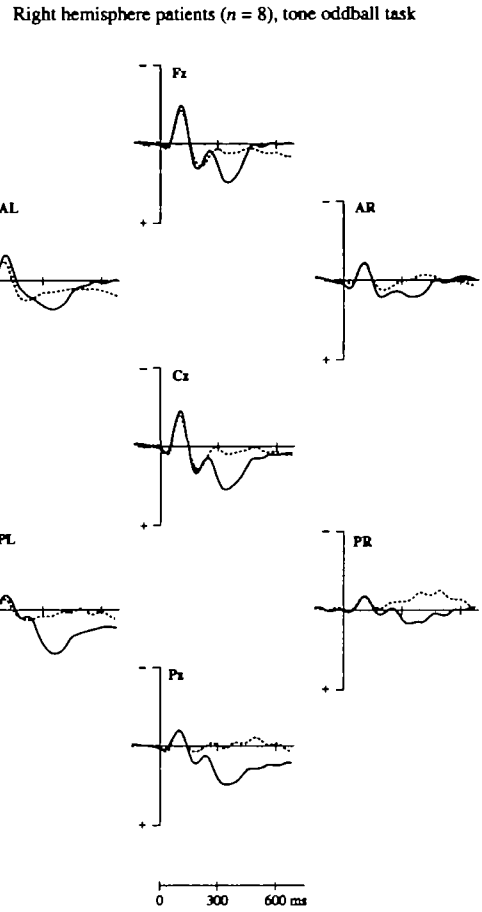


Fig. 15 Grand average ERPs for the patients with a right hemisphere lesion ($n = 8$) to the rare oddball tones (continuous line) and the frequent standard tones (dotted line) in the oddball paradigm.

Patients with a right hemisphere lesion

Figure 15 shows the oddball effect for the patients with right hemisphere lesions. These patients show a fairly peaked P300 to the oddballs, which is larger at PL than at PR. The overall effect of 3.25 µV over the centroparietal electrode sites is significant [$F(1,7) = 14.21$, $MSe = 11.92$, $P = 0.007$]. However, the oddball effect is smaller than in the normal controls, as is shown by a significant Group of Subjects by Probability interaction in the analysis that compared the data of these patients with the normal controls [$F(1,15) = 12.15$, $MSe = 11.32$, $P = 0.003$].

Individual subject data

Figures 16, 17 and 18 present the N400 effects averaged over the four centroparietal electrode sites in the associative list and the semantic list, and the P300 effect in the tone oddball paradigm for the individual subjects in the group of elderly controls, the groups of aphasic patients and the group of non-aphasic patients with right hemisphere lesions, respectively.

All individual control subjects except one, showed N400 effects, but with some variation in size between the individual

Individual subject data

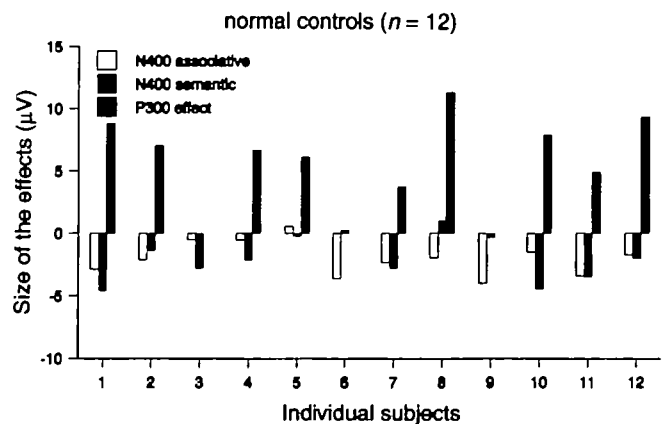


Fig. 16 Mean amplitude of the N400 effects for the associative list and the semantic list, and mean amplitude of the P300 effect in the tone oddball paradigm, for each individual subject in the group of normal controls. The means were averaged over the four centroparietal electrode sites.

