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Spatiotemporal dynamics of neural language processing: an MEG study using minimum-norm current estimates

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Abstract

The inferior frontal and superior temporal areas in the left hemisphere are well-known to be crucial for language processing in most right-handed individuals. This has been established by classical neurological investigations and neuropsychological studies along with metabolic brain imaging have recently revealed converging evidence. Here, we use fast neurophysiological brain imaging, magnetoencephalography (MEG), and L1 Minimum-Norm Current Estimates to investigate the time course of cortical activation underlying the magnetic Mismatch Negativity elicited by a spoken word. Left superior-temporal areas became active 136 ms after the information in the acoustic input was sufficient for identifying the word, and activation of the left inferior-frontal cortex followed after an additional delay of 22 ms. By providing answers to the where- and when-questions of cortical activation, MEG recordings paired with current estimates of the underlying cortical sources may advance our understanding of the spatiotemporal dynamics of distributed neuronal networks involved in cognitive processing in the human brain.

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Introduction

Broca and Wernicke reported the first clear evidence that there are areas in the human brain that specifically contribute to language (Broca, 1861; Wernicke, 1874). Modern neuroimaging, along with more recent neuropsychological investigations, could further confirm the involvement of an inferior frontal area and a superior temporal area in the left hemisphere of most right-handers in language processing (Zatorre et al., 1996; Price, 2000). However, the question of *when* these areas become active in the process of language perception and comprehension could not be addressed until very recently. Here, we use Magnetoencephalography

(MEG) and Minimum-Norm Current Estimates to reveal the time course of cortical activation evoked by spoken language.

As the dependent measure, we chose the magnetic correlate of the Mismatch Negativity (MMN) elicited by spoken words. Whereas a magnetic MMN can be elicited by acoustic stimuli of various kinds, the magnetic MMN to language stimuli, including vowels (Näätänen et al., 1997), syllables (Shtyrov et al., 2000), and words (Pulvermüller et al., 2001), is lateralized to the left and may therefore reveal specific cortical signatures of language processing (Näätänen, 2001). In an earlier study (Pulvermüller, et al., 2001), we had shown that words presented as deviant stimuli in oddball tasks elicit a greater MMN response than meaningless pseudowords, suggesting that the MMN reflects the activation of cortical memory traces for spoken words (Pulvermüller, 2001; Shtyrov and Pulvermüller, 2002b). This makes the word-evoked MMN a promising tool for inves-

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tigating the cortical basis of language processing. Here, we show for the first time that presentation of a spoken word activates superior-temporal cortex immediately and inferior frontal cortex with a slight delay.

Materials and methods

Whole-head MEG recordings (Vectorview-306, Elekta NeuroMag, Helsinki) were obtained from 12 right-handed native speakers of Finnish (age range = 21–29; 5 males). They repeatedly heard the same recording of a Finnish word spoken by a native speaker while seeing a silent video film of their own choice. Subjects were instructed to watch the film and try to ignore the auditory stimuli. The critical stimulus word was the inflected verb *tuon* (*bring*) with the [n] indicating first-person singular present. An oddball paradigm was applied in which the critical word occurred as the infrequent ($P = .167$) deviant stimulus in the context of a frequently occurring standard stimulus that only minimally differed from the deviant toward its end (*tuot*, with the [t] indicating second person singular present). The word stimuli had the same peak sound energy, voice-onset time, F_0 frequency, and similar contours. In a gating study, the recognition point (Marslen-Wilson and Tyler, 1980) of the word *tuon* used as deviant stimulus was found to occur 351 ms after word onset and that of the standard stimulus word, *tuot*, at 415 ms. The word with a recognition point that was later than that of the deviant stimulus word was chosen as the standard stimulus to ascertain that, if there were cortical activation processes driven by the recognition point, they would occur earlier for the deviant stimulus than for the standard.

