

Electrophysiological manifestations of open- and closed-class words in patients with Broca's aphasia with agrammatic comprehension

An event-related brain potential study

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Summary

This paper presents electrophysiological data on the on-line processing of open- and closed-class words in patients with Broca's aphasia with agrammatic comprehension. Event-related brain potentials were recorded from the scalp when Broca patients and non-aphasic control subjects were visually presented with a story in which the words appeared one at a time on the screen. Separate waveforms were computed for open- and closed-class words. The non-aphasic control subjects showed clear differences between the processing of open- and closed-class words in an early

(210–375 ms) and a late (400–700 ms) time-window. The early electrophysiological differences reflect the first manifestation of the availability of word-category information from the mental lexicon. The late differences presumably relate to post-lexical semantic and syntactic processing. In contrast to the control subjects, the Broca patients showed no early vocabulary class effect and only a limited late effect. The results suggest that an important factor in the agrammatic comprehension deficit of Broca's aphasics is a delayed and/or incomplete availability of word-class information.

Keywords: Broca's aphasia with agrammatic comprehension; open- and closed-class words; event-related brain potential; lexical processing

Abbreviations: ERP = event-related brain potential; RH = right hemisphere; VC = vocabulary class

Introduction

In this study we investigated electrophysiological manifestations of vocabulary class (VC) in patients with Broca's aphasia with agrammatic comprehension, as reflected by scalp-recorded event-related brain potentials (ERPs). We focused on the role that closed-class items play in agrammatic comprehension.

Broca's aphasia is a syndrome that includes a complex of impairments in both sentence production and sentence perception. Central among these impairments is the so-called agrammatic comprehension deficit. Many Broca patients suffer from an impairment in the comprehension of sentences that require a full analysis of the grammatical structure for correct understanding. The comprehension of sentences that can be understood largely on the basis of the meaning of the sequence of open-class words, without full analysis of the syntactic structure, seems to be relatively unimpaired (e.g.

Caramazza and Zurif, 1976; Berndt and Caramazza, 1980; Caplan and Hildebrandt, 1988; Sherman and Schweickert, 1989). Open-class or content words, such as nouns, verbs and adjectives, are the main bearers of meaning in language. They contain indispensable semantic information, thus providing the building blocks for the overall sense that is contained in a spoken or written sentence.

Analysis of the syntactic structure of a sentence is a complex process. One of the levels of grammatical analysis, in which Broca patients with agrammatic comprehension are reported to have difficulties, is the processing of closed-class words (e.g. Caramazza and Zurif, 1976; Berndt and Caramazza, 1980; Bradley *et al.*, 1980; Swinney *et al.*, 1980; Friederici, 1983, 1985; Goodglass and Menn, 1985; Rosenberg *et al.*, 1985; Friederici and Kilborn, 1989; Friederici *et al.*, 1991; Pulvermuller, 1995; Biassou *et al.*,

1997). Closed-class or function words, such as articles, conjunctions and prepositions, are relatively devoid of meaning (certainly in comparison with open-class words) and primarily serve a syntactic role in language understanding. They co-determine the syntactic relations between open-class words, thereby making combinations of words interpretable. In other words, closed-class words support the syntactic analysis of a sentence. Broadly speaking, the distinction between open- and closed-class words can be seen as a basic reflection of the separation between semantics and syntax. The agrammatic comprehension of Broca's aphasics has thus often been described in terms of this classical separation of VC into content or function words, or, alternatively, open- and closed-class words. We will use the latter terms.

Just how critical the problems are that agrammatic comprehenders have with closed-class items is an issue that remains controversial in accounts of agrammatic comprehension. Roughly two sets of views have been advanced. In the first set of views, agrammatic comprehension is directly tied to an abnormal processing of closed-class items (e.g. Berndt and Caramazza, 1980; Bradley *et al.*, 1980; Friederici, 1985, 1989; Friederici *et al.*, 1991; Rosenberg *et al.*, 1985; Zurif *et al.*, 1990; Pulvermuller, 1995). The problems associated with the hypothesized direct relationship vary from the (fast) access or retrieval of closed-class words from the mental lexicon, to the processing of the syntactic information carried by closed-class words in sentence analysis. In the alternative set of accounts, no special role is attributed to closed-class items and the processing of closed-class items *per se* is not assumed to be impaired. Rather, some other underlying (syntactic) deficit is postulated, which may result in symptoms that suggest problems with closed-class items (e.g. Linebarger *et al.*, 1983; Kolk and Van Grunsven, 1985; Grodzinsky, 1986, 1995; Schwartz *et al.*, 1987; Caplan and Hildebrandt, 1988; Saffran and Schwartz, 1988; Rosenthal and Goldblum, 1989; Hickok, 1992; Mauner *et al.*, 1993; Hickock and Avrutin, 1995; Swinney and Zurif, 1995; Tyler *et al.*, 1995; for a more extensive review, see Kolk, 1997).

Electrophysiological evidence for a processing distinction between open- and closed-class words

In this study we pursue the question of whether agrammatic comprehension might be related to an impairment in processing closed-class words, by offering real-time electrophysiological evidence on the processing of VC information. This evidence is obtained by recording ERPs, that is, real-time electrical brain activity, related to the processing of open- and closed-class words in Broca patients with agrammatic comprehension and in normal control subjects.

Over the last few years, investigations on the vocabulary type distinction in young normal adults have shown that

ERPs elicited by open- and closed-class words consistently differ in roughly an early and a late time-window, thus reflecting electrophysiological differences in the processing of the two word types. In the early time-window (200–350 ms), differences have mostly been reported in the peak latency and/or in the presence of a frontal negative component between the two VCs. This negative-polarity component is quite consistently elicited by closed-class words, with a maximal amplitude over left anterior electrode sites, on average at 280 ms following stimulus onset (Neville *et al.*, 1992; Nobre and McCarthy, 1994; Pulvermuller *et al.*, 1995; Osterhout *et al.*, 1997; King and Kutas, 1998; Brown *et al.*, 1999). Open-class words elicit either a less distinct or a delayed early negativity. Although precise functional interpretation of the early differences between the two word classes varies between the different studies, they are generally taken as an electrophysiological manifestation of differences in the lexical processing of open- and closed-class words. These differences refer to an early stage of word processing in which the lexical-syntactic and lexical-semantic information of a word is accessed and made available for further sentential processing.

Additional differences in the ERP profiles of the two word classes have been reported for a late time-window (350–700 ms). Closed-class words have consistently been reported to elicit a broad frontal negative shift (Kutas and Hillyard, 1983; Van Petten and Kutas, 1991; Neville *et al.*, 1992; Osterhout *et al.*, 1997; King and Kutas, 1998; Brown *et al.*, 1999). This shift has been classified as a variant of the contingent negative variation (Hillyard, 1973; McCallum, 1988) and has been taken to reflect anticipatory processes associated with the syntactic nature of closed-class items and their role in sentence parsing (Van Petten and Kutas, 1991; Brown *et al.*, 1999). In the same time-window around 400 ms, several differences between the two word classes have been reported in the amplitude of the N400 component (Kutas and Hillyard, 1983; Neville *et al.*, 1992, 1993; Nobre and McCarthy, 1994; Pulvermuller *et al.*, 1995; Osterhout *et al.*, 1997; N400: cf. Kutas and Hillyard, 1980). The posterior N400 to open-class words is generally assumed to reflect real-time semantic processing (Holcomb, 1993; Kutas and Van Petten, 1994). Closed-class words, in contrast, do not elicit a strong N400. It has been argued that the modulation of N400 amplitude is a reflection of lexical-semantic integration processes, related to the insertion of word meanings into the message-level representation of the sentential and discourse context in which they occur (e.g. Brown and Hagoort, 1993, 1999; Kellenbach and Michie, 1996). Thus, ERP profiles elicited by the on-line processing of VC provide information on both the early lexical processing of open- and closed-class words and on the later post-lexical processing of their semantic and syntactic information.

