Correspondence of Event-Related Potential Tomography and Functional Magnetic Resonance Imaging During Language Processing

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Abstract: Combining event-related potentials (ERP) and functional magnetic resonance imaging (fMRI) may provide sufficient temporal and spatial resolution to clarify the functional connectivity of neural processes, provided both methods represent the same neural networks. The current study investigates the statistical correspondence of ERP tomography and fMRI within the common activity volume and time range in a complex visual language task. The results demonstrate that both methods represent similar neural networks within the bilateral occipital gyrus, lingual gyrus, precuneus and middle frontal gyrus, and the left inferior and superior parietal lobe, middle and superior temporal gyrus, cingulate gyrus, superior frontal gyrus and precentral gyrus. The mean correspondence of both methods over subjects was significant. On an individual basis, only half of the subjects showed significantly corresponding activity patterns, suggesting that a one-to-one correspondence between individual fMRI activation patterns and ERP source tomographies integrated over microstates cannot be assumed in all cases. *Hum. Brain Mapping* 17:4–12, 2002. © 2002 Wiley-Liss, Inc.

Key words: ERP; fMRI; distributed source modeling; LORETA; language; multimodal

INTRODUCTION

To achieve a better understanding of the functional circuitry of cognitive processes, it is essential to mea-

sure both time course and localization of functional brain activation. Temporal properties of brain activation can be recorded with high resolution by event-related brain potentials (ERPs) and spatial properties by functional magnetic resonance imaging (fMRI). Before the advantageous characteristics of the two methodologies can be combined, empirical work must first clarify which scalp electric and fMRI BOLD contrast brain responses represent the same neural networks. A simple one-to-one correspondence between the sources of event-related potentials and the localization of BOLD responses is not expected: ERP sources have been described in regions without a corresponding hemodynamic response [McCarthy, 1999], and the phasic activation measured by ERPs may originate

Contract grant sponsor: Swiss National Science Foundation; Contract grant number: 31-50734.97 and NCCR on Neural Plasticity and Repair; Contract grant sponsor: Federal Office for Education and Science; Contract grant number: 95.0314.

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Received for publication 8 February 2001; accepted 20 February 2002
DOI 10.1002/hbm.10038

from other regions than the sustained or summated activation measured in fMRI block designs [Woldorff et al., 1999].

ERP scalp potentials reflect the activity of a large number of pyramidal cells in the gray matter of the cortex. Neighboring cells share the same orientation and can be represented as a single polarized region or current source. A consequence of neuroelectric mass activity is local changes in blood properties. The resulting hemodynamic response in the area of the neuronal activity is represented by the signal intensity of the BOLD-contrast [see Rosen et al., 1998 and Raichle, 1998 for a more extensive discussion].

Contrary to the BOLD response, the scalp ERPs contain no direct information about the location of their sources. Mathematically, the inverse problem (inferring intracranial current distribution from scalp recordings) is ambiguous and thus not solvable without assumptions about the underlying neural generators and the head. The most common simplifying assumption is that polarized regions can be modeled by current dipoles, i.e., by point sources within a spherical head (with multiple shells representing the skin, skull and brain). This dipole fitting approach has produced physiologically meaningful results for early afferent ERP components that can be modeled by one or two dipoles [Butler et al., 1987; Lehmann and Fender, 1969; Scherg, 1993]. It requires, however, a priori knowledge of the number of dipole sources. Furthermore, stable and unique solutions for the best fit between the real fields and those generated by dipole configurations are usually only obtained if the model is limited to few dipoles, which is an unrealistic assumption in studies of higher cognitive functions as they involve multiple sources.

Several studies have combined brain electric and hemodynamic data that were acquired with the same tasks and subjects. In these studies, dipole fitting was used to estimate the source of brain electric data. Matches reported were based on single ERP components reflecting auditory target selection [Menon et al., 1997; Opitz et al., 1999], visual attention [Heinze et al., 1998] or afferent somatosensory [Grimm et al., 1998] processing. All dipole solutions were also constrained by localization information from the hemodynamic results, thereby assuming a priori correspondence between hemodynamic and ERP source locations. To what extent that both methods represent the same neural networks is thus difficult to assess from these studies.

In the current study, the LORETA method was chosen to compute current source densities. LORETA is a *distributed source modeling* method, which makes assumptions about the distribution rather than the number of sources. In addition, no a priori localization

information from hemodynamic data is needed. The LORETA [Pascual-Marqui et al., 1994] algorithm directly computes the smoothest possible 3D current distribution in the brain that generates the observed scalp field. Mathematically, this smoothest solution is unique and provides accurate but possibly “over-smoothed” 3D localization of multiple sources without further assumptions. The physiological rationale for the smoothness constraint is that neighboring neurons are most likely simultaneously and synchronously active; this is also a prerequisite for detectable EEG activity on the scalp.

