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Aphasietherapie im Wandel

Informationen aus
medizinisch-apparativen
Untersuchungsverfahren
für Aphasietherapeuten

4. Rhein-Ruhr-Meeting in Bochum

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Inhalt

Neurophysiological Evidence for a Temporal Disorganization in Aphasic Patients with Comprehension Deficits

Colin Brown, Peter Hagoort* & Tamara Swaab***

In normal conversational settings, the average speaking rate is some 3 to 4 words per second. This rate (which is by no means a performance limit – people can speak even faster) imposes strict limitations on the listener: If an utterance is to be understood, the listener must keep track of the message at much the same rate with which it is produced. In other words, time is of the essence for normal spoken language understanding. In this paper we present a novel line of evidence on comprehension deficits in aphasia, using the registration of event-related brain potentials (ERPs), on the basis of which we argue that an important factor in aphasic comprehension problems is an impairment in the time-course of understanding. We suggest that the comprehension deficits of the aphasic patients that we have investigated, result from an inability to exploit stored linguistic representations in real-time. This characterization of aphasic deficits contrasts markedly with the more traditional perspective on aphasia, which holds that problems in understanding language stem from a loss of linguistic knowledge (for an overview, see Hagoort, 1990).

The research that we present concentrates on the processing of spoken words, both in simple two-word contexts and in sentences. The reason for focusing on lexical processing is that words are fundamental building blocks for understanding, providing a bridge between the spoken sensory input and the ultimate representation of the full meaning of the utterance. A primary condition, therefore, for

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normal language understanding, is a smooth and swift functioning of the lexical analysis process.

The real-time lexical analysis process can be divided into three basic processes: lexical access, lexical selection, and lexical integration (cf. Frauenfelder & Tyler, 1987; Marslen-Wilson, 1987). During lexical access, an initial stretch of the sensory input is mapped onto representations of lexical form in the mental lexicon. This results in the activation of a subset of all the words in the lexicon (roughly some 45,000 in total, cf. Aitchison, 1987; Nagy & Herman, 1987), namely all lexical items that match this initial part of the spoken input. In lexical selection, the number of activated word candidates is narrowed down to the one lexical candidate that best matches the sensory input and the context specifications (although the role of in particular sentential context during lexical selection is contentious, cf. Marslen-Wilson, 1987; McClelland & Elman, 1986; Zwitserlood, 1989). Finally, during lexical integration, syntactic and semantic information at the lexical level is mapped onto a higher-order meaning representation of the whole utterance. If we now consider the already mentioned rate of speech and the size of the mental lexicon (i.e., on average 3 to 4 words per second, from a database of about 45,000 entries) in the light of this functional analysis of spoken word recognition, then it becomes clear that a number of basic processes have to be executed quickly (in less than half a second), and, moreover, need to be carefully orchestrated, such that the right process gets executed at the right moment in time. Both the speed and the orchestration can be problematic for aphasic patients.

The major claim we will be making on the basis of our ERP data, is that comprehension deficits in aphasic patients are due to an impairment in integrating individual words into an overall meaning representation. Specifically, we will argue that comprehension problems result from a temporal mismatch between lexical access and lexical integration, caused by a delay in the integration of lexical information within the context representation. Our analysis of comprehension deficits is in line with an emerging research approach in which temporal factors in aphasia are under investigation (e.g., Friederici

& Kilborn, 1989; Haarmann & Kolk, 1994; Hagoort, 1990, 1993; Hagoort, Brown, & Swaab, 1995; Hagoort, 1990, 1993; Swaab, Brown, & Hagoort, 1995; Swinney, Zurif, & Nicol, 1989).

Although the importance of the role of time in aphasic deficits has been emphasized over the years (e.g., Kolk & van Grunsven, 1985; Lenneberg, 1967; Von Monakow, 1914), in mainstream aphasiological research it has until recently been largely ignored. In part, this has resulted from the use of experimental procedures that do not allow direct evaluation of real-time language processing. In particular, the majority of experimental work on aphasia has used so-called off-line tasks to assess the nature and extent of aphasic deficits. In such tasks, patients are usually asked to make grammatical and/or semantic judgments in, for example, picture-sentence matching or sentence verification tasks. These tasks are off-line because they do not tap the language process as it proceeds over time. Instead, patients are given a relatively large amount of time in which to produce a response, and the response itself is an end-product of a number of preceding on-line processes, none of which can be readily identified on the basis of the final off-line response.

On the basis of results in off-line tasks, it was the predominant view in the seventies that Wernicke's aphasics suffered from a semantic disorder due to a partial loss or disintegration of lexical-semantic knowledge, whereas the impairment of Broca's aphasics was characterized as a loss of syntactic knowledge (for an overview, see Caplan, 1987). Recent years, however, have seen a number of studies which suggest that for many aphasic disorders a characterization of the disorder in terms of a processing impairment might be more adequate than one in terms of loss of representational structures for language. Furthermore, it turned out that a neat distinction between patients with a semantic deficit (Wernicke's aphasics) and patients with a syntactic deficit (Broca's aphasics) was less clear-cut than one would hope. The resulting change of perspective can be illustrated with the issue of lexical-semantic processing in aphasic patients.