In this study the differential characteristics of ERP correlates of open- and closed-class words are exploited to investigate the central issue under debate: are Broca patients with agrammatic comprehension impaired in the processing

Table 1 Individual patient information for the Broca patients and the non-aphasic RH control patients

Patient	Age (years)	Sex	Token Test [†]	Overall comp. score AAT [‡]	Visual comp. score AAT	Syntactic off-line score	Lesion site
1 Broca	74	F	7	108/120	56/60	115/144	Left frontal
2 Broca	70	M	50	90/120	44/60	59/144	Left frontotemporoparietal
3 Broca	68	M	24	105/120	54/60	88/144	Left frontal
4 Broca	63	M	38	67/120	28/60	52/144	Left frontotemporal
5 Broca	42	M	17	94/120	49/60	74/144	Left temporoparietal
6 Broca	50	F	10	97/120	49/60	95/144	Left frontotemporoparietal
7 Broca	68	M	18	103/120	49/60	47/144	Left frontotemporoparietal
8 Broca	52	M	20	109/120	55/60	113/144	Left frontotemporoparietal
9 Broca	63	F	23	80/120	45/60	60/144	Left frontotemporal
10 Broca	64	F	45	65/120	34/60	44/144	Left frontotemporal
11 Broca	43	F	19	115/120	57/60	93/144	Left frontotemporoparietal
12 Broca	61	M	14	98/120	46/60	115/144	No CT information available
13 Broca*	44	M	41	60/120	25/60	56/144	No CT information available
14 Broca*	39	F	45	74/120	33/60	51/144	No CT information available
15 Broca	48	M	42	89/120	44/60	51/144	Left temporoparietal
16 Broca	66	F	18	91/120	46/60	111/144	Left frontotemporoparietal
1 RH*	46	M	0	114/120	58/60	130/144	Right frontotemporoparietal
2 RH*	60	M	0	118/120	58/60	116/144	Right frontotemporal
3 RH	59	M	1	117/120	60/60	134/144	Right frontotemporal
4 RH	65	F		108/120	54/60	108/120	Right frontotemporoparietal
5 RH	49	M		113/120	55/60	134/144	No CT information available
6 RH*	63	M		95/120	54/60	101/144	No CT information available
7 RH	69	F	2	106/120	53/60	89/144	Right frontoparietal
8 RH	67	F	0	102/120	54/60	118/144	Right parietal

*Patients that were excluded from EEG analysis. [†]Severity of the aphasic disorder as indicated by the Token Test: no/minimal disorder (0–6); light (7–23); middle (24–40); severe (41–50). [‡]Severity of the comprehension disorder as indicated by the Aachen Aphasia Test subtest on comprehension (includes word and sentence comprehension in both the auditory and visual modality): no/very mild disorder (107–120); light (90–106); middle (67–89); severe (1–66). comp. = comprehension; AAT = Aachen Aphasia Test.

of closed-class items? On the assumption that the electrophysiological differences between the ERP profiles elicited by the open- and closed-class vocabulary reflect differential processing of open- and closed-class information, a specific impairment in the processing of closed-class items should show up as changes in the ERP profiles elicited by the two VCs.

Methods and subjects

Subjects

Sixteen patients with aphasia secondary to a single cerebral vascular accident in the left hemisphere participated in this study. A group of 15 healthy normal subjects, who were approximately matched in age and education level to the aphasic patients, were tested to control for age and education effects. To account for non-specific effects of brain damage on cognitive ERP components, a group of eight non-aphasic patients with a single cerebral vascular accident in the right hemisphere (RH patients) was tested. The testing procedures were approved by the ethical committee of the Nijmegen University Hospital. All subjects gave informed consent, according to the declaration of Helsinki. The mean age of the aphasic patients was 57.2 years (range 39–74 years), of the RH patients 59.8 years (range 46–69 years) and of the

normal controls 58.7 (range 47–69 years). All subjects had normal or corrected-to-normal vision and were (premorbidly) right-handed according to an abridged Dutch version of the Oldfield Handedness Inventory (Oldfield, 1971). All neurological patients were tested at least 6 months post-onset of their cerebral vascular accident. Median post-onset time for the RH patients was 2.6 years (range 1.4–10.8 years). Median post-onset time for the Broca patients was 8.5 years (range 1.3–19.8 years).

All neurological patients were tested with the standardized Dutch version of the Aachen Aphasia Test (Graetz *et al.*, 1992). Both presence and type of aphasia were diagnosed on the basis of the test results and on the basis of a transcribed sample of the patients' spontaneous speech. All RH patients were diagnosed as non-aphasic and all left-hemisphere patients were diagnosed as Broca patients. According to their scores on the comprehension subtest of the Aachen Aphasia Test, the aphasic patients had severe to mild comprehension deficits. To determine whether the aphasic patients indeed showed agrammatic comprehension, all subjects were administered a Dutch version of an off-line test for syntactic comprehension (Huber *et al.*, 1993). This test assesses the influence of syntactic complexity on sentence comprehension and will be described in more detail below.

Patients' age, gender, results on the Token Test, scores on

Table 2 *The five types of sentences of the syntactic off-line test*

Degree of syntactic complexity	Sentence
I	Active, semantically irreversible sentences, e.g. Het meisje met de strik draagt de bal. (<i>The girl with the ribbon carries the ball.</i>)
II	Active, semantically reversible sentences, e.g. De man met de bal zoekt het kind. (<i>The man with the ball is looking for the child.</i>)
III	Simple passive sentences, e.g. De man met de bal wordt door het kind gezocht. (<i>The man with the ball is being looked for by the child.</i>)
IV	Sentences with an active subject relative clause, e.g. Het kind dat naar de man zoekt heeft een bal. (<i>The child that is looking for the man has a ball.</i>)
V	Sentences with a passive subject relative clause, e.g. Het kind dat door de man gezocht wordt heeft een bal. (<i>The child that is being looked for by the man has a ball.</i>)

Syntactic complexity increases from I–V.

the Aachen Aphasia Test subtest on comprehension, overall scores on the syntactic off-line test and lesion site information are summarized in Table 1. The Token Test is a valid measure of the general severity of the aphasia, independent of syndrome type (Orgass, 1986). The general severity of the aphasia ranged from light to severe. The Token Test results also substantiated that the RH patients were not aphasic. Lesions evident on CT scans of the patients were transcribed on to corresponding CT templates by an experienced neurologist. These CT templates were read into a computer program that permitted the computation of the group-averaged lesions (Frey *et al.*, 1987; see Knight *et al.*, 1988, for detail). Figures 1 and 2 show the average axial reconstructions of the Broca and the RH patients, respectively.

Syntactic off-line test

The syntactic off-line test consisted of five types of sentences (in total 72 items) which differ in their degree of syntactic complexity (see Table 2). Subjects were tested in a quiet room. The experimenter read the sentences aloud to the subject at a normal speaking rate whilst sitting face to face with him/her. The order of presentation of the different sentence types was randomized. For each sentence, subjects performed a sentence-picture matching task with four alternatives which consisted of one picture that correctly matched the target sentence and three distracter pictures (all black and white line-drawings). For the semantically irreversible sentences the distracters were: (i) a picture with an incorrect lexical modifier; (ii) a picture with a lexically incorrect direct object; (iii) a picture with the combination of an incorrect lexical modifier and a lexically incorrect direct object. For the other sentence types the distracters were: (i) a picture with an incorrect assignment of the attribute; (ii) a picture with a reversed agent-patient role; (iii) a combination of (i) and (ii). If the subject explicitly asked for a repetition, the sentence was read again. Responses were scored on a three-point scale: two points for correctly matched

sentences, one point for sentences that were correctly matched after self-correction, one point for correctly matched sentences that were presented twice and no points for incorrectly matched sentences.

Analyses were performed on the percentage-correct scores for the five sentence types of the syntactic off-line test. The data were entered into repeated measures analyses of variance with group (Broca patients, normal controls, RH patients) as a between-subjects factor and sentence type (I–V) as a within-subjects factor. A Huyn–Feldt correction was applied to all repeated measures with >1 d.f. in the numerator, and the Tukey-HSD multiple range test ($\alpha = 0.05$) was used for *post hoc* analysis (cf. Maxwell and Delaney, 1990). The adjusted degrees of freedom and *P*-values are reported.

ERP experiment

A modified version of a fairy-tale like story was selected for visual presentation (Renier, 1989). The text contained 151 sentences of average length of 10 words (range 4–16). Active sentences made up 92% of the story (of which 58% were one-clause, and 34% two-clause sentences). The text contained a total number of 1540 words, including nouns, verbs, adjectives, adverbs, auxiliaries, conjuncts, prepositions, numerals, articles and pronouns. From this set of words, 439 open-class words (202 nouns, 151 verbs, 86 adjectives) and 398 closed-class words (212 articles, 115 prepositions, 71 conjuncts) were included in the analyses reported below. The stimuli selected for analysis did not include the initial or final words of a sentence to avoid contamination from start-up and wrap-up effects (cf. Hagoort *et al.*, 1993; Kutas and King, 1996).