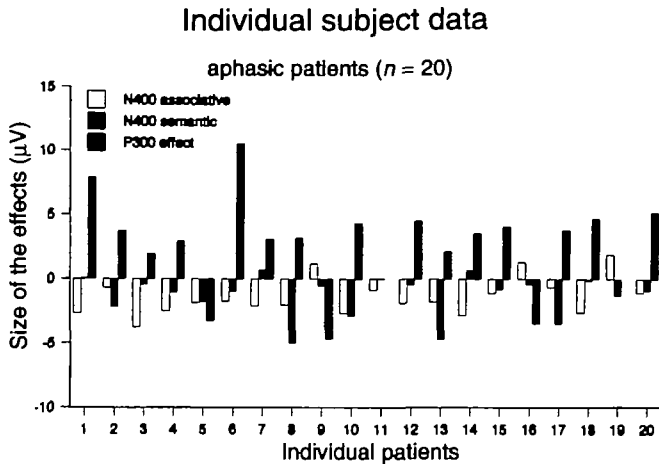


Fig. 17 Mean amplitude of the N400 effects for the associative list and the semantic list, and mean amplitude of the P300 effect in the tone oddball paradigm, for each individual aphasic patient. The means were averaged over the four centroparietal electrode sites. Patient numbers are identical to the ones in Table 1.

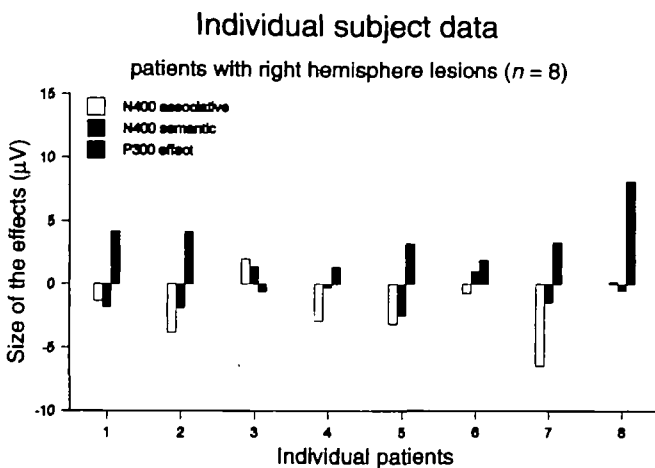


Fig. 18 Mean amplitude of the N400 effects for the associative list and the semantic list, and mean amplitude of the P300 effect in the tone oddball paradigm, for each individual non-aphasic patient with a right hemisphere lesion. The means were averaged over the four centroparietal electrode sites. Patients are numbered in the order given in Table 1 (21–28).

effects for the associative and the semantic list. The nine subjects for whom ERPs were recorded in a tone oddball task, all showed sizeable P300 effects.

N400 effects were also obtained for the majority of the aphasic patients, but again with quite some variation in the individual sizes of the associative and semantic N400 effects. However, much more striking than the individual variation in the N400 effects, is the sizeable variation in P300 effects. At least three patients (Patients 5, 9 and 16) showed what seems like an opposite P300 effect, i.e. their P300 amplitudes are larger compared with the standards than with the oddballs. The opposite oddball effect did relate to the inability to count the rare tones, which was the case for five patients (Patients 5, 8, 9, 14 and 16).

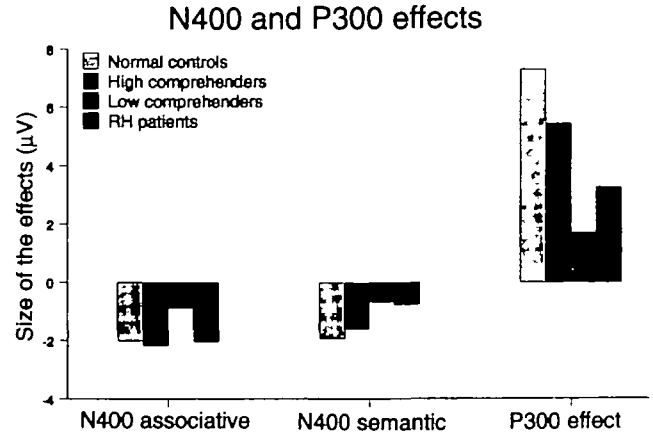


Fig. 19 Summary of the main results. The mean amplitude of the N400 effects in the associative and the semantic list, and the mean amplitude of the P300 effect in the tone oddball paradigm is shown for the normal control group, the aphasic patients with a high comprehension score, the aphasic patients with a low comprehension score, and the patients with a right hemisphere lesion. The aphasic patients were grouped into high comprehenders and low comprehenders on the basis of their language comprehension scores on the AAT.