The claim that Wernicke's aphasics suffer from a loss of lexical-semantic knowledge, whereas in Broca's aphasics the semantic lexicon is largely unaffected, has been challenged in a number of recent word priming studies (Blumstein, Milberg, & Shrier, 1982; Chenery, Ingram, & Murdoch, 1990; Friedman, Glosser, & Diamond, 1988; Hagoort, 1993; Katz, 1988; Milberg & Blumstein, 1981; Milberg, Blumstein, & Dworetzky, 1987; Milberg, Blumstein, Katz, Gershberg, & Rosen, 1995; Ostrin & Tyler, 1993; Prather, Zurif, Stern, & Rosen, 1992). In these studies subjects had to make a lexical decision, that is 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 & Schvaneveldt, 1971; see Neely (1991) for an extensive review of the visual priming literature). These priming effects reflect, directly or indirectly, that lexical concepts in semantic memory are clustered according to some matrix of semantic similarity (cf. Collins & 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. That is, 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; Friedman et al., 1988; Hagoort, 1993; Milberg et al., 1987). Second, surprisingly, Broca's aphasics had a less stable pattern of performance. Some studies reported no priming effects in these patients (Milberg & Blumstein, 1981; Milberg et al., 1987). In other studies, however, Broca patients showed the expected priming effect (Blumstein et al., 1982; Hagoort, 1993; Katz, 1988; Ostrin & Tyler, 1993).

What these studies suggest, then, is that if subjects are not required to explicitly evaluate the semantic characteristics of words, but only have to make a rapid decision about the 'wordhood' of a string of letters or sounds, some subjects no longer seem to be impaired in accessing lexical-semantic information. This implies that under certain conditions information that was thought to be lost can be retrieved; a result which is more compatible with a processing impairment than with a loss of linguistic knowledge.

Although an account of aphasic disorders in terms of a processing impairment has gained a lot of adherents in recent years, the exact nature of the processing deficit is still a matter of debate. One possibility that has been entertained is that especially Broca's aphasics might have an impairment in automatically accessing the semantic lexicon (e.g., Baum, 1989; Milberg et al., 1987; Milberg et al., 1995; Swinney et al., 1989). However, results from recent on-line studies suggest that rather than lexical access, the integration of lexical information into the preceding word or sentence context might be impaired in these patients (e.g., Hagoort, 1990, 1993; Hagoort et al., 1995; Swaab et al., 1995; Tyler & Ostrin, 1994; Tyler, Ostrin, Cooke, & Moss, 1995). The ERP data that we present in this chapter, provide evidence for this latter position. More specifically, we will argue on the basis of our data that the processing impairment is related to pathological changes in the time course of language processing. Especially the temporal fine-tuning between lexical access and lexical integration seems to be lost in aphasic patients with clear comprehension deficits.

In the following we will present two experiments in which ERPs were recorded while aphasic patients and control subjects listened to spoken language. The first experiment focuses on lexical processing in simple two-word contexts, in which the second of two words is preceded by a prime word to which it is either related or unrelated in meaning. The main purpose of this experiment was to investigate the presence and nature of lexical-semantic processing impairments. The second experiment moves beyond the two-word lexical environment, and investigates lexical processing in sentential contexts. Here, patients and control subjects listened to sentences that ended with a word that either fitted the semantic specifications of the preceding context, or that was semantically anomalous. The main purpose of this experiment was to determine whether spoken sentence comprehension problems might result from a deficit in the on-line integration of lexical information into a higher-order semantic representation.

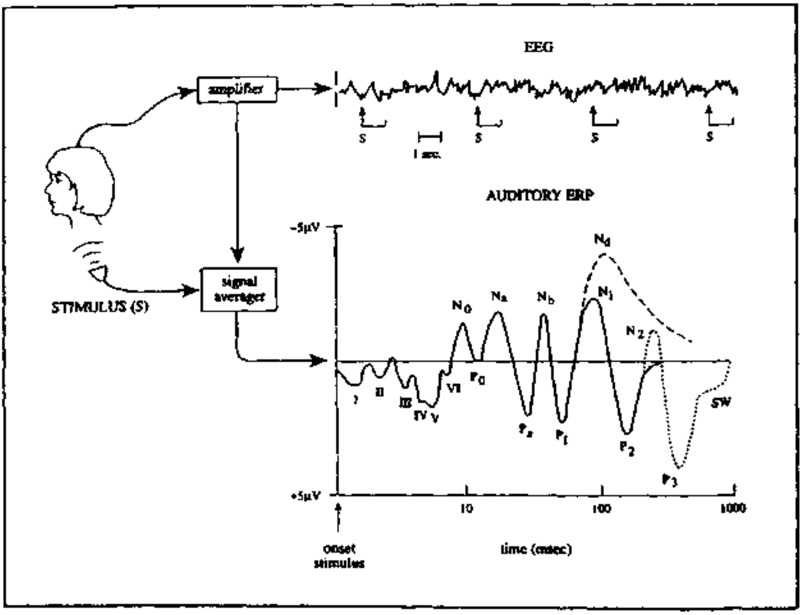

Fig. 1: Idealized waveform of a series of ERP components that become visible after averaging the EEG to repeated presentations of a short auditory stimulus. As a rule, averaging over a number of stimulus tokens is required to get an adequate signal-to-noise ratio. Along the logarithmic time axis the early brainstem potentials (Waves I-VI), the midlatency components (No, Po, Na, Pa, Nb), the shorter latency (P1, N1, P2), and the longer latency components (Nd, N2, P300, Slow Wave) are shown. Negative polarity components are plotted upwards, positive polarity components are plotted downwards.