The open-class words that were selected for analysis ranged in length from 3 to 12 letters. The selected closed-class words ranged from 2 to 5 letters. The frequency of occurrence for the open-class words was between 0.0 and 4.3 and between 2.42 and 4.44 for the closed-class words on a log frequency scale. The frequencies were obtained from a Dutch

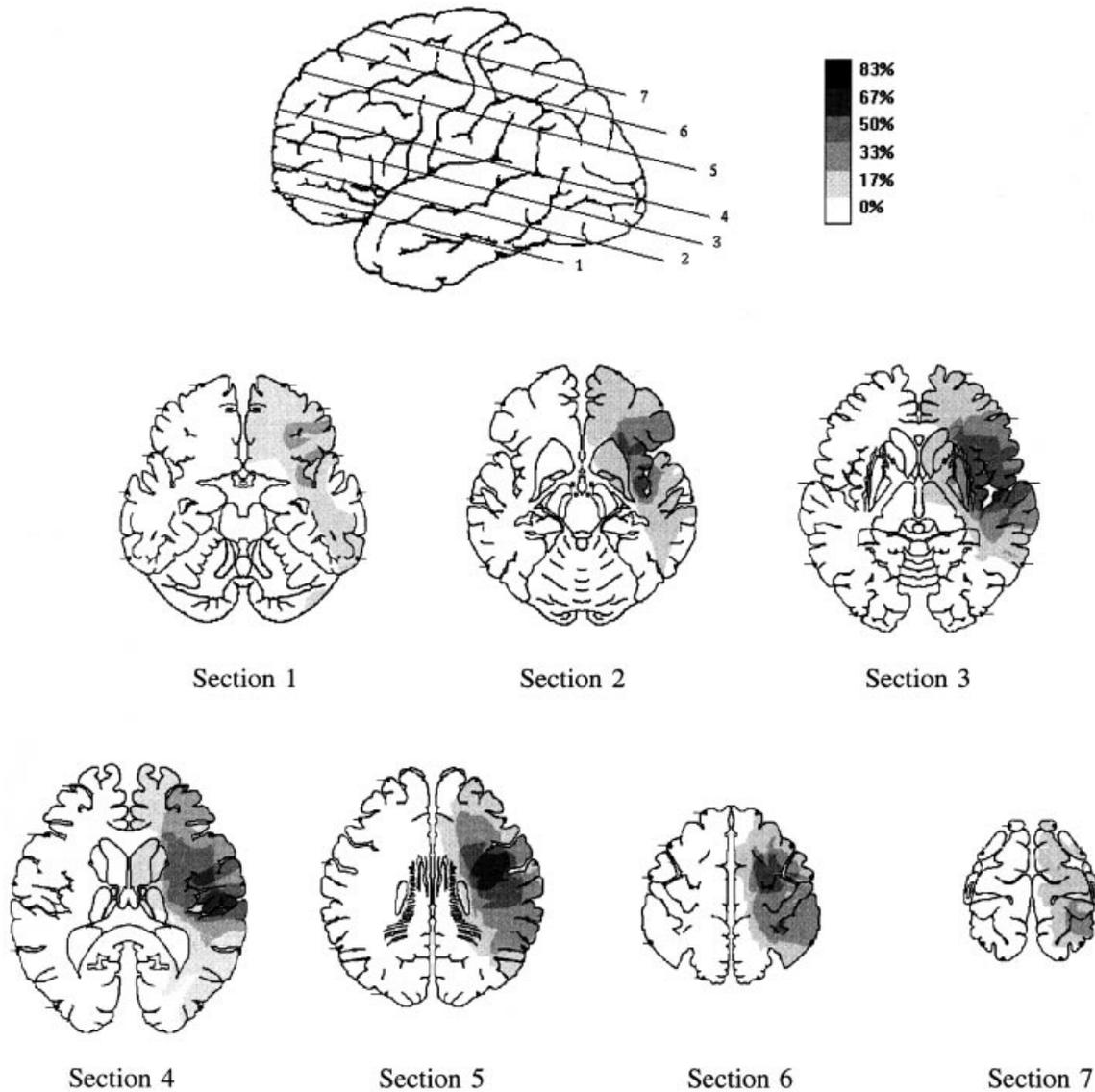


Fig. 1 Lesion information of the Broca patients ($n = 13$). Lesions determined by available CT scans from individual patients were transcribed on to templates 0° to canthomeatal line. These lesion data were then read into a reconstruction program and the digitized data were averaged to generate the group lesion densities. The seven lines through the lateral reconstruction indicate the seven axial sections. The shaded area indicates the percentage of patients with damage in the corresponding area.

frequency-coded corpus based on over 42 million tokens (Baayen *et al.*, 1993).

The test story was preceded by a short practice story to familiarize the subjects with the experimental procedure. A session lasted ~ 2 h, including electrode application and removal. All subjects were tested in a quiet room. The text was presented visually, word by word, for 400 ms in a 10×2.5 cm window on a high-resolution PC screen that was covered by a black non-reflecting shield. Each word was followed by a 400 ms blank-screen interval (i.e. the stimulus-onset asynchrony was 800 ms). Initial words of the sentences were written with an initial capital letter, all other letters were in lower case. Final words in the sentences appeared together with a period, question or exclamation mark, as appropriate. A sentence was followed by a blank-screen

interval of 2200 ms. Viewing distance was between 70 and 80 cm, and the stimuli subtended a vertical visual angle of approximately 3° . Subjects were instructed to read the text carefully for comprehension, with no additional task. They were also instructed to move as little as possible, and to keep their eyes fixated on the window in the centre of the screen. The story was presented in four blocks of ~ 5 min stimulation. To make sure that the subjects were actually reading the text, the experimenter would at various moments during the breaks between the blocks question the subjects about the story.

Continuous EEG was recorded from 29 tin electrodes attached to an electrode cap, each referred to the left mastoid. Figure 3 presents a flat-projection of the electrode configuration with site labels. Activity over the right mastoid was actively recorded on a separate channel to determine

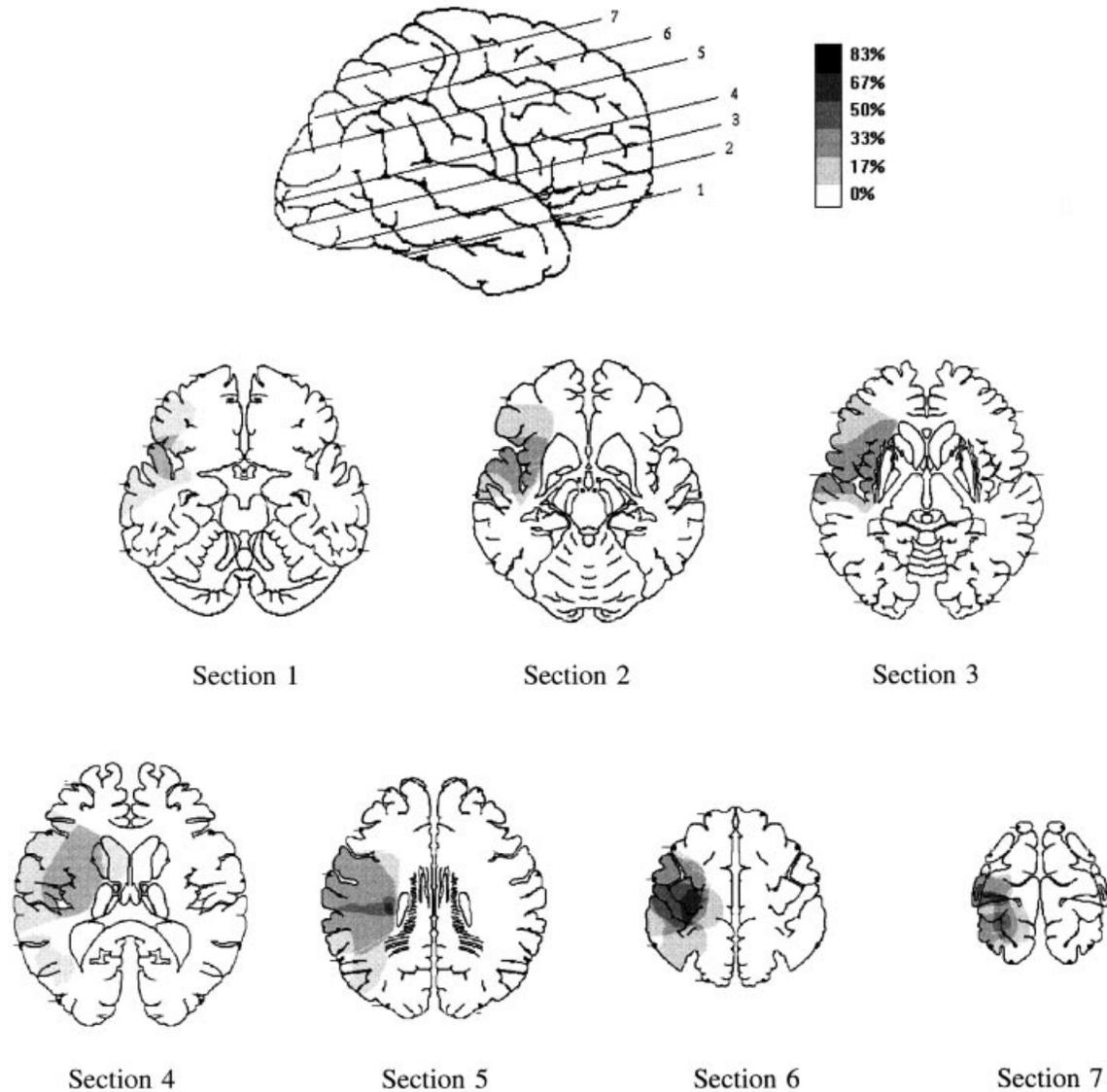


Fig. 2 Lesion information of the RH control patients ($n = 6$). For details, see Fig. 1.

