ERP Correlates of Word Production before and after Stroke in an Aphasic Patient

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Abstract

■ Changes in brain activity characterizing impaired speech production after brain damage have usually been investigated by comparing aphasic speakers with healthy subjects because prestroke data are normally not available. However, when interpreting the results of studies of stroke patients versus healthy controls, there is an inherent difficulty in disentangling the contribution of neuropathology from other sources of between-subject variability. In the present work, we had an unusual opportunity to study an aphasic patient with severe anomia who had incidentally performed a picture naming task in an ERP study as a control subject one year before suffering a left hemisphere stroke. The fortuitous recording of this patient's brain activity before his stroke allows direct comparison of his pre- and poststroke brain activity in the same language production task. The subject did not differ from other healthy subjects before his stroke, but presented major electrophysiological differences after stroke, both in comparison to himself before stroke and to the control group. ERP changes consistently appeared after stroke in a specific time window starting about 250 msec after picture onset, characterized by a single divergent but stable topographic configuration of the scalp electric field associated with a cortical generator abnormally limited to left temporal posterior perilesional areas. The patient's pattern of anomia revealed a severe lexical–phonological impairment and his ERP responses diverged from those of healthy controls in the time window that has previously been associated with lexical–phonological processes during picture naming. Given that his prestroke ERPs were indistinguishable from those of healthy controls, it seems highly likely that the change in his poststroke ERPs is due to changes in language production processes as a consequence of stroke. The patient's neurolinguistic deficits, combined with the ERPs results, provide unique evidence for the role of left temporal cortex in lexical–phonological processing from about 250 to 450 msec during word production. ■

INTRODUCTION

Brain damage can drastically disrupt the fluent and automatic process of language production: Word retrieval becomes effortful and words are substituted or distorted (paraphasias). Investigation on changes in brain activity during language processing after stroke usually compares aphasic patients to healthy controls as prestroke data are normally not available. In electrocortical studies, aphasic patients and healthy control subjects have been recorded with magnetoencephalography or EEG during a variety of language comprehension and language production tasks: word or sentence comprehension (Wassenaar & Hagoort, 2005; Breier et al., 2004; Friederici, von Cramon, & Kotz, 1999; Hagoort, Brown, & Swaab, 1996), lexical decision tasks (Pulvermüller, Mohr, & Lutzenberger, 2004), semantic or syntactic judgment (Hensel, Rockstroh, Berg, & Schonle, 2004; Angrilli, Elbet, Cusumano, Stegagno, & Rockstroh, 2003; Dobel et al., 2001), or picture naming tasks (Laganaro, Morand, & Schnider, 2009; Cornelissen et al., 2003). Some studies have tracked changes in rhythmic activities in aphasic patients after brain lesion or during recovery (especially changes in slow waves: Hensel et al., 2004; Meinzer et al., 2004; Szelies, Mielke, Kessler, & Heiss, 2002), whereas other, more cognitive-oriented investigations analyzed ERP differences between aphasic patients and a control group in the attempt to investigate the temporal course of changes accompanying reorganization of language processes after stroke. These studies aimed to tease apart changes due to specific subprocesses underlying language production or perception. In the language comprehension domain, electrophysiological studies have compared aphasic patients to healthy controls using specific tasks, tapping into semantic or syntactic treatment during word or sentence comprehension (Wassenaar & Hagoort, 2005; Friederici et al., 1999; Hagoort et al., 1996). During single word receptive language tasks, the modification of early ERP components in the aphasic patients, starting about 160–200 msec after stimulus presentation, has been reported with auditory (Breier et al., 2004) or visually presented single words (Pulvermüller et al., 2004). Differences in later time periods, starting around 300 msec after stimulus presentation, have been reported in studies analyzing the electrocortical reorganization after brain damage with

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speech production tasks. For instance, Angrilli et al. (2003) and Dobel et al. (2001) analyzed mean amplitudes of electrodes from four regions of the scalp with tasks demanding semantic or phonological encoding processes. They reported different activation patterns between healthy controls and aphasic patients starting around 300 msec after stimulus presentation. In a recent report comparing two subgroups of aphasic patients to healthy controls with a picture naming task, the time windows of diverging ERPs varied, depending on the underlying anomic impairment (Laganaro et al., 2009). Early ERP divergences (100–250 msec after picture onset) appeared in aphasic patients with lexical–semantic anomia, whereas later ERP divergences (300–450 msec) were observed in aphasic patients with lexical–phonological impairment.