Before turning to the presentation of the data from the two experiments, we will briefly introduce the use of ERPs in language research.

ERPs and language processing

Scalp-recorded ERPs reflect the summation of the synchronous post-synaptic activity of a large population of neurons. ERPs 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. Figure 1 illustrates the basic ERP procedure, and provides an idealized waveform.

For the purposes of neurolinguistically oriented ERP research, the most informative ERP components belong to the longer latency components. These 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 longer latency components as a consequence of some experimental manipulation, usually form the basis for making inferences about the nature of the underlying cognitive processes.

ERP recordings have at least two advantages when investigating language impairments in neurological patients (cf. Hagoort & 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 wants to investigate. The other advantageous aspect of ERPs is that they are tightly linked in time to the underlying language processing events. They therefore not only allow inferences 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.

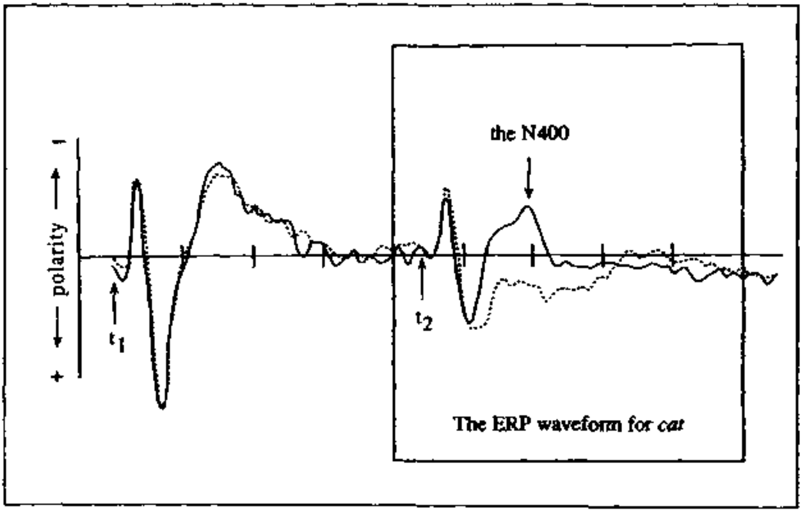

Fig. 2: ERP waveforms for related and unrelated wordpairs. The dashed line represents the related wordpairs (e.g., dog-cat), the solid line the unrelated wordpairs (e.g., lamp-cat). At time t_1 either *dog* or *lamp* is presented. At time t_2 *cat* is presented. As a function of the meaning relationship of *cat* with the word that precedes it, the amplitude of the N400 component varies. The difference in amplitude between the unrelated and the related condition is referred to as the N400 effect.

The most relevant ERP component for the work reported in this chapter 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. For example, 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 & 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. In contrast to semantic anomalies, physically deviant words (e.g., printed in bold-face type) elicit a positive potential rather than a negativity. Other non-semantic deviations such as musical or grammatical violations also do not elicit the N400 effect (Besson & Macar, 1987; Hagoort, Brown, & Groothusen, 1993; Kutas & Hillyard, 1983; Osterhout & Holcomb, 1992). 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 Hagoort & Kutas, 1995; Kutas & Van Petten, 1988, 1994).

N400 effects are not only obtained in a sentence context, but can also be observed 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, McCarthy, & Wood, 1985; Chwilla, Brown, & Hagoort, 1995; Rugg, 1985, 1987; Boddy, 1986; Kutas & Hillyard, 1989; Holcomb & Neville, 1990, 1991). Figure 2 shows a representative example, from our own work, of an N400 semantic priming effect in a two-word context. The N400 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 & 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 postlexical processes that are involved in lexical integration (Brown & Hagoort, 1993; Brown, Hagoort, & Chwilla, 1995; Chwilla et al., 1995; Hagoort et al., 1993; Holcomb, 1993; Rugg, Furda, & Lorist, 1988).

In the two experiments that we will now report, we used our knowledge of the processing nature of the N400, and of its relationship to language processing, to investigate spoken language understanding in aphasic patients.

Experiment 1: ERPs and word priming

The major goal of this first 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 the comprehension subtest of the Aachen Aphasia Test (AAT; Graetz, De Bleser, & Willmes, 1992). This allows us to evaluate the influence of the severity of the comprehension deficit on the N400 priming effects.

The paradigm used is auditory word-word lexical priming, in which subjects listen to wordpairs that are either related or unrelated in meaning. The issue we look at is the modulation of the N400 component for the second word in a wordpair, as a function of its meaning relation with the first word.

Subjects, Materials, Procedure, EEG recording

The subjects in this experiment were 20 aphasic patients, and 12 age-matched controls. None of the control subjects had any known neurological impairment or used neuroleptics.