whether there were any differential effects of the experimental variables on the mastoid recordings. No such effects were observed. Eighteen electrodes (Fp1, Fp2, F7, F8, Fz, F3, F4, T3, T4, C3, C4, T5, T6, P3, P4, Pz, O1, O2) were placed according to the International 10–20 system (Jasper, 1958). Eleven electrodes were placed over non-standard intermediate sites (Fz', Tf1, Tf2, Tfc1, Tfc2, Fc1, Fc2, Tpc1, Tpc2, Pc1, Pc2). Vertical and horizontal eye movements were monitored bipolarly via sub- and supra-orbital electrodes, and left and right external canthal montages, respectively. The ground electrode was placed on the standard midline central site Cz.

The EEG and EOG recordings were amplified by a Neurotop MME-3100 multi-channel bio-electric amplifier system, using a band-pass filter of 0.016–35 Hz. Impedances were kept below 5 k Ω . The EEG signal was digitized on-line by a BEST recording system with a sample frequency of 200 Hz.

Trials that were contaminated by eye movements, muscular activity, excessive electrode drift or amplifier saturation were removed, first by an automatic procedure and subsequently on visual inspection by a manual procedure prior to averaging. Excessive EEG and EOG artefacts led to the exclusion of the results of two Broca patients and three RH patients from the EEG analyses. Furthermore, for three Broca and one RH patient only a limited number of overlapping channels ($n = 18$, apart from the mastoid channel) could be adequately analysed for all four. Therefore, in all three subject groups these 18 electrodes were used for subsequent statistical analysis, but more sites ($n = 24$) are displayed in the different figures. As a result, for the 15 normal control subjects, 26% of the open-class trials and 24% of the closed-class trials (in total 24% of the trials) were removed prior to averaging. For the 14 Broca patients, in total, 34% of the trials were removed and these were equally divided over the open- and closed-

class items. For the five RH patients, 42% of the open-class items and 34% of the closed-class items (in total 38%) were removed.

In the analyses reported below, different subsets of electrodes were taken together to investigate the topographical distribution of the ERP effects. For purposes of brevity, we use the following labels: anterior left (AL; F7, F3, Tfc1, Fc1), anterior right (AR; F8, F4, Tfc2, Fc2), anterior (AL + AR), posterior left (PL; TpC1, Pc1, T5, P3), posterior right (PR; TpC2, Pc2, T6, P4), posterior (PL + PR), left hemisphere (F7, F3, Tfc1, Fc1, TpC1, Pc1, T5, P3, O1) and right hemisphere (F8, F4, Tfc2, Fc2, TpC2, Pc2, T6, P4, O2).

On the basis of visual inspection of the waveforms of the different subject groups, two latency windows were selected for statistical analysis: 210–375 ms and 400–700 ms. Analyses were performed on the mean amplitude values determined via a computerized procedure in the specified time-windows. First, for each subject the waveform elicited by each word was normalized, point by point, with respect to the averaged activity in the 100 ms preceding that word. Then, in selected epochs, the mean amplitude was computed in the waveform, for each VC, for each subject. The resulting values were entered into repeated measures analyses of variance with VC (open- versus closed-class) and electrode site as within-subjects factors. The Huyn-Feldt correction was applied when evaluating effects with >1 d.f. in the numerator. The adjusted degrees of freedom and P -values are reported. The Tukey-HSD multiple range test ($\alpha = 0.05$) was used for *post hoc* analysis (cf. Maxwell and Delaney, 1990). Effects involving the factor electrode site are only reported for significant interactions with VC. For these interactions, analyses of variance were computed after performing a Z -score normalization procedure to equalize the overall mean amplitudes across experimental conditions. This procedure is described by Rosler *et al.* (1993) and is equivalent to the normalization procedure suggested by McCarthy and Wood (1985).

Finally, to test directly for differences between the results for the control groups and the Broca patients, group analyses were performed in the specified time-windows over restricted electrode sites. Repeated measures analyses of variance were performed with VC as a within-subjects factor and group (controls, Broca patients, RH patients) as a between-subjects factor.

Given the role that lexical-statistical factors play in any performance differences obtained between open- and closed-class words (closed-class words are in general shorter and more frequent) we also tested whether the observed differences in the waveforms could be attributed to lexical frequency and length rather than to VC. The contribution of lexical frequency and length in number of letters to the ERP profiles for open- and closed-class words was analysed for all three subject groups. We approached this issue by performing analyses collapsing over all word types (i.e. ignoring VC). In the analyses on the effect of lexical frequency, waveforms averaged as a function of different

frequency ranges, keeping the word length constant at 4, 5 and 6 letters, were compared. For 4 letters, log frequency bins 0.2–2.0, 2.2–2.8 and 3.0–3.8 were contrasted. For 5 and 6 letters, frequency bins 0.2–2.0 and 2.2–2.8 were contrasted. In the analyses on word length, we compared waveforms that were averaged as a function of different word lengths within particular frequency bins. Words with lengths of 4–8 letters were compared within frequency bin 0.2–2.0, lengths of 4–6 were compared within bin 2.2–2.8, and lengths of 3 and 4 letters were compared within bin 3.0–3.8. The rationale behind this approach is that if, for example, the frequency of occurrence was the only determinant of the differences in ERP profiles between open- and closed-class words, the respective profiles should show up as a function of frequency. The selection of particular lengths or frequency bins was dictated by having a sufficient number of words available over which to compute an averaged potential.

Results

Syntactic off-line test

Figure 4 shows the comprehension scores (in percentage correct) on the off-line test for syntactic comprehension of the Broca patients, the normal controls and the RH patients. For the five types of syntactic complexity see legend to Fig. 4. Analyses with group as factor showed that syntactic complexity has a differential effect on the comprehension scores of the different subject groups [sentence type: $F(3.45, 124.22) = 30.25$, $MSe = 119.82$, $P < 0.0001$; group: $F(2, 36) = 30.98$, $MSe = 940.02$, $P < 0.0001$; sentence type \times group: $F(6.90, 124.22) = 8.03$, $MSe = 119.82$, $P < 0.0001$]. *Post hoc* analyses ($P = 0.05$) revealed that the Broca patients performed significantly worse than the normal controls on all sentence types and significantly worse than the RH patients on sentence types III–V. The two control groups did not differ significantly from each other on any sentence type. In contrast, the size of the difference in comprehension scores between the Broca patients and the two control groups increased with increasing syntactic complexity. For the most complex sentence type their performance was close to chance level.

This pattern of results substantiates the syntactic comprehension problems of the Broca patients in this study and on the basis of these results they can be classified as agrammatic comprehenders.

ERP experiment

The ERP data for the 15 normal control subjects, the 14 Broca patients and the five RH patients are presented in separate sections.