A major problem for the interpretation of results emanating from the comparison of stroke patients to healthy controls concerns intersubject variability. Between-subject variability of EEG patterns has been observed not only among brain-damaged subjects but also among healthy control subjects (Campanella et al., 1999). By contrast, intraindividual EEG patterns have been reported to be quite stable, even over several months (Vuga, Fox, Cohn, Kovacs, & George, 2006; Condacs & Szabó, 1999).

Between-subjects electrophysiological variability might preclude teasing out differences due to the pathological conditions from those due to other sources of between-subjects variability. Showing that a single subject does not differ from other subjects *before* the occurrence of brain damage, but presents electrophysiological changes *after* brain damage, provides strong evidence that the divergent pattern in brain-damaged subjects is due to changes in cognitive processing caused by the stroke. This conclusion is further strengthened if the neural changes can be related to task-specific changes in behavior or cognition.

In the present study, we had the opportunity to compare the electrophysiological activation pattern of the same subject before and after a left hemisphere stroke. The patient presented here was recorded during a language production (picture naming) task as a control subject, one year before suffering a left hemorrhagic stroke which caused severe aphasia. If differences observed after stroke appear both in the within-subject comparison of his activation pattern before and after stroke and in the comparison to a control group of healthy subjects, the observed changes in ERP patterns could reliably be attributed to stroke rather than to interindividual variations.

Our word production task was known to elicit two ERP patterns associated with distinct processes of speech production: lexical–semantic and lexical–phonological processing. If only one of those patterns were altered, we would expect the patient to show a congruent pattern of neurolinguistic impairment and ERP divergences. The subject presented a severe anomia after stroke, characterized by many phonological paraphasias and response failures. Impaired lexical–phonological processes should be associated with changes in the 300–450 msec time period that has previously been linked with lexical–phonological processes during picture naming.

METHODS

Participants

The patient is a 68-year-old man with a university education (a retired psychologist) who suffered a left frontotemporal parietal hemorrhagic stroke (Figure 1). At the acute stage he was described as a Wernicke aphasic. Due to persistence of concomitant medical complications, the patient was transferred to neurorehabilitation only 2.5 months poststroke. A detailed neuropsychological evaluation was carried out 4 months poststroke. At this time his language was fluent, but marked by frequent phonological paraphasias and neologisms (e.g., "moto" produced [mato]; "trompette" (/tRõpEt/–trumpet) produced [pRõtEt]; cigarette produced [asEs]); he experienced word finding difficulties. Naming was severely impaired in the French version of Boston Naming Test (Thuillard-Colombo & Assal, 1992) with predominance of omission and phonological errors. Repetition and reading aloud were also severely impaired with comparable performance on words and pseudowords and a length effect in all production tasks.

Auditory comprehension was preserved for single words and simple sentences (Montreal–Toulouse 86 Aphasia Battery; Nespoulous et al., 1992), but some errors were observed for complex sentences; written sentence and text comprehension were at ceiling on the subtest of the French version of the Boston Diagnostic Aphasia Examination (Mazaux & Orgogozo, 1981). Semantic assessment revealed normal performances on the Pyramid and Palm Trees Test (Howard & Patterson, 1992). He exhibited severe central agraphia with preserved automatic writing and letter formation. A mild orofacial apraxia was observed with no signs of