Artifact-free MEG recordings (0.03- to 200-Hz band pass; sampling rate-600 Hz) from 204 MEG gradiometer sensors were averaged separately for each subject and stimulus (at least 120 trials per average) and again filtered with a 1- to 20-Hz band pass. Event-related fields obtained for the standard stimulus were subtracted from those of the deviant stimulus in the usual way to obtain the magnetic MMN. The cortical sources of the measured neuromagnetic activity were calculated using Minimum-Norm Current Estimates. This method is known to solve the inverse problem of localizing neurophysiological activity in the brain from surface recordings by revealing the unique constellation of current elements that models the recorded magnetic field distribution with the smallest amount of overall current (Hämäläinen and Ilmoniemi, 1984; Hämäläinen and Ilmoniemi, 1994; Ilmoniemi, 1993). Among the, in principle, infinitely many constellations of activity that can explain a given scalp topography of the magnetic field, there generally exists one that does so with the least amount of overall activity and thus in the most parsimonious way. Thus, minimum-norm estimates apply the general scientific principle of parsimony to the inverse problem of localizing neurophysiological current sources in the brain.

In contrast to modeling using several individual dipoles, Minimum-Norm Current Estimates can thus be performed without prior assumptions about the number or loci of the sources. This was our main reason to prefer this localization technique to multiple dipole fits. The norm selected for the source estimate defines how the overall current amplitude is calculated from the individual sources. The L1 Minimum-Norm Current Estimate (Uutela et al., 1999), which was applied here, minimizes the integral of the current amplitude and reveals a realistic and robust constellation of generators. The computation time for L1 norm solutions is much larger than for the L2 norm; in the former, linear-programming techniques are generally used, whereas in the latter, the solution is found by computing the Moore-Penrose pseudo-inverse using singular-value decomposition. The L1 Minimum-Norm Current Estimate is applicable if it can be assumed *a priori* that the source distribution consists of discrete areas of neuronal activity. This assumption is justified in the investigation of language, because neuroimaging results obtained with different methodologies proved the activation of discrete cortical areas during a variety of language tasks (Price, 2000; Pulvermüller, 2001). In the context of the present study, the L1 norm was preferred to the L2 norm, because the former has been shown to be capable of separating sources a few centimeters apart (Uutela et al., 1999), whereas the latter is known to lead to blurring of sources. In the realm of language, where it is important to allow for a separation of sources in the inferior frontal and superior temporal cortex, the L1 norm might therefore be preferable.¹

Singular value decomposition was applied for reducing the influence of noise. Minimum-norm current estimates were calculated for each subject individually for consecutive time steps. For each point in time, up to 30 simultaneously active current sources were allowed at 1231 possible loci placed on an ellipsoid approximating an averaged cortical surface. Three orthogonal current components (in x , y , and z directions) were calculated at each location and their RMS yielded the source strength at a given locus. Source solutions were projected on a triangularized surface of the averaged brain. Statistical analyses were performed for the time interval where the magnetic MMN was most pronounced, between 100 and 250 ms after the word recognition point. The maximal amplitudes of source currents and their latencies were obtained for each subject in two predefined regions of interest, inferior-frontal and superior-temporal. These values were analyzed using t test.

¹ We acknowledge that there are further source localization techniques that could serve the same purpose, for example, approaches compromising between the L1 and L2 norms (e.g., L1.85 norm), although a “pure” L1 or L2 approach might be preferable over a mixture, especially considering the need of justifying additional parameters.