Normal control subjects

Figure 5 shows the grand average waveforms for the open- and closed-class category. Both VCs elicit the early visual

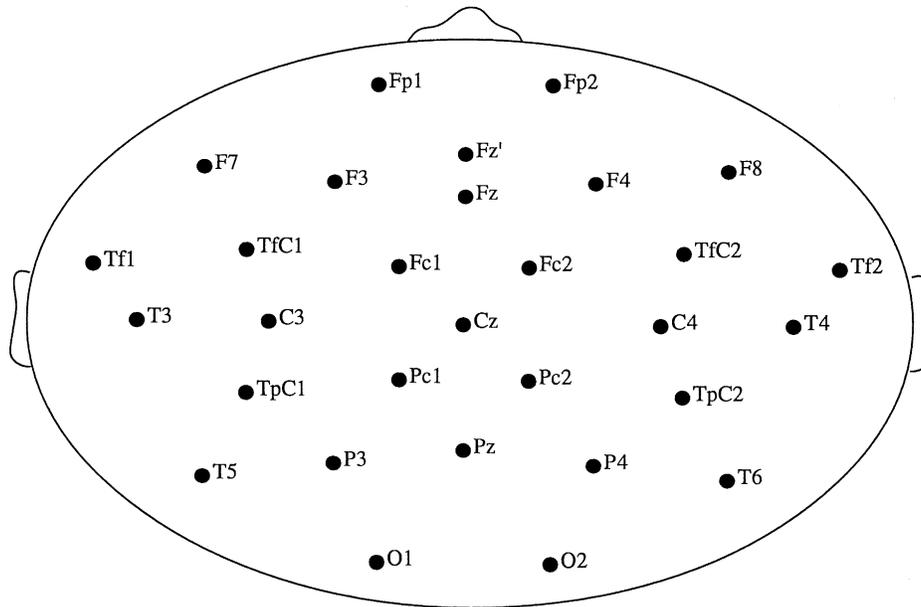


Fig. 3 Flat projection of the electrode configuration.

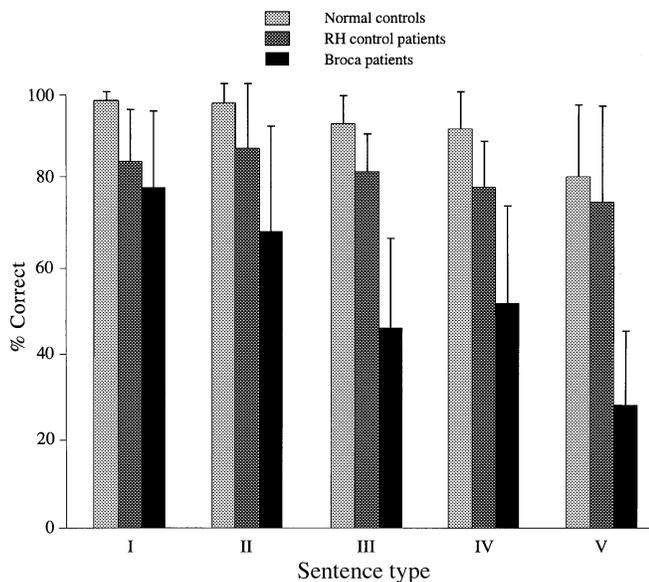


Fig. 4 Scores of the group of normal controls ($n = 15$), the RH control patients ($n = 8$) and the group of Broca patients ($n = 16$) for the off-line test for syntactic comprehension; for the five types of syntactic complexity: I = active, semantically irreversible; II = active, semantically reversible; III = simple passive; IV = sentences with active relative clause; V = sentences with passive relative clause.

components P1 and N1, which are a standard response to physical visual stimulation, and a P2 whose amplitude is reduced in the closed-class words [overall analysis in the 150–200 ms epoch: $F(1,14) = 7.77$, $MSe = 3.70$, $P = 0.015$]. Following these early visual components, the ERP profiles elicited by the open- and closed-class vocabulary show roughly an early and a late time-window within which differences between the two VCs occur.

Early VC differences. In the early time epoch, between approximately 210 and 375 ms, a clear negative shift is elicited by the closed-class words. It peaks at ~263 ms, has a predominant anterior distribution and is somewhat larger over the left than the right hemisphere. The open-class words also elicit a negative shift, but the amplitude is much smaller. This component shows a biphasic morphology with peaks at 237 and 317 ms, and it has essentially the same anterior distribution as the early negative response to the closed-class words, although it is slightly more restricted to anterior sites.

The difference in mean amplitude between the two word classes is significant [$F(1,14) = 16.55$, $MSe = 4.13$, $P = 0.001$]. Analyses on the topography of the VC effect demonstrated that the effect is largest over left anterior electrode sites: the effect is larger over anterior than posterior electrode sites [$A/P \times VC: F(1,14) = 5.17$, $MSe = 0.39$, $P = 0.039$] and somewhat larger over left than right anterior electrode sites [$AL/AR \times VC: F(1,14) = 5.28$, $MSe = 0.24$, $P = 0.038$].

Late VC differences. In the late time epoch, from ~400 ms until the presentation of the next stimulus, the closed-class items elicit a broad negative shift with a left-hemisphere preponderance and no obvious peak, whereas the open-class words elicit a positive shift with no obvious peak over predominantly frontal electrode sites. For both VCs the waveforms at ~550 ms show the off-potential elicited by the disappearance of the stimulus.

Analyses of the mean amplitude between 400 and 700 ms confirmed the presence of a VC effect [$F(1,14) = 23.19$, $MSe = 10.64$, $P < 0.0001$], with the closed-class words eliciting a more negative waveform than the open-class words. This effect was largest over the left anterior electrode

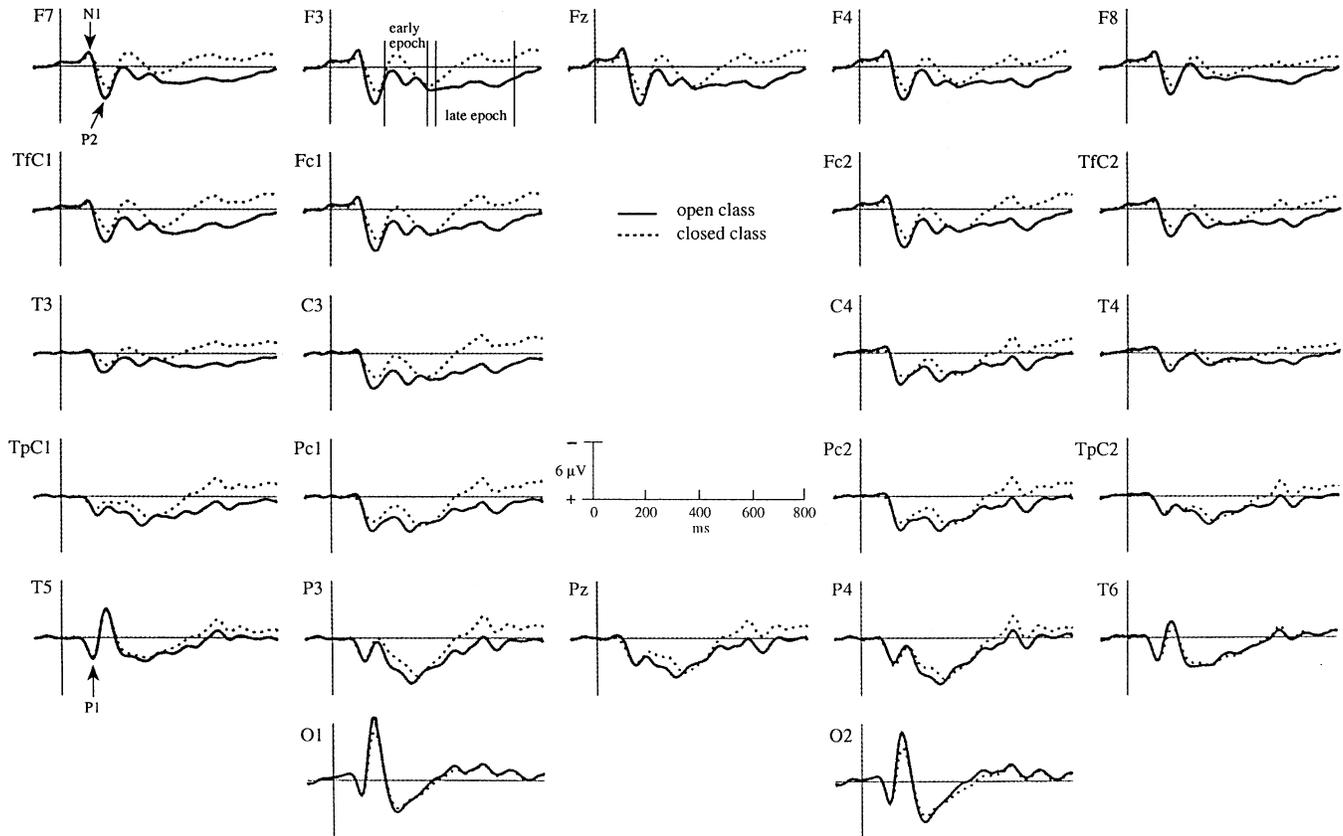


Fig. 5 Grand average waveforms elicited by the open- and closed-class categories for the group of normal control subjects ($n = 15$). Negativity is plotted upwards. The total epoch is 900 ms long, starting 100 ms before a word was presented. The stimulus appeared at 0 ms and disappeared at 400 ms.

sites. In separate analyses, significant interactions between VC and hemisphere [$F(1,14) = 21.37$, $MSe = 0.93$, $P < 0.0001$] and between VC and anterior/posterior regions [$F(1,14) = 8.05$, $MSe = 1.88$, $P = 0.013$] reflect the fact that the size of the VC effect is larger over left than right and over anterior than posterior electrode sites. Furthermore, an analysis of anterior left/anterior right confirmed that the size of the difference was larger over anterior left sites [$VC \times AL/AR$: $F(1,14) = 25.09$, $MSe = 0.43$, $P < 0.0001$].