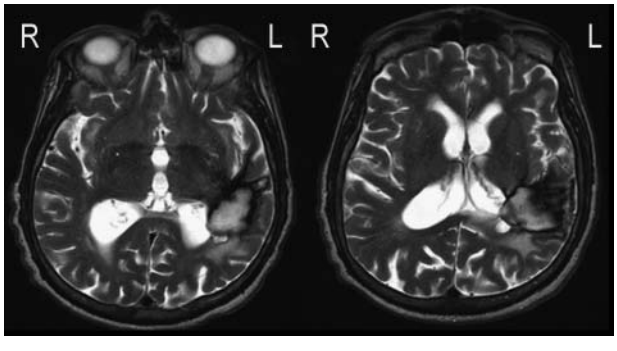

Figure 1. The lesion. A T2-weighted MRI (TE = 122 msec; TR = 8690 msec) at 4 months shows a left temporal–parietal hematoma in resorption with extended destruction of the posterior superior temporal lobe (area 22, including Wernicke's area) and the white matter underlying areas 22 and 40, including the arcuate fasciculus in the temporal stem.

limb apraxia; visual or spatial agnosia; or neglect. Performances were in the normal range on mental flexibility and autoactivation tasks (Frises de Luria and figural fluency; Regard, Strauss, & Knapp, 1982) but performance on the Trail Making Test was somewhat impaired (Reitan & Wolfson, 1985). Nonverbal intellectual processes were in normal range (short version of the progressive matrices; Raven, Court, & Raven, 1998).

In summary, 4 months poststroke, the patient presented with severe expressive aphasia, characterized by anomia with phonological transformations in spontaneous and elicited speech as well as in repetition and reading aloud, relatively spared auditory and written comprehension, and severe agraphia.

The patient was recorded three times, at 3, 4, and 5 months after the stroke, using the same picture-naming task that he had already performed as a control subject 1 year before stroke.

Fifteen other healthy subjects from the original group (Laganaro et al., 2009), from which the patient's data before the stroke were removed, made up the control group (mean age = 55 years; range: 34–72 years; 4 men). One of them (65-year-old woman, hereby "Control subject S") was recorded again 1 year later. The control subjects scored at ceiling on the picture naming task (97.4% correct, SD = 2.7%).

Task and Material

High-resolution (128 channels) EEG was recorded during a delayed picture naming task. The stimuli were 144 black-and-white line drawings selected from French databases (Bonin, Peerman, Malardier, Méot, & Chalard, 2003; Alario & Ferrand, 1999): they corresponded to mono-, di-, and trisyllabic words (nouns) with name agreement above 65%. The pictures were presented at the center of a white computer screen as black outlines. Subjects sat 0.7 m in front of the screen, viewing pictures of approximately 0.09 m with a visual angle of 3.67°.

Each picture was displayed for 2000 msec, followed by a response cue (question mark). The participants were asked to prepare the name matching the picture and to say it aloud when the question mark appeared on the screen. This procedure was adopted to avoid possible artifacts during motor preparation for overt naming.

EEG Acquisition and Preanalyses

The EEG was recorded continuously using the ActiveTwo BioSemi EEG system (BioSemi V.O.F., Amsterdam, Netherlands) with 128 channels covering the entire scalp. EEG signals were sampled at 512 Hz with band-pass filters set at 0.1–100 Hz.

Epochs from −100 to 600 msec relative to picture onset were averaged for each subject. Individual data were recalculated against the average reference and band-pass filtered to 1–30 Hz. In addition to automated amplitude threshold detection, trials were visually inspected, and epochs contaminated by eye blinks, movements, or artifacts were rejected. Baseline correction was applied to the 100 msec prestimulus period. A minimum of 78 epochs were averaged in each subject's data.

Waveform Analyses

The ERPs were first subjected to waveform analysis to determine the time periods in which amplitude differences over all electrodes were found between the patient and the control group, and between the patient's pre- and poststroke data.

t tests were applied to compare voltages of the averaged ERP data (at each electrode and each time point over the whole period, from 0 to 600 msec in 2-msec steps) between the patient and the control group (Crawford t tests; Crawford & Howell, 1998). For the comparison between the patient's prestroke and poststroke data, paired t tests (Bonferroni corrected) were computed on 50 randomly selected single epochs aligned to the stimulus onset. The same procedure was applied to compare the two recording sessions of a control subject (Control subject S), who, as we recall, was recorded again 1 year later (but not suffering a stroke in between).