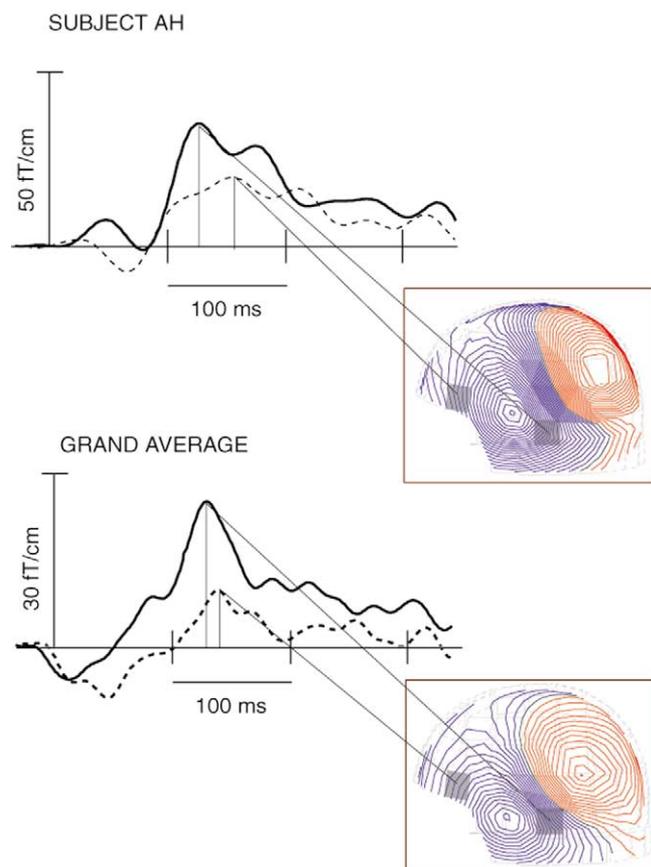


Fig. 1. Field gradients of the magnetic MMN (deviant response – standard response) recorded from a typical subject (diagrams at the top) and grand-average event-related fields calculated for the entire group (diagrams at the bottom). Dynamics recorded at a superior temporal sensor (solid line) are contrasted with those at an inferior frontal sensor (dashed line; sensor locations are indicated by gray boxes in the insets). Note the slightly earlier maximum recorded at the temporal sensor as compared with that of the frontal sensor. The magnetic field distributions at peak activation of the stronger source are shown for the individual subject and the group (insets).

Results

The spoken word presented as the deviant stimulus elicited a magnetic MMN that peaked around 130 ms after the recognition point of the deviant stimulus and was maximal over the left hemisphere (Fig. 1). Recordings at temporal sites tended to peak earlier than those at frontal sensors, but the time difference did not reach significance in the analysis of raw event-related fields. The magnetic field distribution indicated the typical superior temporal source but did not in itself give evidence of an additional left-hemispheric source underlying the MMN (Fig. 1, insets). In contrast, the current estimate revealed two pronounced left-hemispheric sources of the MMN, one in superior temporal areas and the other in inferior frontal areas. The superior-temporal source was significantly stronger than the one in inferior-frontal cortex [peak amplitudes: 56 vs 27 nAm; $t(11) = 2.87$, $P < 0.007$, one-tailed]. Examination of the time course of superior-temporal and inferior-frontal activation indicated that, in the

average, the temporal source became active before the one in frontal cortex (Fig. 2). The time difference was 22 ms and reached statistical significance [$t(11) = 2.27$; $P < 0.02$]. Relative to the earliest point in time when the acoustic input included the information necessary for unambiguously identifying the critical word, the average delays of peak activation in superior-temporal and inferior-frontal areas were 136 and 158 ms, respectively (Fig. 3). Analysis of the event-related field elicited by the standard stimulus alone revealed a comparatively weak superior-temporal activation with no evidence of an inferior frontal source.

Discussion

In summary, the processing of spoken language coincided with near-simultaneous activation in superior-temporal and inferior-frontal areas in the left language-dominant hemisphere. The minimal delay of ~ 20 ms between superior temporal and inferior frontal activation may be caused by the conduction of action potentials through the most common myelinated corticocortical fibers (Aboitiz et al., 1992; Braitenberg and Schüz, 1998), possibly in the *arcuate* and *uncinate fasciculi*, and matches well with estimates of corticocortical conduction delays on the basis of combined use of transcranial magnetic stimulation and neurophysiological recordings (Ilmoniemi et al., 1997).