Non-aphasic RH control patients

Figure 6 shows the grand average waveforms for the open- and closed-class category. Notwithstanding the lower signal-to-noise ratio of the waveforms due to the limited number of subjects, the RH patients show ERP profiles elicited by open- and closed-class words similar to those of the normal control subjects. Following the early visual P1–N1 complex and the P2 component which has a reduced amplitude in the closed-class items [overall analysis: $F(1,4) = 7.07$, $MSe = 6.58$, $P = 0.056$], similar VC effects were obtained in both the early and the late epoch.

In the early epoch, closed-class words elicited a component with a more negative shift than open-class words [overall analysis: $F(1,4) = 12.63$, $MSe = 3.42$, $P = 0.024$]. In the

RH patients this effect is largely restricted to the anterior left electrode sites [VC: $F(1,4) = 7.01$, $MSe = 1.19$, $P = 0.057$; VC \times AL/AR: $F(1,4) = 6.73$, $MSe = 0.24$, $P = 0.060$], whereas in the normal controls it is present over all anterior sites.

In the late epoch a clear negative shift was elicited by the closed-class words [overall analysis: $F(1,4) = 142.63$, $MSe = 0.63$, $P < 0.001$]. The VC effect was largest over the left anterior side of the scalp [VC \times AL/AR: $F(1,4) = 8.86$, $MSe = 0.88$, $P = 0.041$; VC \times PL/PR: $F < 1$].

Broca patients with agrammatic comprehension

Figure 7 shows the grand average waveforms for the open- and closed-class category. As a consequence of the results for the control subjects, analyses in the early and late epoch were restricted to anterior sites. As with the control subjects, both VCs elicit the P1–N1 complex and a P2 whose amplitude is reduced in the closed-class words [analyses over AL/AR: VC: $F(1,13) = 12.99$, $MSe = 2.34$, $P = 0.003$]. Following these early visual components, the ERP profiles elicited by the open- and closed-class vocabulary show both divergencies and commonalities with the waveforms elicited by the two groups of control subjects.

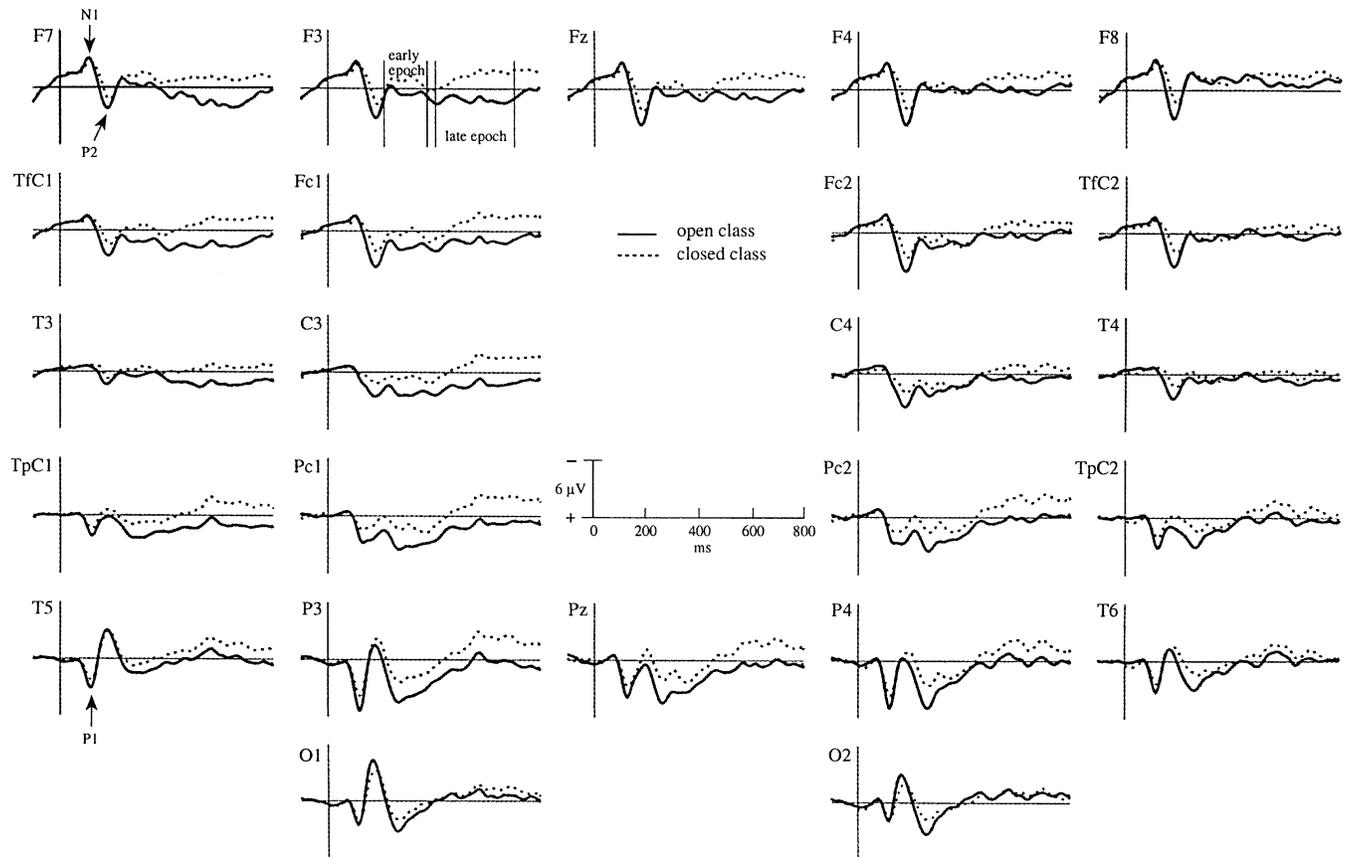


Fig. 6 Grand average waveforms elicited by the open- and closed-class categories for the group of non-aphasic RH patients ($n = 8$). Negativity is plotted upwards. The total epoch is 900 ms long, starting 100 ms before a word was presented. The stimulus appeared at 0 ms and disappeared at 400 ms.

Early anterior VC differences. In the early time-window between about 210 and 375 ms, both open- and closed-class items elicit a negative shift over anterior sites which is approximately equal over the left and right side of the head. However, in contrast to the control subjects there is no VC effect [$F(1,13) = 0.01$, $MSe = 2.19$, $P = 0.934$]. The component is of approximately equal amplitude for the two VCs.

Late anterior VC differences. In the late time-window between approximately 400 and 700 ms, a negative shift is elicited by the closed-class items over anterior sites which is similar to that observed with control subjects. However, no positive shift is elicited by the open-class items. The visible differences between the VCs reached significance only over one right anterior electrode site, F4 [$F(1,13) = 5.53$, $MSe = 1.28$, $P = 0.035$] and showed a trend towards significance over electrode site F8 [$F(1,13) = 3.98$, $MSe = 1.75$, $P = 0.068$].

Late posterior VC differences. In a late time-window from about 300–500 ms over posterior sites additional VC differences are visible. In accordance with the results obtained for control subjects, a positive waveform is elicited by the closed-class items. However, unlike the control subjects, a

clear negative shift with a peak at approximately 412 ms is elicited by the open-class items. This shift is more pronounced over the left side of the head. Analyses over posterior left/right electrodes confirmed the presence of a VC effect [$F(1,13) = 5.05$, $MSe = 5.68$, $P = 0.043$], with open-class words eliciting a waveform that consistently showed a more negative shift than that obtained from the closed-class words. The waveforms elicited from the left posterior sites tended more towards the negative than those from homologous right sites and this effect was more pronounced for the open- than closed-class items [PL/PR: $F(1,13) = 7.79$, $MSe = 9.53$, $P = 0.015$; VC \times PL/PR: $F(1,13) = 6.07$, $MSe = 0.52$, $P = 0.028$].