All of the patients except one had suffered a CVA (the lesion of one patient (pt. 13) was due to a bacterial meningitis). The patients were administered the standardized Dutch version of the AAT. Time of administration was at least six 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. Thirteen patients were diagnosed as Broca's aphasics, and seven were diagnosed as Wernicke's aphasics. According to their scores on the comprehension subtest of the AAT, the patients had severe to mild comprehension deficits. 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. 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.

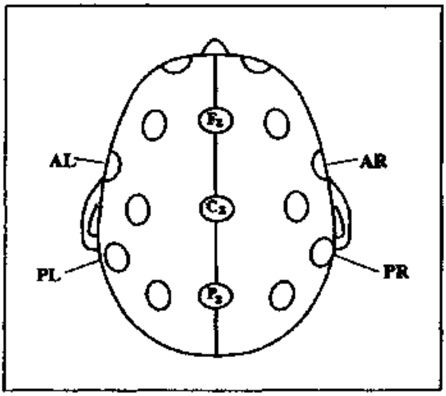

Fig. 3: **Electrode placement**
Schematic flat projection of the scalp, showing the approximate locations of the electrodes.

The stimuli consisted of a list of 166 auditorily presented Dutch word pairs, 83 of which were related in meaning (e.g., 'bread-butter'). A pair was considered to be related if the target word appeared as an associate of the prime in published Dutch word association norms (De Groot, 1980; De Groot & De Bil, 1987; Lauteslager, Schaap, & Schievels, 1986).

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 wheelchair). Subjects were asked to listen attentively to the words. No additional task demands were imposed.

EEG activity was recorded using an Electrocap with 7 scalp tin electrodes, each referred to the left mastoid. Three electrodes were placed according to the International 10-20 system (Jasper, 1958) at frontal (Fz), central (Cz), and parietal (Pz) sites. Symmetrical anterior temporal electrodes (AL, AR) 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. Figure 3 gives a schematic of the electrode placement.

Table 1: Individual patient information for the Broca's aphasics and the Wernicke's aphasics. The patients were clustered on the basis of their comprehnsion scores into High Comprehenders (HI) and Low Comprehenders (LO).

Patient	Age	Sex	Token Test*	Comprehension Score AAT**	Auditory Compreh. Score AAT	Lesion Volume in cm^3***
01 Broca HI	40	m	17	94/120	45/60	59.60
02 Broca HI	49	m	31	92/120	44/60	66.40
03 Broca HI	60	f	18	104/120	49/60	–
04 Broca LO	37	f	31	85/120	49/60	112.10
05 Broca LO	68	m	34	65/120	37/60	72.90
06 Broca HI	71	f	7	108/120	52/60	127.10
07 Broca LO	42	m	41	65/120	33/60	219.06
08 Broca HI	53	m	13	98/102	49/60	49.55
09 Broca –	72	f	20	87/120	41/60	–
10 Broca HI	64	m	25	108/120	50/60	60.35
11 Broca LO	58	f	20	82/120	48/60	85.05
12 Broca LO	66	m	28	76/120	42/60	–
13 Broca –	27	m	24	93/120	47/60	141.85
14 Wernicke HI	45	f	21	99/120	48/60	64.65
15 Wernicke LO	51	m	43	66/120	37/60	67.20
16 Wernicke HI	65	m	45	–	39/60	123.65
17 Wernicke HI	52	m	30	95/120	48/60	110.90
18 Wernicke HI	60	m	33	87/120	45/60	25.40
19 Wernicke HI	67	m	44	84/120	40/60	88.25
20 Wernicke LO	62	m	47	84/120	42/60	26.90

* 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 sentence) is specified. Ranges of severity are based on the norms of the Dutch version of the AAT.

*** Lesion volume was calculated by means of a CT-reconstruction program (see Knight et al., 1988, for details).

Results

Average waveforms were computed by subject over all artifact-free trials of the related and unrelated target words in the 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, 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 (Gunter, Jackson, & Mulder, 1992; Harbin, Marsh, & Harvey, 1984). 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. For purposes of exposition, we will in the following figures present the waveform of one representative electrode site: Pz.

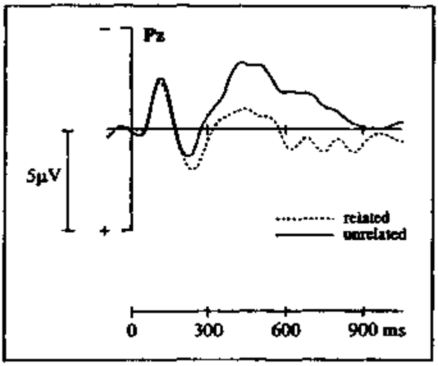

Fig. 4: **Control subjects (N=12)**
Grand average ERPs for the control subjects to the unrelated (solid line) and related second words (dotted line). Electrode site Pz.

Control subjects

Figure 4 shows the average waveforms for the second word of the wordpair as a function of its meaning relationship with the first word.