Topographic Analyses

The differences observed in amplitudes can be a consequence of a modulation in the strength of the electric field, of a topographic change of the electric field (revealing distinguishable brain generators), or of latency shifts in brain processes. To differentiate these effects, topographic analyses were also performed. This approach allows one to summarize ERP data into a limited number of electrocortical map configurations and to identify time periods during which different populations or different conditions evoke different electrocortical configurations.

Topographic (map) pattern analysis, based on a modified spatial k-means cluster analysis, was used to identify time periods with distinct electric field configurations (Michel et al., 2001; Pascual-Marqui, Michel, & Lehmann, 1995) and to determine the optimal number of maps that best explained the averaged datasets ("temporal segmentation"). This method is independent of the reference electrode and is insensitive to pure amplitude modulations across conditions (topographies of normalized maps are compared). Statistical smoothing was used to eliminate temporally isolated maps with low strength; a given topography had to be present for at least 15 time frames (30 msec).

Spatio-temporal segmentation was performed on the averaged group control data, together with the patient's pre- and the three poststroke datasets. The pattern of maps observed in this analysis was then statistically tested by

comparing each map with moment-by-moment scalp topography of each individual control subjects' ERPs (Murray, Brunet, & Michel, 2008). This "fitting" procedure allowed us to establish how well maps explained patient's and individual control's patterns of activity. In order to take into account interindividual variability among the control participants, the patient's data were compared to individual subjects' measures instead of the grand mean data. A map was considered divergent from the control group when its global explained variance (GEV) and its duration (number of time frames) were beyond the maximum or the minimum values displayed by the control subjects and the topographic map was not observed in his own data before stroke.

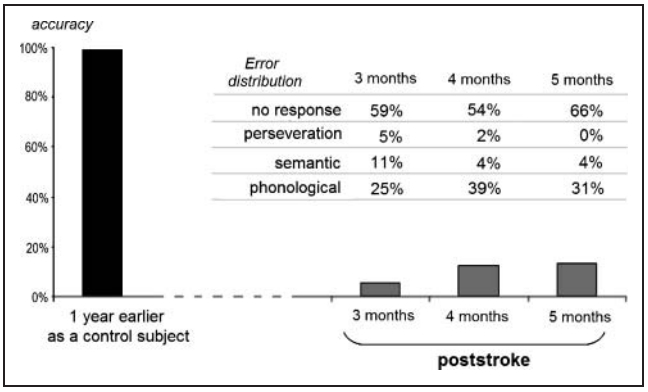

Figure 2. Performance on the naming task (accuracy) before and after stroke and error distribution at 3, 4, and 5 months poststroke.

Source Localization

Estimation of the location of intracranial generators was carried out using a linear distributed inverse solution (LAURA; Grave de Peralta, Gonzalez Andino, Lantz, Michel, & Landis, 2001). This source imaging method is based on the physical law that the strength of a source regresses regularly with distance. Using a regular grid of solution points, the method incorporates this law in terms of a local autoregressive average with coefficients depending on the distance between solution points (Michel et al., 2004). In the current analysis, solution points were distributed within the gray matter of a standard MRI for the control group and the patient's prestroke data and on the patient's poststroke MRI. The latter was used for the source localization of the divergent microstates in the patient's poststroke data. A spherical head model with an anatomical constraint was used, applying the SMAC transformation method (Spinelli, Gonzalez Andino, Lantz, Seeck, & Michel, 2000). In this head model, the solution space is restricted to gray matter subspace. The parameters used for the LAURA calculation were fixed at a neighborhood size of 26 solution points and a regression with the inverse of the cubic distance (for vector fields). The regularization parameter was fixed to Alpha = 1 for all maps (Pascual-Marqui, Sekihara, Brandeis, & Michel, 2009).