This opposite P300 effect has also been observed in brain damaged patients by other research groups (M. Rugg, personal communication; cf. Knight *et al.*, 1988, 1989), but is still without an adequate explanation. It is even unclear whether it should be labelled as a P300 effect, or is better characterized as a larger negativity to the rare tones in the absence of a P300. However, whatever the exact characterization of these abnormal oddball effects, they do not seem to have strong predictive value with respect to the N400 effects. Two patients (Patients 9 and 16) with opposite P300 effects do not show a clear N400 effect, but the third patient (5) does show a normal pattern of N400 effects.

The patients with right hemisphere lesions also show variation in their N400 effects, but for the majority of patients with clear N400 effects, the effects for the associative list are consistently larger than the effects for the semantic list. Most patients with right hemisphere lesions show a P300 effect, but these effects are smaller than the ones for the individual control subjects and fall within the range of the individual P300 effects for the aphasic patients.

Discussion

In this study, we investigated impairments of lexical–semantic processing in aphasic patients with a lesion in the left hemisphere, and non-aphasic patients with right hemisphere lesions. This was done by recording ERPs while subjects listened to word pairs and, in a control task, to high and low tones. In both types of patients, changes in the N400 effects were observed. The main findings are summarized in Fig. 19, and are discussed below. The following findings are particularly relevant.

Among the aphasic patients, the low comprehenders showed a reduced N400 effect, both for associatively and for semantically related targets. In contrast, the N400 effects of the high comprehenders were close to normal. Although overall the Wernicke's aphasics showed a larger reduction in the size of the N400 effect than the Broca's aphasics, there were no qualitative differences in the pattern of results for these two aphasic patient groups.

In tendency, the patients with right hemisphere lesions showed a pattern of results that was qualitatively different from that of the aphasic patients. Overall, the patients with right hemisphere lesions showed a normal N400 effect for the associatively related targets, but a reduction was observed in the size of their semantic N400 effect. Additional research is required to determine how reliable this reduction is in patients with right hemisphere lesions, and to what degree we see variation in these patients in relation to their lesion site within this hemisphere.

Relative to the group of elderly normal controls, all patient groups showed a reduction in the amplitude of the N1 and in the size of the P300 effects. However, the reduction in neither of these components had any predictive value with respect to the pattern of results for the N400 component. The N1 amplitude was reduced in all brain damaged patients, even in the ones who showed normal N400 effects (e.g. the high comprehenders). Therefore, there does not seem to be an obvious relationship between the N1 amplitude on the one hand, and the presence, absence or size of the N400 effects on the other hand.

P300 effects were also reduced in all patient groups. But again, no clear relationship could be detected between P300 effects and N400 effects. For instance, inspection of Fig. 19 suggests that the P300 effects were smaller in the low comprehenders than in the patients with a right hemisphere lesion, whereas these same groups of patients did not differ in the size of their semantic N400 effect. In addition, the groups of Broca's aphasics and Wernicke's aphasics showed P300 effects of similar size, whereas the N400 effects were clearly reduced in the Wernicke's aphasics compared with the Broca's aphasics. Finally, the computation of a Pearson product-moment correlation between the N400 effects collapsed over the two lists, and the P300 effects for the 26 patients (including the aphasic patients and the patients with right hemisphere lesions) participating in both the word pair listening and the oddball task, resulted in the absence of a significant correlation ($\rho = -0.27$; $P = 0.19$). This further substantiates the conclusion that the N400 results can not easily be interpreted in terms of a general, aspecific lesion effect, equally affecting different endogenous ERP components.