Group analyses on the early and late anterior VC differences

Given that for the control subjects the VC effects were largest over left anterior sites, analyses comparing all three subject groups in the early and late anterior time-window were restricted to the anterior left electrode sites. The analyses confirmed a main effect of VC [early: $F(1,31) = 47.84$, $MSe = 0.61$, $P < 0.0001$; late: $F(1,31) = 109.56$, $MSe = 1.15$, $P < 0.0001$] and, more importantly, a significant

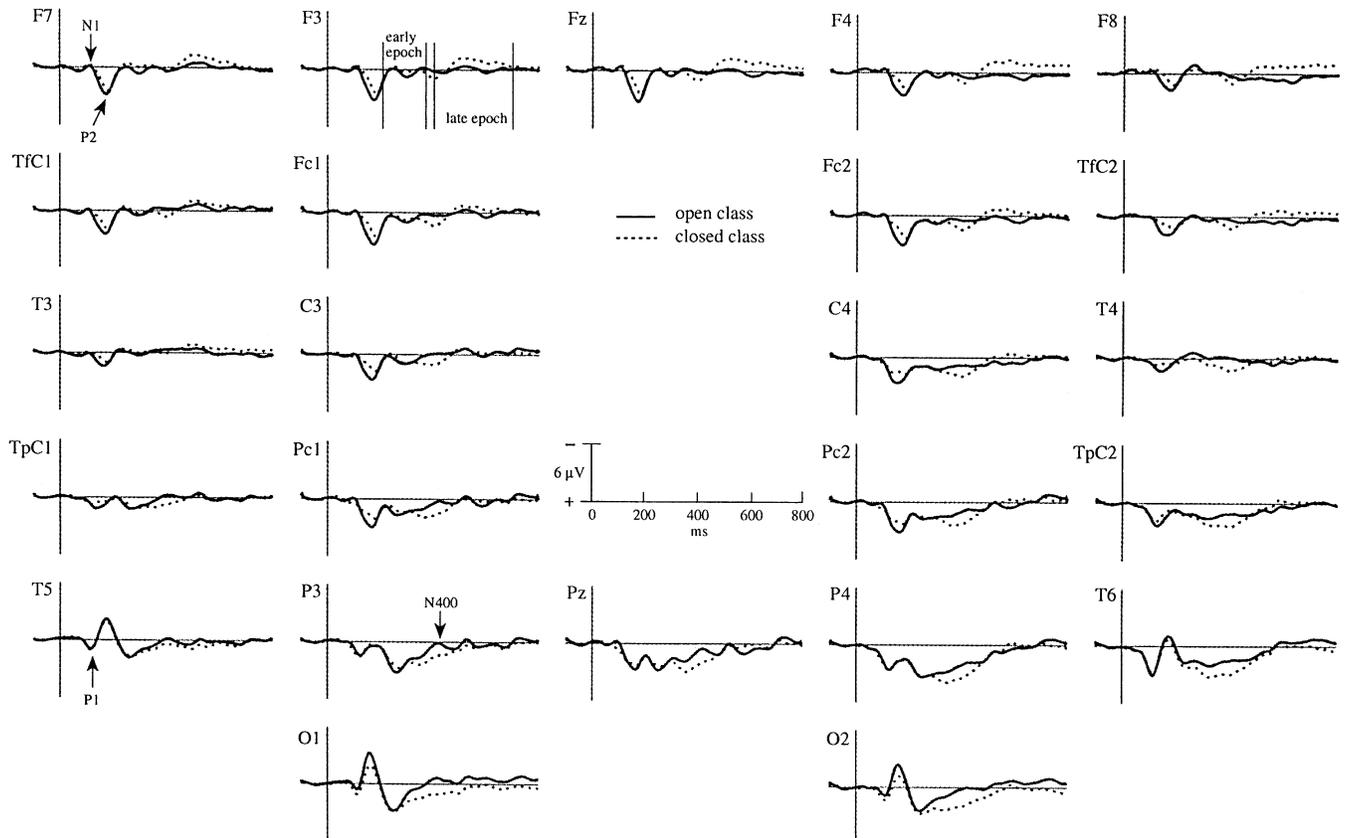


Fig. 7 Grand average waveforms elicited by the open- and closed-class categories for the group of Broca patients ($n = 14$). Negativity is plotted upwards. The total epoch is 900 ms long, starting 100 ms before a word was presented. The stimulus appeared at 0 ms and disappeared at 400 ms.

interaction between VC and group [early: $F(2,31) = 20.92$, $MSe = 0.61$, $P < 0.0001$; late: $F(2,31) = 35.12$, $MSe = 1.15$, $P < 0.0001$]. Planned comparisons between the subject groups demonstrated that in both time-windows the group of Broca patients differed significantly from both the group of normal control subjects [group \times VC: early: $F(1,27) = 37.99$, $MSe = 0.61$, $P < 0.0001$; late: $F(1,27) = 55.92$, $MSe = 1.24$, $P < 0.0001$] and the group of RH patients [group \times VC: early: $F(1,17) = 51.12$, $MSe = 0.20$, $P < 0.0001$; late: $F(1,27) = 192.30$, $MSe = 0.20$, $P < 0.0001$]. The two control groups did not differ significantly from each other in either time-window (group \times VC: $F < 1$ in both time-windows).

Effects of lexical frequency and length on the early VC differences

The frequency and length of word analyses in the early epoch for the three subject groups were restricted to anterior electrode sites. For the group of normal control subjects no effects of length of word were found. With respect to the effects of frequency on the mean amplitude of ERPs, only one analysis, on all words of length of 4 letters in three separate frequency bins, yielded a significant effect [$F(1.3,18.26) = 10.94$, $MSe = 12.13$, $P = 0.002$]. Here, the

highest frequency words were associated with the smallest mean amplitude. The effect is most likely due to a confounding with VC as the two lower frequency bins are composed almost entirely of open-class words, whereas the highest frequency bin has an open- to closed-class ratio of 1 : 2.

With respect to the group of Broca patients and the group of RH patients, neither lexical frequency, nor word length was found to affect the early waveform. This absence of any length and frequency effects reinforces earlier results of a similar study with young healthy subjects (Brown *et al.*, 1999).

Summary

Table 3 shows a summary of the VC effects in the ERP profiles of the normal control subjects, the non-aphasic RH patients and the Broca patients. Both groups of control subjects showed clear differences in an early (210–375 ms) and a late (400–700 ms) latency window of the electrophysiological profiles elicited by open- and closed-class words. These differences were maximal over left anterior electrode sites. In contrast, the group of Broca patients failed to show a VC effect in the early time epoch, exhibited an effect similar to that of the control subjects over only one

Table 3 Summary of the VC effects in the ERP profiles of normal control subjects, non-aphasic RH control patients and Broca patients

	Normal control subjects	Non-aphasic RH patients	Broca patients with agrammatic comprehension
Effect in early epoch 210–375 ms Distribution	Present, with closed class more negative than open class Wide, largest over left anterior electrodes	Present, with closed class more negative than open class Left anterior electrodes	Absent
Effect late epoch 400–700 ms Distribution	Present, with closed class more negative than open class Wide, largest over left anterior electrodes	Present, with closed class more negative than open class Largest over left anterior electrodes	Limited, with closed class more negative than open class Right anterior electrode F4
Effect in late epoch 300–500 ms Distribution	Absent	Absent	Present, with open class more negative than closed class (N400) Posterior electrodes

electrode in the late anterior time-window and showed a clear VC effect in an additional, partially overlapping time-window (300–500 ms), that was largest over posterior electrode sites.

Discussion

In this study we focused on whether Broca patients' agrammatic comprehension might be related to a specific impairment in the processing of closed-class words. An off-line test for syntactic comprehension was used to assess the influence of syntactic complexity on sentence comprehension. The results confirm that the patients we tested showed a syntactic comprehension deficit. In an ERP experiment electrophysiological evidence on the processing of open- and closed-class words was collected and the results show a clearly deviant pattern for the processing of open- and closed-class words in the Broca patients when compared with the control subjects.

P2 effects

In addition to the early and late negative VC effects, we also found differences in the P2 amplitude (150–200 ms) between open- and closed-class words. These differences have also been observed in other studies (e.g. Osterhout *et al.*, 1997; King and Kutas, 1998; Brown *et al.*, 1999). Although the exact characterization of these effects awaits further research, they are most likely due to aspects of the stimuli that are not language-related. These include the overall length differences between the two word types and possibly attentional differences (cf. Mangun and Hillyard, 1995). It is, therefore, unlikely that the P2 effects are related to linguistically relevant aspects of open- and closed-class words and of agrammatic aphasia.