LORETA is only one of infinitely many inverse solutions. The reasons for using only this solution include the following. Unlike dipole localization methods that are explicitly capable of finding only some few “hot spots,” LORETA is a 3D distributed inverse solution. This means that LORETA shares the same type of solution space as fMRI. LORETA performs similar to other published 3D distributed inverse solutions for epileptic spike sources [Michel et al., 1999], but has the additional advantage of correctly localizing deep sources [Pascual-Marqui et al., 1994].

Before the correspondence of brain electric and BOLD contrast data can be evaluated, the basic common and distinct factors of both methodologies have to be considered. In this study, the common factors are the subjects and the experimental tasks. As a result, both brain electric and BOLD contrast data within subjects should represent the same mental processes. Distinct factors are the spatial and temporal properties of both acquisition methods.

A direct consequence of the smoothness constraint in LORETA is a low spatial resolution blurred beyond the already coarse 7 mm³ voxels, which contrasts with the high spatial fMRI resolution (2 mm³). To *overcome the differences in spatial resolution*, the nearest distances between each LORETA local maxima to every fMRI local maxima was computed in Talairach space [Talairach and Tournoux, 1988]. The use of local maxima also resolves the problem of different scaling between both methods (LORETA values vs. Z-scores in fMRI, both representing brain activation). Due to the coarser resolution of the LORETA maps, the resulting LORETA local maxima were fewer than the local maxima found for the neuroimaging data. To compensate for this, a unidirectional correspondence approach was used and only distances between each LORETA local maxima with the nearest found fMRI local maximum were computed. This unidirectional approach should be insensitive to mismatch due to additional fMRI activation in deep structures not represented in the LORETA source space (confined to cortical and hippocampal gray matter).

Neurons respond within 10 msec of a perceptual stimulus, whereas the subsequent rise time of the BOLD contrast signal occurs a few seconds after stimulus onset. Due to the fast response of neurons, the acquisition and analysis of brain electric data can be made on temporal scales that are measured in milliseconds. In the analysis of fMRI data, an activation map is created that collapses the entire time-series into one statistical map that represents correlated areas to a hypothesized model and has low temporal resolution. To overcome the differences in temporal resolution, the LORETA results were collapsed over time to evaluate the correspondence of both methods via volumes of the entire information processing time-series, i.e., without the temporal resolution.

The aim of our approach is to evaluate the *statistical* correspondence of activity of the whole common volume and of the entire time series of both acquisition methods to investigate if both methods represent the same neural networks. Once correspondence at this common, low resolution (i.e., with EEG data collapsed over time) is established, multimodal integration can proceed toward a description of the activation sequence at both the full temporal resolution of the EEG, and the full spatial resolution of the fMRI method. Because no a priori knowledge of location or amount of current source densities are needed by the LORETA program, we tested the correspondence of brain electric and BOLD-contrast activity that was evoked by a semantic monitoring task.

MATERIALS AND METHODS

Subjects and stimuli

Subjects were 10 healthy 21–41-year-old volunteers (mean age 26.8 years, SD 5.5 years). Two subjects were females and all but one were right-handed. Subjects gave written informed consent and had no known neurological disorder or history of reading disability. Magnetic Resonance Imaging and EEG data were acquired in two separate sessions using the same experimental task. The sequence of acquisition sessions was balanced between subjects: six subjects completed the MRI and four subjects the EEG measurement before completing the other method. Both measurements of each subject were at least one week and not more than three weeks apart.

Stimuli were well-known Swiss-German 4–6 letter words that were presented one by one with a stimulus duration of 400 msec and a inter-stimulus interval of 1,100 msec. A 'rest' block – 'word' block presentation cycle was repeated five times. During the 'rest' condi-

tion, a small white cross-hair was presented in the middle of the computer monitor continuously. Subjects were asked to fixate this cross-hair and to suppress conscious thought during the resting condition. The main task was the silent reading of the Swiss-German words. The additional task was to monitor for words of the category food (one-third of the stimuli were targets). For this, subjects had a computer mouse and pressed a button every time they read a target word to ensure that subjects were actively processing the stimuli. The answers and their reaction time were saved to disk for later analysis. Unfortunately, due to malfunction of the equipment, the behavioral data acquired during the fMRI session is no longer accessible. The sequence of words was randomized between subjects and acquisition methods. The stimuli were shown in white on a black background in the middle of the computer monitor. Words had a vertical visual angle of approximately 0.53° for both acquisition methods.