RESULTS

The naming scores of the patient were at ceiling before stroke and were severely impaired at 3, 4, and 5 months poststroke (see Figure 2), with a slight but significant improvement from 3 to 4 months (McNemar Change Test: $\chi^2 = 6.231, p = .012$) and stable performance between 3 and 4 months ($\chi^2 = 1.6, p = .2$). His error distribution reveals a preponderance of omission and phonological errors; some semantic errors were also observed, especially at the first (3 months poststoke) recording session. Error distribution also differed between the first and second assessment sessions [Pearson $\chi^2(3) = 8.2, p < .04$], but not between the last two sessions [$\chi^2(3) < 1$].

The patient's poststroke ERPs were compared to the control group of 15 healthy subjects and to his own data before stroke.

The analyses indicated similarly distributed differences in amplitudes after stroke when comparison was carried out with the control group (Figure 3A) and with himself (Figure 3B). In all comparisons, amplitudes consistently differed after stroke from about 250–270 to 400–450 msec after stimuli presentation, especially in the posterior right and left regions and on the left anterior and central electrodes. A second period of diverging amplitudes appeared in the 4 and 5 months poststroke recordings from 450 msec to the end of the recording period on the anterior (right and left) electrodes. By contrast, the patient did not differ from the rest of the control group before stroke (Figure 3C, top); also, Control subject S did not display any significant changes in amplitudes at the 1-year interval.

A strong divergent electrocortical response with a unique map topography appeared after stroke relative to his prestroke data and to the control group in the 250–400 msec time window (Figure 4). The same divergent topography was observed in the three poststroke recordings in the same time window.

This topographic map was observed neither in his own data before stroke nor in the grand average of the control group. Abnormality was further confirmed by a spatial fitting procedure that showed higher GEV and longer duration of this map in the patient as compared to the individual control subjects (GEV: patient after stroke, 86–94%; maximum controls, 48%; duration: patient after stroke, 162–168 msec; maximum duration in control subjects, 138 msec).

More crucially, the template map observed in this time window in 13 out of the 15 control subjects and in his own prestroke data was not present in the patient poststroke data. Source localization computed with the patient's own poststroke head model indicated a left inferior and middle temporal activation after stroke during the 250–400 msec time window, whereas the left middle temporal and anterior and superior temporal lobe was activated in the control subjects and in the patient's data before stroke (source localization for map template in Figure 4).

DISCUSSION

Similar results were observed when comparing ERPs recorded during picture naming in an aphasic patient to his own ERPs recorded with the same task 1 year before stroke and to a control group. Different amplitudes and topographic maps after stroke appeared across all comparison around 250 msec after picture presentation and remained very stable at 3, 4, and 5 months poststroke. These results, together with the observation that the patient did not differ from the control group before stroke and that no changes appeared in a healthy subject at a 1-year interval, indicate that the observed ERP divergences in the aphasic patient are linked to the stroke and cannot be attributed to interindividual or intraindividual (intersession) variability.

Below, we discuss the main implications that can be drawn from these reliable findings for the cognitive changes in language processing in aphasia.

First, changes in ERP patterns after stroke during a picture naming task consistently appeared around 250 msec after stimuli presentation. These results confirm that divergent ERP patterns observed during a language production task after stroke appear in a specific time window,