Both waveforms show sizeable N1 and P2 components following the onset of the second word. These components are followed by a broad negative deflection that is very similar to previously observed N400s to spoken words (Holcomb & Neville, 1990). The N400 is

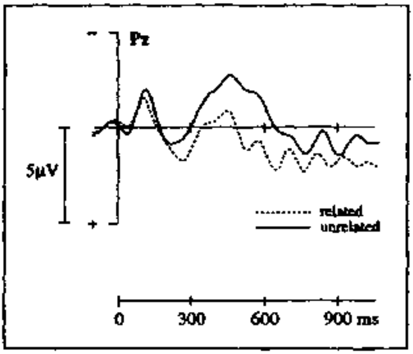

Fig. 5: **Broca's aphasics (N = 13)**
Grand average ERPs for the Broca's aphasics to the unrelated (solid line) and related second words (dotted line). Electrode site Pz.

substantially larger to unrelated than to related words. This N400 effect of -2.01 μV is statistically significant.

Aphasic patients

Figure 5 shows 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 control subjects. Just as for the controls, the waveforms of the Broca's aphasics show clear N1 and P2 components, albeit that the N1 is slightly reduced in amplitude relative to the control subjects.

The N400 is clearly present in the waveforms, and its amplitude is larger for the unrelated than for the related target words. This N400 effect of -1.79 μV is statistically reliable.

The average waveforms of the 7 Wernicke's aphasics are shown in Figure 6. Both N1 and P2 components are reduced in the Wernicke's aphasics relative to the control subjects. The N400 is also clearly reduced, but a statistically significant N400 effect of -0.78 μV is present.

High vs. 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. Bates, Appelbaum, & Allard, 1991; Caplan, 1988; Caramazza, 1984, 1986; Shallice, 1988). 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. That is, the 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.[5]

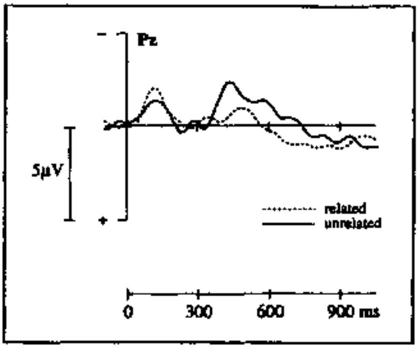

Fig. 6: **Wernicke's aphasics (N=7)** Grand average ERPs for the Wernicke's aphasics to the unrelated (solid line) and related second words (dotted line). Electrode site Pz.

The statistical analysis on 18 aphasic patients with Group of Subjects (high comprehenders, low comprehenders) as an additional factor showed that the N400 effect was significantly larger in the high comprehenders (-1.89 μV) than in the low comprehenders (-0.75 μV).

Discussion

In this study we investigated impairments of lexical-semantic processing in aphasic patients. The low comprehenders showed a reduced N400 effect. 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

5 Two patients were excluded from this analysis. One patient (Table 1, pt. 13) was excluded because his age and etiology deviated from that of the other patients, thereby potentially compromising a straightforward comparison of 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, pt. 09). The resulting group of 9 high comprehenders had a mean score of 98.3 (s.d.: 7.2) on the comprehension subtest of the AAT. The group of 9 low comprehenders had a mean score of 71.9 (s.d.: 14.7).

than the Broca's aphasics, there were no qualitative differences in the pattern of results for these two aphasic patient groups.

Relative to the group of control subjects, the aphasic patients showed a reduction in the amplitude of the N1. However, this reduction does not have any predictive value with respect to the pattern of results for the N400 component. The N1 amplitude was reduced in all patients, even in the High Comprehenders, who showed normal N400 effects. Therefore, there does not seem to be an obvious relation between the N1 amplitude on the one hand, and the presence, absence or size of the N400 effects on the other hand. Hence, changes in the size of the N400 component in the aphasic patients will be interpreted in terms of their language comprehension deficit, and not in terms of spurious effects of brain damage on ERP components.

Before we can discuss the nature of the comprehension deficit in the patients we tested, we first need to have a better understanding of what the N400 effects are reflecting about the real-time operations of the language system. In the experiment, the stimulus-onset asynchrony (SOA) between the first and the second word of each word-pair was 1183 ms, with the silent interval between first and second words 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 mainly 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 & Loftus, 1975; Neely, 1977). That is, activation spreads from the semantic node associated with the first word to the semantic node associated with the second, thereby reducing the processing time of the second word upon its presentation. In contrast, priming observed at longer SOAs is largely due to using the first words to generate expectancies about possible following words (Becker, 1980, 1985; Posner & Snyder, 1975) and/or to a postlexical process, that has been referred to as postlexical meaning integration (De Groot, 1985) or semantic matching (Neely & Keefe, 1989). This latter mechanism searches for semantic overlap between members of a wordpair after they have been accessed in the mental lexicon.

The SOA between the first and second words in this experiment is beyond the latency range in which the activation spreading mechanism is active (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 (Brown et al., 1995). Together, the relatively long SOA between members of a wordpair, the absence of a task other than listening to wordpairs, 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 the members of a wordpair for semantic similarity. A successful match leads to a reduction of the N400 amplitude.