One may ask whether the pattern of brain activity found here is related to language processing per se or to a more global process of auditory perception that can also be invoked by elementary acoustic stimuli. When investigating cortical activation elicited by simple tones, neuromagnetic activity was strongest over the right temporal and frontal cortex compared with the homotopic areas on the left side (Rinne et al., 2000), whereas in the present study, as in several earlier language experiments, activation was predominantly on the left. The cortical signature of the MMN response obtained in the present study may therefore reflect language-specific processes per se, a conclusion further confirmed by neurophysiological investigations of phoneme, syllable, and word processing (Näätänen et al., 1997; Shtyrov et al., 2000; Näätänen, 2001; Pulvermüller, 2001; Pulvermüller et al., 2001). We do not know, however, whether the spatiotemporal pattern of activity observed in this experiment does reflect a general property of the processing of spoken language or, more specifically, the recognition of words and their status as lexical elements of a language. A further possibility is that the processing of the inflectional affix with which the word ended was reflected at the neurophysiological level. This would be consistent with earlier findings of a left-perisylvian activation process elicited by regular inflectional affixes (Shtyrov and Pulvermüller, 2002b) and with the degradation of these affixes after lesions of the left-perisylvian network seen in agrammatic patients and in neural network simulations modeling the effect of such lesions (Pulvermüller and Preissl, 1991).

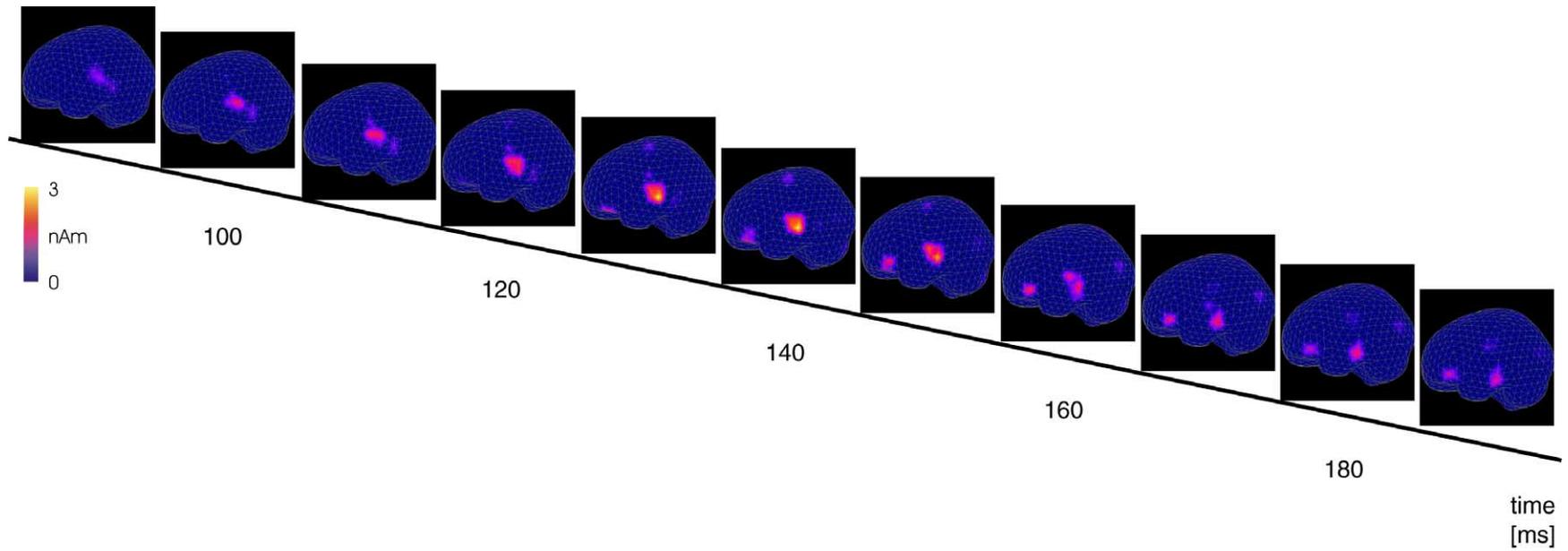


Fig. 2. Spatiotemporal pattern of cortical activation elicited by a spoken word. Minimum-Norm Current Estimates of the sources underlying the magnetic MMN calculated for 10-ms-wide time bins and averaged over all subjects are shown on the triangularized surface of an average brain. The time scale indicates ms after the point of word recognition. A superior-temporal source starts to build up early (~ 90 ms) and reaches its maximum activation at ~ 140 ms. A second inferior-frontal source appears later (~ 120 ms) and peaks at ~ 160 ms. A film showing the spatio-temporal dynamics over ~ 500 ms is available at www.sciencedirect.com.