The early VC effect

The presence, the latency (210–375 ms) and the predominantly left anterior topography of the early VC

differences in the ERP profiles of the group of non-damaged control subjects is consistent with earlier ERP studies that explicitly compared the open- and closed-class categories, albeit in young normal subjects, (Neville *et al.*, 1992; Nobre and McCarthy, 1994; Pulvermuller *et al.*, 1995; Osterhout *et al.*, 1997; King and Kutas, 1998; Brown *et al.*, 1999). The early, predominantly anterior negative response in the waveform elicited by the closed-class items between 210 and 375 ms after stimulus onset, with a peak at 263 ms, agrees well with previous ERP reports on the open- and closed-class distinction (Neville *et al.*, 1992; Nobre and McCarthy, 1994; Pulvermuller *et al.*, 1995; King and Kutas, 1998; Brown *et al.*, 1999). The same holds for the anterior component elicited within the same time-window by the open-class items (Pulvermuller *et al.*, 1995; Osterhout *et al.*, 1997; King and Kutas, 1998; Brown *et al.*, 1999). However, the two different peaks for open-class words (at 237 and 317 ms) have not been reported before. This biphasic modulation might be an age-related effect, since all other ERP reports so far have included only young (adult) subjects. However, at this moment it is impossible to determine whether the biphasic modulation reflects the peaks of two separate components with a similar topography, or one component modulated by an additional process. Clearly, further research is needed to determine the precise (functional) nature of this modulation.

The second group of control subjects, the RH patients, showed essentially the same consistent pattern for the early VC effect, except for its absence over right anterior electrode sites. However, where the effect has been consistently found, the presence of the effect over left anterior electrode sites suggests that the processing of open- and closed-class words was normal in these patients.

Given the similar latency and topographical distribution of the early negative shift elicited by the open- and closed-class items in the two groups of control subjects, we suggest that this is an electrophysiological manifestation of the same underlying process for the two VCs (see also, Van Petten and Kutas, 1991; Osterhout *et al.*, 1997; King and Kutas,

1998; Brown *et al.*, 1999). The component itself has been classified as an early marker of lexical processing (Neville *et al.*, 1992; King and Kutas, 1998; Brown *et al.*, 1999) but which aspect of lexical processing it reflects is still a matter of debate. Consequently, so are its differences as a function of VC. In our data, as in the data of Neville *et al.* (1992) and of Brown *et al.* (1999), neither the existence nor the morphology of the VC effect was affected by lexical-statistical factors such as word frequency or length. This makes it less likely that the early differences are related to the initial stage of lexical processing, i.e. lexical access. On the basis of our results, we interpret the early VC effect as the first electrophysiological manifestation of the availability of word-category information from the mental lexicon.

In contrast to either group of control subjects, the group of Broca patients did not show any signs of an early VC effect over either the left or the right anterior electrode sites. The underlying negative component, however, does seem to be present. This suggests that, at least during the early time-window, the information that distinguishes between the open- and closed-class category has not yet or has only partially become available to these patients. In other words, lexical-categorical information does not seem to be available to Broca patients with agrammatic comprehension to a similar extent or at the same moment in time in on-line word processing as it is to non-aphasic subjects. Although we cannot decide on the basis of an absence of the early effect whether the abnormal processing reflected in this early time-epoch is specifically tied to the open- or closed-class vocabulary, it is obvious that both the full availability of lexical-categorical information and the availability of this information at the right moment in time is an important prerequisite for successful on-line sentence processing. A delayed or incomplete availability of this information will have serious effects on sentence comprehension.

The late VC effect over posterior sites

Interestingly, only the group of Broca patients showed a VC effect in a partially overlapping time-window (300–500 ms) over posterior sites. On the basis of its morphology, its peak latency at 412 ms and its posterior topography, we classify the negative shift elicited by the open-class words as the N400 component (Kutas and Hillyard, 1983). The N400 to open-class words has been reported in previous ERP studies on the reading of open- and closed-class words (Kutas and Hillyard, 1983; Neville *et al.*, 1992, 1993; Nobre and McCarthy, 1994; Pulvermüller *et al.*, 1995; Osterhout *et al.*, 1997; Brown *et al.*, 1999). The N400 primarily reflects real-time post-lexical semantic processing (cf. Holcomb, 1993; Kutas and Van Petten, 1994). In context, the modulation of the N400 amplitude seems to reflect the ease with which a word can be integrated into the preceding context, with larger amplitudes for words that are difficult to integrate (Brown and Hagoort, 1993, 1999). Although each open-class word elicits an N400, its amplitude is strongly reduced when words

are easy to integrate into sentence or discourse context. Presumably, this explains why we see no differential N400 for open- and closed-class words between the two control groups. The fact that the Broca patients do show an N400 effect indicates that they experience difficulties with integrating the lexical-semantic information of the open-class words into the message-level representation of the preceding sentential and discourse context in which they occur, as has been suggested previously (e.g. Hagoort, 1993; Tyler and Ostrin, 1994; Tyler *et al.*, 1995; Hagoort *et al.*, 1996; Swaab *et al.*, 1997). This makes sense if, as reinforced by the absence of an early VC effect, the word-category information necessary for constructing a phrasal configuration of the sentence does not become fully available at the right moment in time.

The late VC effect over anterior sites

Finally, the presence, the latency and the topographical distribution of the late VC effect (400–700 ms) over predominantly anterior sites in the two control groups is consistent with previous ERP reports (Kutas and Hillyard, 1983; Van Petten and Kutas, 1991; Neville *et al.*, 1992; Osterhout *et al.*, 1997; King and Kutas, 1998; Brown *et al.*, 1999). The slow ascending negative shift which is elicited solely by the closed-class items has generally been classified as a variant of the contingent negative variation. In contrast to the control subjects, the Broca patients only show a late VC effect over two anterior electrode sites.

Van Petten and Kutas (1991) have speculated that the late effect might reflect anticipatory processes related to the fact that closed-class items often serve as a syntactic signal to the reader that a new head of a phrase is imminent. The absence of the early effect and an indication of a late, albeit reduced, effect in the Broca patients, would mean that some of the lexical-syntactic information associated with closed-class items must have become available at a later moment in time than in the control subjects. This would favour the view of a delay in the availability of word-class information as a factor underlying agrammatic comprehension, rather than a complete loss of this information. This position is akin to the proposals of Friederici and colleagues (e.g. Friederici, 1985; Friederici and Kilborn, 1989).

Brown and colleagues (Brown *et al.*, 1999) proposed a less parsing-specific explanation for the late effect, which is still based on the syntactic nature of the closed-class words. They suggested that the predictive processes involved serve a more general expectation, simply that following a closed-class word, the next word is likely to be a meaningful word. The distinction between meaning-devoid and meaning-bearing words maps quite naturally on to the closed- and open-class distinction. For the Broca patients this would mean that the late effect could be present solely on the basis of the availability of lexical-semantic information. The relative lack of lexical-semantic information in the case of

closed-class items could, in itself, be enough to generate an expectancy for a following meaningful word.

Implications for accounts of agrammatic comprehension

What does the real-time electrophysiological evidence on the processing of open- and closed-class words presented in this study imply for accounts of agrammatic comprehension? The absence of an early VC effect is the major finding, with two implications. First, Broca patients with agrammatic comprehension have specific problems with the on-line processing of VC. Secondly, these problems already occur at a relatively early stage, which can be associated with the lexical processing of words. Thus far the results could be interpreted as supporting the claim in the literature that a direct relationship exists between problems with the lexical processing of closed-class words and agrammatic comprehension. However, we found no evidence to indicate that the lexical processing problems are restricted to closed-class words only. The early negative response in the waveforms in the Broca patients is elicited by open- and closed-class words alike, and does not differ as a function of VC.

One of the problems, then, that Broca patients are faced with is that the lexical-categorical information associated with open- and closed-class words does not seem to be available to them to a similar extent or at the same moment in time during on-line word processing as it is to non-aphasic subjects. This could easily result in asyntactic comprehension. For on-line sentence processing to be successful, it is essential that the syntactic information of a word is available and at the right moment in time. Crucial within this information is word category (noun, verb, article, etc.).

The presence of an N400 effect in the Broca patients suggests that the lexical integration problems associated with agrammatic comprehension might be related to problems with getting word-class information available at the right moment in time during on-line sentence processing. The presence of the N400 component evident in response to open-class words implies that the lexical-semantic information of these words has become available. However, as indicated by the N400 effect, the Broca patients do seem to have problems with integrating individual word meanings into the message-level representation of the preceding sentential and discourse context. This makes sense if the word-class information necessary for building up a higher-order structural representation has not become available in time.

Conclusion

In the present study we addressed the issue of whether Broca patients' agrammatic comprehension might be related to a specific impairment in the processing of closed-class words, by investigating electrophysiological manifestations of on-

line VC processing. No evidence was found for an impairment restricted to the processing of closed-class words only. Rather, the results are compatible with the view that an important factor in Broca's agrammatic comprehension is a delayed and/or incomplete availability of word-class information.

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