What, then, does the observed pattern of N400 effects for the aphasic patients imply about the nature of their comprehension deficit? Note first that our data demonstrate that even the low comprehenders do not suffer from a full loss of lexical-semantic knowledge. Although the semantic priming effect is reduced, it is present, showing that the patients must have gained access to the individual words (at least to a significant number of them), and are (at least to some degree) sensitive to the meaning relationships that exist in their mental lexicon. Second, the most relevant aspect of the aphasic patient data is the relation between the size of the N400 effects and the severity of the comprehension deficit in these patients as revealed by the AAT. Patients with clear comprehension deficits (i.e., the low comprehenders) show a sizeable reduction of the N400 effect. Given the processing nature of the N400, what this implies is that these patients have a reduced capacity to match words for their semantic similarity.[6]

At first glance, a reduced capacity to match words for meaning might not sound too dramatic. But if we consider the central role that words play in achieving understanding, in combination with the speed at which they have to be processed, then there are good reasons to suppose that comprehension will be seriously affected by a semantic matching problem. In particular, such matching problems might have very negative consequences for the processing of sentences or discourse. The reasoning here is 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 (cf. Brown & Hagoort, 1993; Neely, 1991). In both cases word meaning has to be matched against the semantic specifications of the context, which in this first experiment was another word meaning, but usually consists of the meaning representation derived from a series of words in the sentence context. If we were to generalize the results of our experiment 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 to integrate activated word meanings into the overall representation of sentences and discourse, within the time frame that is required for complete and successful comprehension. We would, then, 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. Exactly this issue was addressed in the second experiment.

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6 For a more extended presentation and discussion of these data, see Hagoort, Brown, and Swaab (1996).

Experiment 2: ERPs and lexical integration in sentence contexts

In this experiment the N400 was used to test whether the severity of the aphasic comprehension deficit interacted with the ability to rapidly integrate lexical information into the preceding sentence context. This was done by presenting subjects with sentences that either ended normally, as for example in: „The children like to play in the garden", or with semantically anomalous words, as for example in: „The girl dropped the candy in the sky". The task of the subjects was to listen attentively to these sentences, with the understanding that sometimes a question about the content of the sentence would be asked. In accordance with results in the literature (e.g, Kutas & Hillyard, 1980; Holcomb & Neville, 1991; Gunter, et al., 1992), an N400 effect was expected for the control subjects. This means that the amplitude of the N400 to sentence-final congruent words („garden" in the example) will be reduced when compared to the amplitude of the N400 to sentence-final anomalous words („sky" in the example). This results from the fact that the meaning of an anomalous word does not match the semantic specifications of the sentence context, which makes the integration of this word difficult, if not impossible. If comprehension deficits in aphasia affect the rate at which lexical information is integrated into the higher order representation of the preceding sentence context, a delay of the N400 effect is expected in these patients. To the degree to which such a delay reduces the efficiency of lexical integration, an amplitude reduction of the N400 effect might also be seen. Finally, it might be the case that the severity of the comprehension deficit interacts with the N400 effect, which means that the largest deviation from the normal N400 effect is expected for those patients with the most severe comprehension deficits.

Table 2 Individual patient information for Broca´s aphasics and Wernicke´s aphasics. The aphasic patients were clustered on the basis of their comprehension scores into High Comprehenders (HI) and Low Comprehenders (LO)

Patient	Age	Sex	Token Test*	Overall Comp. Score AAT**	Sent. Comp. Score AAT	Aud. Comp. Score AAT	Lesion in Volume in cm^3***
01 Broca HI	40	m	17	94/120	35/60	45/60	59.60
02 Broca HI	36	f	19	97/129	47/60	53/60	75.10
03 Broca LO	62	m	38	67/120	27/60	39/60	120.90
04 Broca HI	62	m	20	96/120	48/60	50/60	34.60
05 Broca LO	38	f	31	85/120	38/60	49/60	112.10
06 Broca LO	69	m	34	65/120	28/60	37/60	72.90
07 Broca HI	72	f	7	108/120	53/60	52/60	127.10
08 Broca LO	43	m	41	65/120	32/60	33/60	219.05
09 Broca HI	53	m	13	98/120	55/60	49/60	49.55
10 Broca LO	73	f	20	87/120	42/60	41/60	---
11 Broca HI	65	m	25	103/120	45/60	58/60	60.35
12 Wernicke HI	44	f	21	99/120	47/60	48/60	64.65
13 Wernicke LO	51	m	43	66/120	25/60	37/60	67.20
14 Wernicke LO	65	m	45	---	---	39/60	123.65

* 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); no/very mild disorder (107-120). Ranges of severity are based on the norms of the Dutch version of the AAT (Graetz et al., 1993).

*** Lesion volume was calculated by means of a CT-reconstruction program (see Knight et al., 1988, for details).

Subjects, Materials, Procedure, EEG recording

A group of 12 control subjects, and 14 aphasic patients participated in the experiment. Patients were diagnosed with the same procedure as for Experiment 1. Eleven patients were diagnosed as Broca's aphasics, and three as Wernicke's aphasics. According to their scores on the comprehension subtest of the AAT, 7 of the aphasic patients had a moderate to severe comprehension deficit (low comprehenders), and 7 had a light to very mild comprehension deficit (high comprehenders). Table 2 gives the relevant patient information.