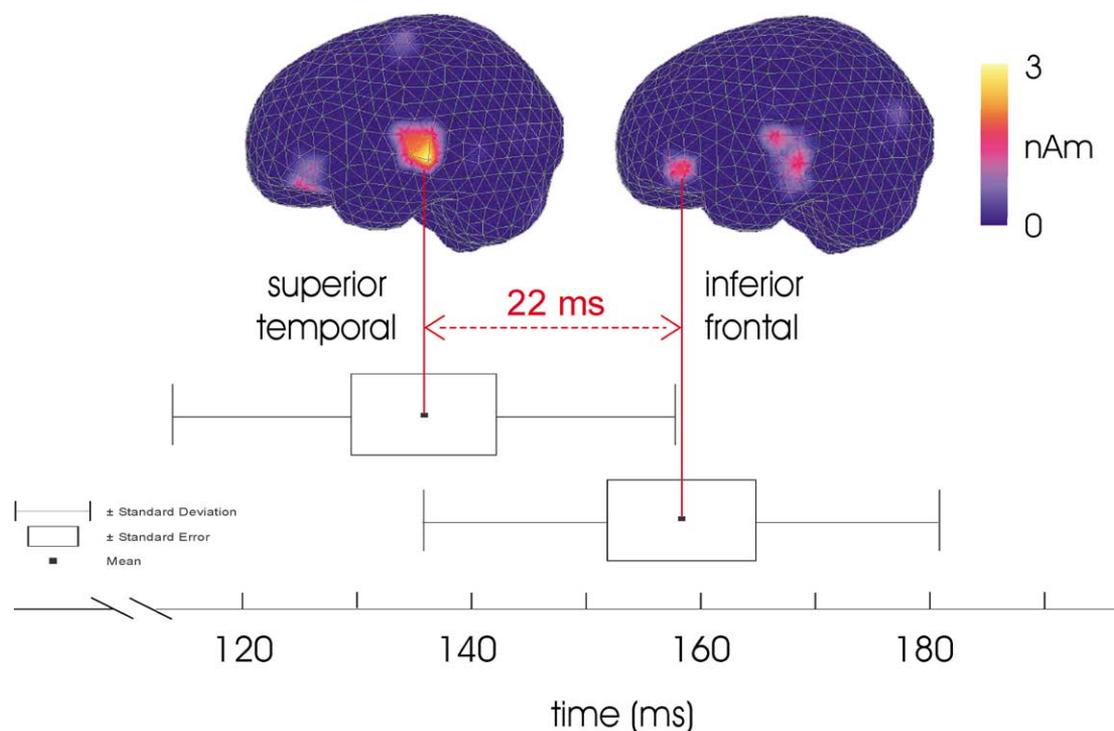


Fig. 3. Space-time plot of the activation pattern: Minimum-Norm Current Estimates of the distribution of cortical sources of the magnetic MMN for the average points in time when maximal activation was found in superior temporal areas (136 ms after the word recognition point; upper left) and in inferior frontal areas (158 ms; upper right). The horizontally arranged box plots (bottom) give the means of the latencies of the activity peaks, calculated for both regions of interest and for each subject individually, along with their standard errors (boxes) and standard deviations (bars).

We should call attention to the fact that estimations of current sources in the brain are always estimates and may, as such, be affected by errors (a statement that is probably true for all brain imaging methods alike). In the context of the present study, the clearest restriction applies with regard to the spatial resolution, which is, as simulations show, in the centimeter range (Uutela et al., 1999). Thus, conclusions in terms of parts of cortical lobes but not Brodmann areas may be appropriate. An advantage of the approach taken here is that it allows for generalized conclusions on the basis of parametric statistics performed over a large group ($n = 12$) of subjects for each of whom source localization has been performed individually.

We conclude that the use of the L1 Minimum-Norm Current Estimation for determining the cortical sources of multichannel MEG recordings can reveal the time course of cognitive brain processes with millisecond precision. The newly available information about the temporal structure of the activation of cortical areas may be relevant for future theorizing about the brain basis of language and cognition (Braitenberg, 1997; Pulvermüller, 2003).

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