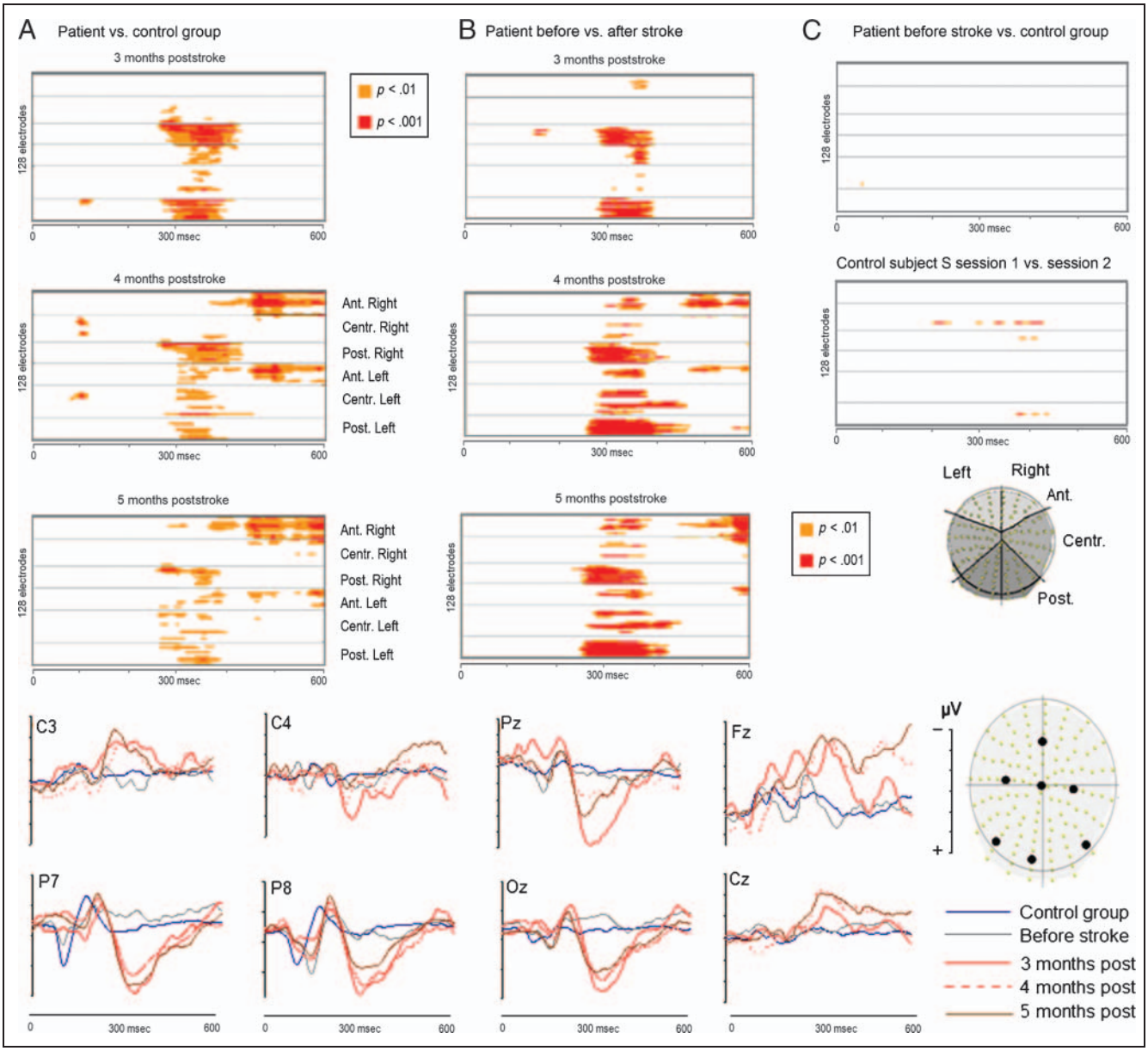

Figure 3. Significant differences (p values, at $p < .01$ and $p < .001$) in electrode amplitude observed for 128 electrodes (y-axes) in time (x-axes): (A) between the patient and the control group at 3, 4, and 5 months poststroke; (B) for the patient before and after stroke (intraindividual comparison); (C) between the patient before stroke and the control group as well as between the two recording sessions of Control subject S. Bottom: evoked potential curves in the control group and the patient at eight specific electrode positions Cz, C3, C4, Fz, Pz, P7, P8, and Oz (marked as black dots on the arrangement of all 128 scalp electrodes).