Together, these results suggest that the pattern of N400 effects can not be explained in terms of a non-specific, straightforward consequence of brain lesion on the characteristics of ERP componentry. Most likely, changes in the pattern of N400 results are related to the nature of the language processing deficit in the patients studied.

Before interpreting the results of the aphasic patients and the patients with right hemisphere lesions in terms of their language comprehension impairment, a few more words should be said about what N400 effects as elicited in this experiment most likely reflect.

In our experiment, the SOA between the auditory primes and targets was 1183 ms, with the silent interval between primes and targets varying between 300 and 840 ms. A well-established finding in the priming literature (*see* Neely, 1991) is that the mechanism responsible for the observed priming effects depends on the length of the SOA. With short SOAs, priming effects are assumed to be largely due to automatic spreading of activation within a lexical-semantic network (Collins and Loftus, 1975; Neely, 1977), i.e. activation spreads from the semantic node associated with the prime to the semantic node associated with the target, thereby reducing the processing time of the target upon its presentation. In contrast, priming observed at longer SOAs is largely due to using primes for generating expectancies about possible targets (Posner and Snyder, 1975; Becker, 1980, 1985) and/or to a post-lexical process, which has been referred to as post-lexical meaning integration (de Groot, 1985) or semantic matching (Neely and Keefe, 1989). This latter mechanism searches for semantic overlap between primes and targets after they have been accessed in the mental lexicon.

The SOA between primes and targets in this experiment is beyond the range of the activation spreading mechanism (Neely, 1977, 1991). Moreover, Brown and Hagoort (1993) have shown that the N400 amplitude is not modulated by automatic spreading of activation within a lexical-semantic network. Recent research suggests that in the absence of an overt task such as lexical decision, N400 priming effects are largely due to semantic matching (C. M. Brown, P. Hagoort and D. Chwilla, unpublished results). Together, the relatively long SOA between primes and targets, the absence of a task other than listening to word pairs and the evidence about the processing nature of the N400, suggest that the N400 priming effects that were observed in this experiment were generated by a semantic matching process. In this process, subjects match primes and targets for semantic similarity. A successful match leads to a reduction of the N400 amplitude.

Lexical-semantic impairments in aphasia

The most relevant aspect of the aphasic patient data was the relationship between the size of the N400 effects and the severity of the comprehension deficit in these patients as revealed by a standardized aphasia test battery (the AAT). Patients with clear comprehension deficits (e.g. the low comprehenders) showed a sizeable reduction of the N400 effect, indicating a reduction in their capacity to match words for their semantic similarity. This reduction was independent of the type of semantic relationship between the presented word pairs.

It has been argued that the mechanism underlying semantic matching in a word priming paradigm is not unlike the

integration process that occurs in the more common processing of sentences or discourse (Neely, 1991; Brown and Hagoort, 1993). In both cases, word meaning has to be matched against the semantic specifications of the context, which in this study was another word meaning, but usually consists of the meaning representation derived from a series of words in the sentence context. If we generalize from the results of this study to a context larger than one word, they suggest that comprehension deficits in at least a subset of aphasic patients might arise from an impairment in integrating activated word meanings into the overall representation of sentences and discourse. We therefore predict that low comprehenders also show an abnormal N400 effect when words have to be matched against a whole sentence context instead of a single word context. In fact, that is exactly what we found in a recent study, in which low comprehenders showed both reduced and delayed N400 effects to sentence-final words that were semantically incongruent with the preceding sentence context (Swaab *et al.*, 1996).