The stimuli consisted of a list of 222 auditorily presented Dutch sentences, of which 120 sentences were critical. These critical stimuli were divided over two conditions. In one condition the sentences ended with a word that matched the sentential-semantic constraints, the congruent condition, for example: „The children like to play in the garden". In the other condition the sentences ended with a word that violated the sentential-semantic constraints, the anomalous condition, for example: „The girl dropped the candy on the sky". In addition, 102 filler sentences were constructed that contained a semantic violation at varying positions in the sentence. These materials were included to prevent subjects developing a strategy of predicting the position of the anomalous word.

Subjects were told that they would hear sentences, some of which had words in them that did not fit the context. They were asked to listen attentively to the sentences, and were told that the experimenter would sometimes stop the tape to ask a question about a sentence they had just heard. No additional tasks were imposed.

The testing room, the general testing conditions, and the EEG montage and recording were identical to Experiment 1.

Results

Average waveforms were computed for each subject over the anomalous and the congruent sentence-final words. Statistical analyses were done on the amplitude of the N400 for all 7 electrode sites, in three time windows: The 300-700, the 300-500, and the 500-700 ms epochs after onset of the sentence-final words, relative to a 100 ms baseline preceding the sentence-final words. These epochs were determined after visual inspection of the waveforms, and based on prior literature (Hagoort et al., 1995; Gunter et al., 1992). The overall epoch of 300-700 ms was divided into an early (300-500 ms) and a

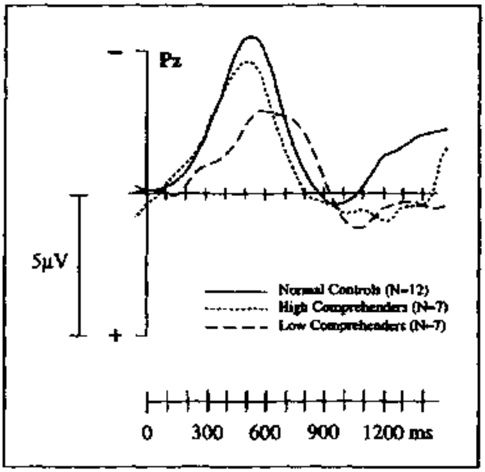

Fig. 7: Difference waveforms, Sentence-final word
Grand average difference waveforms (anomalous minus congruent) for the control subjects (thin solid line), the high comprehenders (dotted line), and the low comprehenders (d ashed line). Electrode site Pz.

late (500-700 ms) window to help quantify an apparent latency shift of the N400 effect in the low comprehenders.

To facilitate insight into the overall pattern of effects, we provide in Figure 7 an overlay of the difference waveforms for the Pz electrode site. In this figure, we have subtracted, for each subject group separately, the waveform for the anomalous condition from the waveform of the congruent condition. The resulting difference waveform gives a clear picture of the effects of the experimental congruity manipulation.

For the control subjects, the N400 effect of -3.09 μV was highly significant in the 300-700 ms epoch after sentence-final word onset. The same was true for the early (300-500 ms: -3.27 μV) and late (500-700 ms: -2.91 μV) temporal windows.

The N400 effect of the high comprehenders is comparable in size to that of the normal controls. The N400 effect of -2.23 μV for the 300-700 ms epoch was significant, as was the effect in the early epoch (-2.50 μV). The effect in the late epoch (-1.96 μV) fell just short of significance ($p < .06$).

For the low comprehenders, the effect is reduced compared to the controls, and it appears to have a later onset. The N400 effect in the full epoch (-1.87 μV) was statistically significant, as were the effects in the early (-1.46 μV) and the late epoch (-2.29 μV).

In sum, in this study the aphasic patients with only a mild comprehension deficit were clearly sensitive to the congruity of sentence-final words. This was evident from their N400 effect that, although slightly smaller, was statistically indistinguishable from the normal controls. Just as for the normal controls, the effect was larger (-0.54 μV) in the early epoch than in the late epoch.

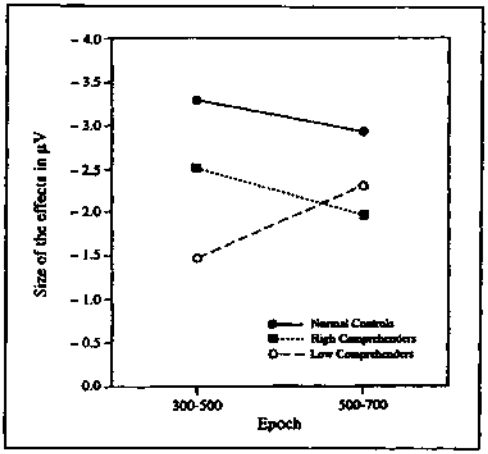

Fig. 8: **N400 effect in early and late epoch**
Mean amplitude of the N400 effect (collapsed over the 7 electrode sites) for the three subject groups, in the early (300-500 ms) and late (500-700 ms) epochs.

When comparing the low comprehenders with the controls, no significant differences were found for the overall 300-700 ms window, or for the late 500-700 ms window. However, in the early 300-500 ms window the two groups did differ significantly. This was due to a delay of the N400 effect in the low comprehenders relative to the normal controls. In contrast to the normal controls and the high comprehenders, the N400 effect in the low comprehenders reached its maximum amplitude in the late measurement epoch, where it was -0.83 μV larger than in the early epoch. This salient difference between the low comprehenders and the other subject groups is further illustrated in Figure 8, where we show the N400 effect (collapsed over all 7 electrodes) in the early versus the late window, for the three subject groups.