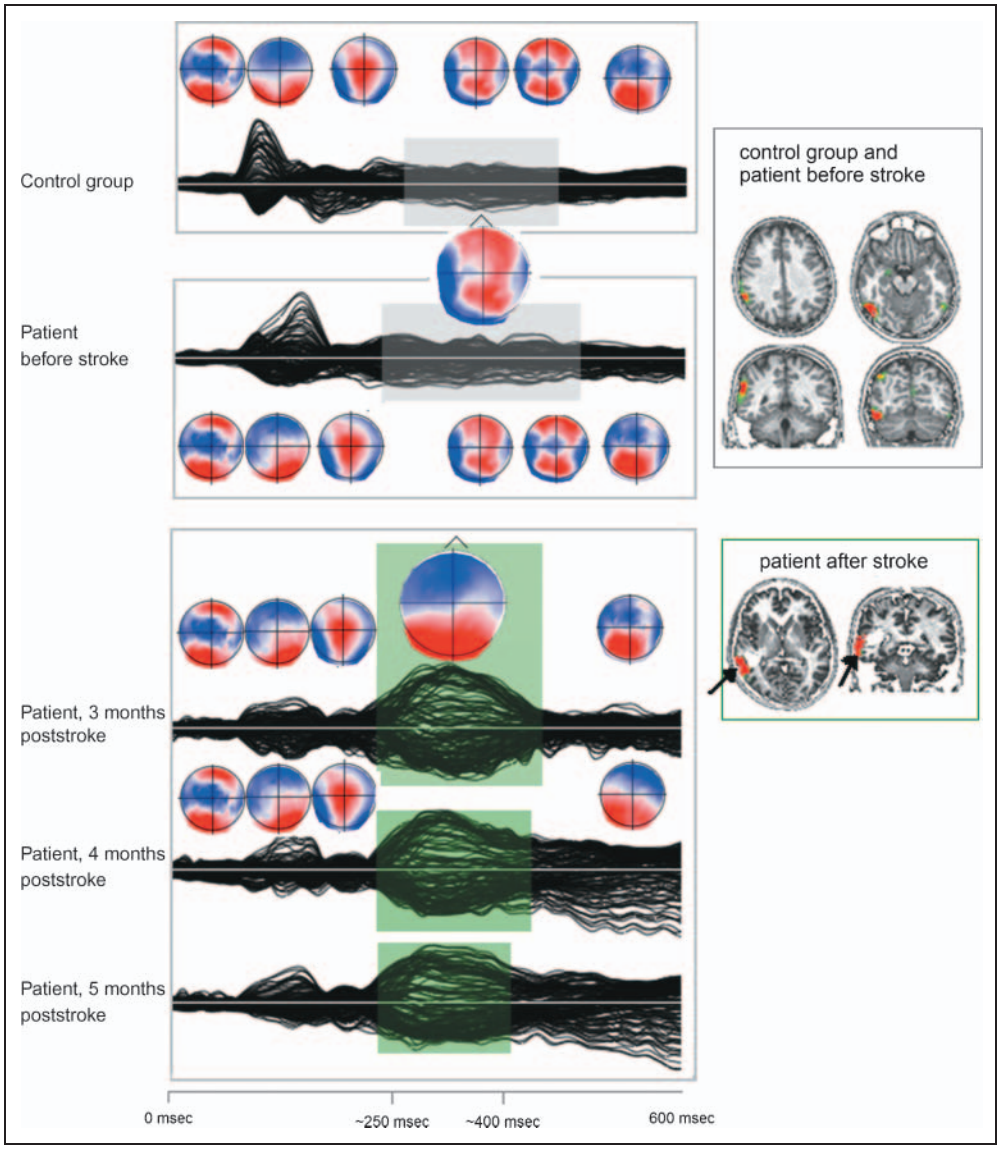

Figure 4. Grand-average ERPs (128 electrodes) of the control group and patient before stroke (top) and of the 3, 4, and 5 months poststroke data (bottom), and sequences of stable topographic maps in each data (positive values in red and negative values in blue). Topographic maps for the 250–400 msec time period for which the analysis revealed different map templates between the poststroke data and the prestroke data are highlighted. (Top, right) Source localization for the map in the data of the control group (within a standard MRI). (Bottom, right) Source localization for the divergent microstate in the patient after stroke (calculated on the patient's poststroke MRI).