In addition, no qualitatively different patterns of results were observed in the Broca's and the Wernicke's aphasics. The N400 effects in the Wernicke's aphasics were more reduced than the N400 effects in the Broca's aphasics, but this was equally true for associative and semantic word pairs. Moreover, to a large extent the reduction in N400 effects in the Wernicke's aphasics can be explained as resulting from the relatively high number of low comprehenders in this subject group. This supports earlier claims based on reaction time priming studies (Hagoort, 1993), arguing that qualitative differences in lexical-semantic processing are not observed between Broca's and Wernicke's aphasics, provided that the patients are not asked to consciously elaborate on aspects of activated word meanings (Graf and Mandler, 1984). In experimental tasks that require subjects to judge explicitly the semantic relationships between words, Wernicke's aphasics often perform much worse than Broca's aphasics (Hagoort, 1993). This difference, however, does not necessarily reflect a differential impairment in the on-line, implicit language processing events executed by the language system. Therefore, on-line measures such as ERPs, tapping language comprehension both implicitly and as it unfolds in real time, provide essential information for an adequate characterization of the functional locus of language comprehension deficits in aphasic patients. The cognitive-functional locus of comprehension deficits might be the same in many Broca's and Wernicke's aphasics, but the degree of impairment can vary (cf. Kolk and Van Grunsven, 1985).

Finally, the similarity of the results for associatively related word pairs and purely semantically related word pairs does not support the claim that the effects elicited by these two types of relationships originate from different levels of representation, namely form level representations and semantic representations (Fischler, 1977; Shelton and Martin, 1992). Most likely, both types of relationships have their effect at the lexical-semantic level (for supporting evidence, see de Groot, 1990), but differ in their strength.

Lexical-semantic impairments after right hemisphere lesion

Despite the lack of convergence between studies on lexical-semantic processing in patients with right hemisphere lesions, on the whole a substantial number of observations suggest that in right-handed individuals, the presence of an intact right hemisphere contributes to the adequate semantic processing of words (for review, see Joannette *et al.*, 1990). Recent visual half field studies in normal subjects report differential lexical-semantic processing in the left and right hemisphere that could be accounted for in terms of the distance of semantic relationships (Rodel *et al.*, 1992; Beeman *et al.*, 1994). The results of these studies suggest a special role of the right hemisphere in the processing of semantically more distant relationships. The right hemisphere is claimed to facilitate the process of connecting more distantly related items (Beeman *et al.*, 1994).

All related word pairs in our study showed some form of semantic overlap. Word pairs in the associative list contained a number of different semantic relationships, including antonymy, (near-)synonymy and hyponymy. The word pairs in the semantic list all consisted of cohyponyms. However, the degree of semantic overlap varied between the two lists of word pairs. The word pairs in the semantic list were clearly more distantly related than the items of the associative list. Not only were the word pairs of the associative list based on the immediacy with which their relationship could be produced by subjects in an association test, the meaning relationships of the associative word pairs (e.g. 'dark-light', 'crime-murder') appeared to be also more direct and stronger than the relationships of the semantic word pairs (e.g. 'bicycle-bus', 'church-villa').

Provided that semantic distance is one of the major distinguishing features between the associatively and semantically related word pairs in this study, the right hemisphere lesions seem to have specifically affected the processing of the semantically more distant relationships. Matching strongly related elements was, however, largely unimpaired in the patients with right hemisphere lesions.

A comparison between the results of the aphasic patients and the patients with right hemisphere lesions suggests that both cerebral hemispheres are involved in lexical-semantic processing, but in a qualitatively different way. The left hemisphere is crucial for the computation of semantic overlap, independent of strength or distance of the semantic relationships. The right hemisphere becomes increasingly relevant to establish coherence between elements with diminishing semantic overlap. This difference is compatible with the notion that semantic information is more coarsely coded in the right hemisphere than in the left hemisphere (Beeman *et al.*, 1994).

Conclusion

Finally, we should like to remark upon the usefulness of ERP research for studying language processing deficits in

brain damaged patients. To our knowledge this is one of the first neurolinguistically motivated ERP studies on aspects of language comprehension impairments in aphasic patients and non-aphasic patients with right hemisphere lesions (for review, *see* Hagoort and Kutas, 1995). This study has shown that reliable ERP effects, uncontaminated by potential task artifacts, can be obtained in brain damaged patients with a language impairment. These effects, however, will only be revealing about the functional nature of the neurolinguistic deficit if, in addition, dissociations between language related and non-linguistic ERP effects are observed. Provided that this and some other methodological concerns are borne in mind (cf. Hagoort and Kutas, 1995), the exploitation of language-related ERP effects such as the N400 (Kutas and Hillyard, 1980) and the Syntactic Positive Shift (Osterhout and Holcomb, 1992; Hagoort *et al.*, 1993) offers a fruitful additional approach to studying language deficits related to brain lesion.