As can be seen in this figure, the low comprehenders clearly showed an increase in the size of the N400 effect in the late window relative to the early window, while the two other groups showed a decrease of the N400 effect in the late relative to the early window.

Discussion

The control subjects showed the expected N400 effect: The N400 to sentence-final congruent words was reduced when compared to the N400 to sentence-final anomalous words. This result is in agreement with the well documented N400 effect in the literature, and replicates the finding of Holcomb and Neville (1991), demonstrating that the N400 effect can be obtained when presenting subjects with naturally produced connected speech. In the controls, the N400 effect was maximal in the 300-500 ms window, indicating the immediacy of the lexical integration process in normal neurologically unimpaired subjects.

The N400 data for the aphasic patients were analyzed according to the severity of their comprehension deficit. This was done for a number of reasons. First, the results of the previous experiment showed that the severity of the comprehension deficit determined the size of the N400 effect in a word-word priming situation. In the second experiment, we therefore examined whether the severity of the comprehension deficit was correlated with the N400 effect, or in other words with the ability to integrate lexical information in sentence contexts. Second, since both the Broca's and Wernicke's aphasics in our study showed comprehension deficits with varying degrees of severity on the comprehension subtest of the AAT, an analysis in terms of the severity of the comprehension deficit seemed appropriate.

The aphasic patients with a mild comprehension deficit showed essentially the same pattern of results as their controls. That is, neither in size nor in latency did their N400 effect differ statistically from that of the control subjects. This shows that standard N400 effects can be obtained in brain damaged patients with aphasia.

The aphasic patients with moderate to severe comprehension deficits also showed a clear N400 effect. However, these patients differed from the two other groups in the latency of the effect. The controls and the high comprehenders showed an N400 effect that had its maximum amplitude in the 300-500 ms epoch. In the low comprehenders, however, the effect had its maximum amplitude in the 500-700 ms epoch. In these patients the N400 effect showed a delay of approximately 100 ms relative to the controls and the high comprehenders.[7]

What does the change in the N400 effect of the low comprehenders mean in terms of their language comprehension deficit? The results of our second experiment suggest that the low comprehenders show a relative delay in the integration of lexical meaning into the overall representation of the utterance. The magnitude of the delay is in the order of 100 ms (see Figure 7). Given the speed at which language processing normally proceeds, a delay of this magnitude is quite substantial, and can seriously affect on-line comprehension. When time is of the essence, one cannot afford to persistently lag behind the ongoing speech stream.[8]

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7 For a more extended presentation and discussion of these data, see Swaab, Brown, and Hagoort (1996).

8 It should be noted that in addition to a prolonged latency of the N400 effect, we also observed a reduction in the overall size of the effect for the low comprehenders. One could argue that we should have seen an increased N400 effect, because low comprehenders seem to have more problems than control subjects in integrating a word into the context. However, the reduction in the N400 effect can be explained if we consider the effect that delayed integration could have on the processing of the sentence-final congruent and anomalous words. It is conceivable that a delay in the process of lexical integration yields an incomplete or degraded higher order context representation. Under such circumstances, the notion of congruent versus anomalous becomes somewhat relative. Note that both sentence-final congruity and sentence-final anomaly is defined in terms of a semantic match cq. mismatch with an adequate representation of the sentence context. However, if the context representation is degraded compared to the normal case, the congruent and the anomalous words could well be more similar with respect to the preceding context. This results in less of a difference in the N400 between conditions, and hence, in a reduced rather than increased N400 effect.

Concluding remarks

The two experiments that we have reported in this chapter are among the first to investigate aphasic comprehension problems with ERPs. Our research shows that ERPs can be a valuable tool in aphasia research. The possibility of assessing aphasic deficits without having to impose an extraneous and possibly contaminating task, together with the possibility to track the real-time comprehension process as it unfolds over time, offers new opportunities for the study of the impaired language system.

Moreover, the results of the two experiments reported here are compatible with results from reaction time studies (Hagoort 1990), suggesting that comprehension deficits in aphasic patients might be related to changes in the time course of language processing events. More specifically, relative to accessing lexical information on the basis of the speech input, the integration of this lexical information into a higher-order representation of the utterance seems to be delayed. Since speed is such a central aspect of language processing, this delay most likely has consequences for the construction of an adequate representation of sentences. The ultimate interpretation of the utterance is no longer adequate. The greater the temporal mismatch between lexical access and lexical integration, the more severe the comprehension deficit will be, with in the limit a complete failure to construct an overall representation of the utterance. This account of language comprehension deficits is not only compatible with results from a large series of on-line studies (e.g., see Tyler et al., 1995), including the ERP studies we discussed, but also easily explains one of the overriding phenomena in aphasic patients, namely the large variation between patients in the degree of severity of their comprehension deficits. This variation in degree of severity might be related to the between-patient variation in the degree of temporal mismatch between lexical access and lexical integration.

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