Functional magnetic resonance imaging

Subjects were examined on a 2 T unit (Tomikon S200A, Bruker Medical, Switzerland) using a quadrature head coil. For anatomical imaging, Inversion Recovery (inversion time = 530 msec) sequences were used. A gradient-echo echo-planar imaging (EPI) sequence (TE = 32 msec; image acquisition time of 82 msec totaling in a slice package repetition time of 1,611 msec; in-plane resolution of $2.34 \text{ mm} \times 4.17 \text{ mm}$) was performed for the functional images. Ghosting artifacts were corrected using an image-based phase correction algorithm [Hennel, 1998]. The slice package consisted of 16 6-mm thick axial-oblique contiguous slices placed along the anterior and posterior commissure plane. One experimental cycle ('rest' block – 'word' block) consisted of the acquisition of 24 slice packages (12 each for the 'rest'- and 'word' block), totaling in 120 images per slice. Using the above-mentioned EPI acquisition parameters, each 'block' lasted 19.33 sec. Head padding was used to suppress non-rigid head movements. Scanner noise was minimized by an active noise-cancellation headset.

Analysis was done with the image processing and analysis software MEDx (Sensor Systems, Sterling, VA). Motion correction was performed by registering all functional volumes to a selected reference volume using a 3D linear algorithm (rigid body 6 parameter model). To standardize the signal at each voxel in relation to the global signal, intensities were normalized based on the average intensity in the brain. For this, each voxel in a scan was divided by the mean of

all voxels. All functional volumes (each of $128 \times 128 \times 16$ matrix size) were registered to the anatomical volume using the AIR3 program [Woods et al., 1998] with a tri-linear interpolation. This resulted in functional volumes of $256 \times 256 \times 16$ matrix size each. All volumes were registered to Talairach space. A voxel-wise correlation analysis [Bandettini et al., 1993] was performed using a gaussian distributed (2 FWHM) boxcar model with a lag of one volume scan. The resulting output are Z-score maps. Critical thresholding was applied (RESEL) [Worsley et al., 1992]. For this work, a corrected probability 0.0004 (corresponding to a z-value of >3.5) was used for individual data. Local maxima of significant activity (any voxel with an intensity greater than any of the immediately adjacent voxels) were read out for each subject separately in Talairach space coordinates using voxels of the size 2 mm^3 . Due to a wide dispersion of individual activity, 'statistical' power was lost in the mean fMRI image. Thus, for the mean of the Z-score maps, z-values above 1.5 (maximum $z = 2.7$) were included in the lists. The result of this analysis generated 11 lists of significant fMRI local maxima (10 subjects, 1 mean), the individual lists ranging from 118–288 local maxima per list.

Brain electric data

The EEG was acquired using 43 Ag/AgCl electrodes that were integrated in an elastic custom-made cap. Next to the 19 standard electrodes of the International 10-20 System [Jasper, 1958], the following electrodes were placed according to the 10-10 system [American Electroencephalographic Society, 1991]: FPz, Oz, C1, C2, FC1, FC2, FC5, FC6, CP1, CP2, CP5, CP6, FT9, FT10, TP9, TP10, PO1, PO2, PO9, PO10, AF1, AF2, and two eye electrodes (EOGs). The EOG-electrodes were placed below the outer canthus of both eyes. The impedance of each electrode was kept under 10 k Ω . Subjects were seated in a soundproof, electrically shielded cabin. The 43-channel EEG was digitally recorded at 500 Hz with filter settings of 0.1–70 Hz and calibrated technical zero baselines using the NEUROSCAN software (Neurosoft, Sterling, VA). FPz was the recording reference. Artifacts due either to eye and body movements, sweating or electrode contact problems were monitored and corrected during the whole session. At the end of the session, the exact 3D position of all electrodes on the scalp were measured with a 3D digitizer (POLHEMUS Inc., Colchester, VT). The position of nasion, inion and both ears were acquired both at the beginning and end of the measurement to ensure that possible movement during the acquisition

did not contaminate the 3D electrode position measurement.