In conclusion, the impairments that aphasic patients with clear comprehension deficits showed in matching related words for their semantic similarity, suggest that one functional locus of language comprehension impairments in these patients is at the level of integrating individual word meanings into the overall message representation of the whole utterance. Patients with right hemisphere lesions tended to show a relatively focal impairment in the semantic matching of more distantly related words. This is compatible with the claim that sentence and discourse processing in these patients is particularly affected when the mutual relationships between the constituting elements are rather loose or indirect.

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Appendix*Associative list*

	Related word pairs		Unrelated word pairs			Related word pairs		Unrelated word pairs	
	Prime	Target	Prime	Target		Prime	Target	Prime	Target
1	aardig	lief	accu	jeugd	43	lijm	plakken	puinhoop	wolf
2	ader	bloed	aktie	kloof	44	links	rechts	put	spot
3	antwoord	vraag	antiek	zeker	45	maaltijd	eten	rot	vrij
4	bal	rond	bewust	boter	46	man	vrouw	rots	passen
5	ballet	dansen	blind	bedrijf	47	misdaad	moord	saldo	plein
6	ballon	lucht	boom	dienen	48	naald	draad	schaduw	slaan
7	beven	trillen	cirkel	nijdig	49	nauw	eng	sieraad	letsel
8	boek	lezen	dom	tillen	50	oorlog	vrede	ski	roepen
9	chef	baas	duel	taal	51	oorzaak	gevolg	smoel	paal
10	dame	heer	eisen	tomaat	52	papier	pen	spleet	verbod
11	dag	nacht	gedicht	knop	53	raak	mis	spoor	tapijt
12	deksel	pan	gelei	getal	54	zeep	wassen	spul	grens
13	dicht	open	gratis	elftal	55	rijmen	dichten	staf	park
14	dik	dun	half	baby	56	rimpel	oud	stel	pers
15	dol	gek	hertog	olie	57	ritme	muziek	stelling	zoen
16	dorp	stad	heks	deel	58	rozijn	krent	stier	vers
17	dier	beest	honger	struik	59	ruig	stoer	stof	veilig
18	donder	bliksem	hooi	lapje	60	schaal	fruit	studie	slok
19	donker	licht	intens	adres	61	schaar	knippen	suiker	uniek
20	durf	moed	kachel	sport	62	schep	zand	team	japon
21	egel	stekels	keer	kind	63	schrijver	auteur	tenger	weelde
22	emotie	huilen	kern	orkest	64	serie	reeks	traan	tellen
23	faam	roem	kleven	molen	65	grijpen	pakken	tube	nota
24	geloof	god	klok	baard	66	slee	sneeuw	uitval	slang
25	gooien	werpen	kapper	meer	67	slordig	netjes	vak	steek
26	haai	vis	koek	traag	68	smelten	ijs	vast	schok
27	haastig	vlug	kraken	stroom	69	spaak	wiel	verschil	vallen
28	herder	schaap	lastig	koel	70	sparen	geld	villa	wolk
29	humor	lachen	lijn	top	71	ster	hemel	visie	perk
30	jongen	meisje	luxe	maan	72	storm	wind	vorst	gezicht
31	kennis	vriend	mand	ets	73	taart	lekker	vreten	post
32	kil	koud	natie	lol	74	tabak	roken	vriezen	sociaal
33	kip	ei	nevel	lek	75	tasten	voelen	wenk	triest
34	koorts	ziek	oceaan	paar	76	vallei	dal	werf	figuur
35	kop	schotel	oerwoud	ober	77	vlam	vuur	woord	zak
36	kust	zee	opstel	graf	78	vochtig	nat	wraak	lip
37	kwast	verf	oven	bestaan	79	vroeg	laat	ziel	rit
38	lang	kort	planeet	loket	80	winst	verlies	zucht	basis
39	lawaaï	herrie	pols	plaats	81	woest	kwaad	zweet	tekst
40	leeg	vol	preek	probleem	82	zomer	winter	wieg	weten
41	lepel	vork	premier	regen	83	berouw	spijt	pudding	debat
42	levend	dood	pril	rus					