which we can relate to impairment in specific cognitive processes. Behavioral and ERP studies with healthy subjects estimated that lexical–semantic processes (conceptually driven lexical selection) occur between 150 and 250 msec after stimuli presentation in picture naming (Vihla, Laine, & Salmelin, 2006; Indefrey & Levelt, 2004; Maess, Friederici, Damian, Meyer, & Levelt, 2002). Word-form (lexical–phonological) encoding has been estimated to start later, around 250–275 msec (around 300 msec in Vihla et al., 2006) after stimulus presentation. According to these estimations, the unchanged ERP correlates from 0 to about 250 msec and the time window of electrophysiological changes observed in this patient after stroke suggest unimpaired visual and semantic processes. This fits with the patient's anomic pattern: He did not display any semantic impairment and his pattern of errors revealed impaired word-form retrieval and encoding (lexical–phonological impairment). The specific changes in the patient's ERPs are also in line with results from a previous group study on patients with either lexical–semantic or lexical phonological anomia (Laganaro et al., 2009, see the Introduction). Taken together, the results indicate that divergent ERPs starting around 250–300 msec after picture presentation characterize impaired single word production in aphasic patients with impaired lexical–phonological encoding.

Second, the modified neurophysiological pattern observed after stroke remained quite stable over several months. The same sequence of topographic maps and similar modification of amplitudes appeared across the three poststroke recordings. The results reported here contrast with previous studies where patients that underwent successive EEG recordings during picture naming tasks after stroke displayed modifications of topographic maps, amplitudes, or both across the recording sessions (Laganaro, Morand, Schwitter, Zimmermann, & Schnider, 2008; Cornelissen et al., 2003). However, the modifications observed were accompanied by behavioral changes, as all patients in these studies displayed some degree of recovery across the study

periods. By contrast, the stable ERP pattern after stroke in the present study was observed together with an unchanged behavioral response (severe anomia), especially during the 4 to 5 months poststroke period. However, an increase in divergent amplitudes from 450 to 600 msec characterized the last two recording sessions relative to the 3 months poststroke data. A minor, but significant, behavioral change was also observed between the first and the following poststroke recordings (10% improved naming accuracy and a slight different distribution of errors); this pattern might be associated with the ERP differences observed between the first and the following two recording sessions.

Source localization applied to the 250–400 ms time window of divergent ERPs indicated activation on a posterior perilesional area while the superior temporal lobe was activated before stroke during this time window. The cortical generator of the divergent topographic map was localized with the patient's own poststroke head model using a procedure of source localization. This procedure has been validated in a recent investigation on patients with focal epilepsy (Brodbeck, Lascano, Spinelli, Seeck, & Michel, 2009), showing that localization was no less accurate in patients with large brain damage than in patients without brain damage; this finding therefore increases our confidence in the accuracy of source localization in stroke patients as well.

Although perilesional activation has been shown to accompany recovery from aphasia (Léger et al., 2002; Belin et al., 1996), in this case, it seems that the generators remain circumscribed to posterior areas of the middle and inferior temporal lobe with a lack of activation of the superior temporal lobe; this latter activation was observed in the prestroke recording and is a very likely locus thought to be implied in the encoding of word form (Indefrey & Levelt, 2004; Levelt, Praamstra, Meyer, Helenius, & Salmelin, 1998). This finding suggests that the lesion disconnects the superior temporal lobe from the inferior and posterior temporal regions, severely disabling word-form encoding. The stability of the divergent electrocortical response over several months also suggests a lack of cortical reorganization in brain-damaged subjects, with limited behavioral changes during the same period.

In conclusion, the same ERP modifications in a specific time period were observed during word production in an aphasic patient in comparison to his own prestroke data and to a group of healthy control subjects. These findings increase our confidence that the observed electrophysiological modifications at 250–400 msec characterize word production impairment at the level of lexical–phonological encoding.

Acknowledgments

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