Post-processing was performed using the NEUROSCAN analysis software. EEG epochs of 1-sec length after stimulus onset markers were computed. EEG epochs were reduced to 256 Hz using a spline-fit algorithm. Data were then band-pass filtered from 1–30 Hz. An artifact rejection was performed, excluding epochs with amplitudes exceeding $\pm 75 \text{ mV}$ in any channel. For each subject separately, EEG epochs were averaged, resulting in 10 individual ERPs. All averages contained at least 40 sweeps. Averaged data was always computed versus the average reference [Lehmann, 1987]. For the calculation of the correspondence over subjects, the grand mean ERP was computed. Microstates (= time range of stable map configuration corresponding to distinct ERP components [Lehmann, 1990]) were defined using the extrema of the grand-mean ERP Global Dissimilarity and Global Field Power [Lehmann, 1987] curves. The resulting time window consisted of five consecutive segments representing different levels of information processing, ranging from the onset of the P1 (90 msec) to the end of the N4 (539 msec) component.

LORETA

In a first step, transformation matrices were calculated for each subject separately using the LORETA program, after fitting their individually measured 3D electrode positions to the standardized Talairach skull surface [described in Pascual-Marqui et al., 1999]. For the source estimation of the grand mean ERP, the mean of each subjects' electrode position was used to compute the mean transformation matrix. Standardized LORETA source estimations of ERP data were then computed for these individually fitted volumes of 2,394 fixed voxels (representing gray matter) in Talairach space. LORETA source estimations were calculated in two fashions: as 1) the mean of each LORETA analysis of every single data point in time between 90–539 msec (mean of the source analysis of 115 separate data points with the given digitization rate of 256 Hz); and as 2) the LORETA analysis of the mean map of every microstate, resulting in five separate source volume solutions. The main result of the LORETA analysis is two source estimation volumes collapsed over time for each subject (thus with different weighting of the ERP data), and analogously two source estimation volumes of the grand mean ERP. Areas of current source densities were then reported in Talairach space. For this, local maxima above a specific LORETA-value threshold ($v = 0.001$) were read out in Talairach space with the predefined spatial

resolution of the LORETA program of 7 mm^3 . This threshold ensured that the number of local maxima in the LORETA list resembled but never exceeded the number in the fMRI list (range 50–100% across subjects), consistent with the lower spatial resolution of LORETA. As in the fMRI analysis, the local maximum is defined as a voxel with an intensity greater than any of the immediately adjacent voxels. The result of this analysis generated 22 lists of LORETA local maxima (2 weighting conditions $\times$ 10 subjects + 1 grand mean), the individual lists ranging from 97–116 (local maxima of each microstate collapsed into one file) and 27–43 (local maxima of mean over all data points) local maxima per list.

Quantification of correspondence

The correspondence between both methods (subsequently termed ‘match’) is quantified in terms of mean nearest 3D distance found between local maxima of both methods. The probability of the match is calculated via the bootstrapping method.

Calculation of mean 3d nearest distance

For each LORETA local maximum (all local maxima were in the format of one point in Talairach space) within a list, the distance to every fMRI local maximum was calculated and each nearest distance found was written to disk. The mean of each nearest found distance within the list was then calculated, resulting in one mean nearest distance per match.

Bootstrap estimation of match significance

The bootstrapping method was used to estimate the probability of the match. For each match, 5000 randomly generated LORETA local maxima lists were created in the size (number of LORETA local maxima within a list) of the original data. The mean nearest found distance between each of these randomly generated lists and the fMRI local maxima list was calculated as described above. The match probability was then based on the order of the actual mean nearest found distance within the randomly generated mean nearest found distances: the probability was calculated from the rank of the mean nearest match distance of actual data within the 5,000 randomly generated mean nearest match distance with the formula $\text{rank}/5,000$.

The LORETA program computes current sources for the full brain volume. The fMRI acquisition was limited to 16 slices. For the match analysis, only the local maxima of the common volume was used thus

reducing the LORETA current sources to local maxima of and above $z = -6 \text{ mm}$. Analogously, the location of randomly generated LORETA local maxima was reduced from a volume of 2,394 to 1,784 voxels.

RESULTS

Behavioral

The overall mean reaction time was 733 msec. Task accuracy (percentage of the sum of correct hits and non-hits) was above 90% in all but one subject. Questioned about this, the subject answered that he understood that targets were only of the category fruits and vegetables, and not food (e.g., toast) in general. A subsequent analysis of his data taken this into account yielded a task accuracy of 90% and reduced the amount of targets in his data by the factor two.

fMRI

For the correspondence of both methods within subjects, individual fMRI data were analyzed. Figure 1 illustrates typical results from two subjects. In these and the other subjects studied, similar activation patterns were found with different degrees of lateralization between subjects. In the majority (8 out of 10) of subjects, BOLD-contrast activity ($P < 0.0004$), evoked by the semantic monitoring of word lists, was found in the cuneus (Brodmann area 17, 18), middle occipital gyrus (18), lingual gyrus (17, 18), precuneus (7), inferior (40) and superior (7) parietal lobe, middle (21, 39) and superior temporal gyrus (22), cingulate gyrus (24), inferior (45), middle (6, 8, 9, 46) and superior frontal gyrus (6), insula (13) and precentral gyrus (6) of the left hemisphere. In the right hemisphere, activity was found for the majority of subjects in the cuneus (18), middle occipital gyrus (18), lingual gyrus (18), precuneus (7), inferior parietal lobe (40), and the middle frontal gyrus (9, 10).