Semantic list

	Related word pairs		Unrelated word pairs			Related word pairs		Unrelated word pairs	
	Prime	Target	Prime	Target		Prime	Target	Prime	Target
1	roos	narcis	oma	anjer	43	kerry	marjoraan	lila	knoflook
2	crocus	fresia	cello	madelief	44	basilicum	zout	schouder	kaneel
3	den	eik	aap	berk	45	schaatsen	voetbal	kardinaal	zwemmen
4	beuk	spar	limonade	esdoorn	46	tennis	boksen	dressoir	handbal
5	appelboom	els	beige	iep	47	zeilen	hockey	penny	roeien
6	tijger	beer	oranje	geit	48	judo	korfbal	kousen	honkbal
7	kat	paard	eeuw	hond	49	minuut	kwartier	komkommer	etmaal
8	cola	wijn	druif	bier	50	maand	uur	vliegtuig	week
9	port	thee	roze	koffie	51	tram	auto	vink	trein
10	cognac	water	fluit	sherry	52	fiets	bus	turnen	motor
11	vader	oom	linde	broer	53	taxi	boot	dijen	metro
12	nicht	zus	schaaf	neef	54	papegaai	ekster	lariks	kievit
13	boor	beitel	luis	hamer	55	spreeuw	eend	bridge	duif
14	zaag	vijl	muts	tang	56	mus	uil	bes	valk
15	kaarten	dammen	bloemkool	schaken	57	zwaluw	parkiet	wodka	meeuw
16	scrabble	kwartet	kever	halma	58	aardbei	banaan	romp	citroen
17	sla	worteltjes	schroeven	kool	59	perzik	appel	mot	meloen
18	andijvie	boontjes	moeder	paprika	60	ananas	peer	volleybal	kers
19	tor	bij	kar	vlo	61	bof	griep	kin	pokken
20	mug	vlinder	pet	vlieg	62	tyfus	mazelen	toepen	malaria
21	wesp	spin	borst	mier	63	pistool	mes	telex	kanon
22	trui	jurk	ezel	hemd	64	geweer	raket	bisschop	dolk
23	broek	vest	hobo	jas	65	degen	tank	spion	sabel
24	bloes	sokken	reiger	hoed	66	arts	jurist	mitrailleur	leraar
25	das	schoenen	peseta	sjaal	67	timmerman	slager	blaas	bakker
26	paars	grijs	brommer	zwart	68	chauffeur	agent	speer	groenteboer
27	bruin	groen	seconde	blauw	69	staal	koper	garage	ijzer
28	geel	rood	lijster	wit	70	goud	aluminium	kolonel	platinum
29	been	hand	rat	hoofd	71	museum	kerk	zilver	huis
30	knie	arm	mees	voet	72	flat	school	dokter	schuur
31	elleboog	teen	whiskey	vinger	73	telefoon	radio	metselaar	televisie
32	buik	neus	pruim	rug	74	brief	fax	hal	krant
33	nek	enkel	beha	hals	75	muur	deur	tin	raam
34	mond	oren	stoel	ogen	76	gang	kamer	gal	zolder
35	bed	buro	rok	kast	77	plafond	trap	onderzoeker	vloer
36	tafel	bank	aster	kruk	78	korporaal	officier	boer	generaal
37	dubbeltje	mark	kastanje	cent	79	sergeant	mariniers	dak	matroos
38	stuiver	dollar	sambal	kwartje	80	non	broeder	bom	monnik
39	gulden	yen	billen	lire	81	rabijn	pastoor	kantoor	priester
40	saxofoon	piano	leeuw	harp	82	nieren	hart	kozijn	maag
41	viool	orgel	shilling	trommel	83	lever	longen	sateliet	darmen
42	gitaar	trompet	peper	fagot					