The correspondence of both methods was also evaluated for the mean over subjects. For this, the mean fMRI activity was computed in Talairach space as the mean of Z-score maps over subjects. An excerpt of the resulting images is displayed in the second row of Figure 3, showing predominantly left lateralized activity in regions similar as discussed above and displayed in Figure 1.

ERP

Reading Swiss-German words evoked five ERP components with standard patterns as already seen in sentence reading paradigms [Brandeis et al., 1994]. The re-

Figure 1.

Regions of BOLD-contrast activity evoked by the semantic monitoring of Swiss-German words. Typical results from two subjects (see text). Scale represents Z-scores between 4.0–9.2.

sulting ERP microstate maps of the grand mean ERP subjects is shown in Figure 2. The first two ‘visual’ microstates (P1: 90–145 msec, N1: 148–203 msec) show the characteristic topography of visual components with strong gradients over the posterior area: P1 with characteristic occipital positivity (red), and N1 with the reversed pattern, occipital negativity (blue). The P2 microstate (207–410 msec) displays bilateral temporo-occipital negativity peaks and posterior positivity. Two main global field power peaks were found in the range of the ‘cognitive’ N400 microstate, resulting in two distinct N400 microstates, N4a (344–410 msec) and N4b (414–539 msec), both with fronto-central negativity of slightly different topography. N4a shows a more posterior and left-lateralized negative topography than N4b. In addition, bilateral anterior positive peaks can be observed in the N400 time range. These microstates exhibit strong gradients between fronto-polar (positive) and antero-temporal (negative) electrodes, arguing against a possible influence of a blinking artifact in the map configuration.

LORETA

The first row of Figure 3 shows the result of the mean LORETA analysis of every single data point in

time between 90–539 msec of the grand mean ERP (same data as used to derive the maps shown in Fig. 2). Displayed are eight contiguous LORETA slices of 7 mm thickness in Talairach space.

In the left hemisphere, current source densities were found by the LORETA program in the cuneus (Brodmann area 17, 18, 30), middle (19) and superior (7) occipital lobe, lingual gyrus (17, 18), precuneus (7, 19), angular gyrus (39), inferior (40) and superior parietal lobe (7), posterior cingulum (31), middle (19, 37, 39) and superior temporal gyrus (22, 39), precentral gyrus (6), cingulate gyrus (32), and the middle and superior (6, 8, 9, 10), and medial (6, 8) frontal gyrus. Current source densities within the right hemisphere were

Figure 2.

Scalp distribution of successive microstate segments of the mean ERP data. Different map topographies characterize different processing stages. See text for description. Maps seen from above, nose on top. Scale is $\pm 4 \mu\text{V}$.

Figure 3.

Correspondence of both acquisition methods illustrated in eight contiguous slices (z = Talairach inferior-superior axis in mm). (a) The top two rows ('Mean Analysis') show the results of the LORETA and fMRI analyses over all 10 subjects. On visual inspection, both methods detected activation of the left prefrontal and left posterior cortex, and activity of the medial superior frontal cortex. (b) The bottom two rows ('Local Maxima') illustrate the

correspondence method. The circled red voxel locations in the first row of (b) display the local maxima found for the LORETA analysis of the mean ERP. The circled green voxel locations in the bottom row display the nearest found fMRI voxel. This nearest distance is represented by the black arrows (light gray arrows refer to slice $z = 57$ that is not shown).

found in the cuneus (17, 18, 30), middle occipital gyrus (19), lingual gyrus (17, 18), precuneus (7), supramarginal gyrus (40), posterior cingulum (31), postcentral gyrus (1, 2), inferior (19, 37), middle (19, 37 & 39) and superior temporal gyrus (22, 39), precentral gyrus (4, 6), cingulate gyrus (32), and the middle, medial and superior frontal gyrus (8, 6).

Correspondence

The correspondence of fMRI and brain electric tomography activity maps was calculated for the mean over subjects and for each individual subject.

Mean over subject

On visual inspection (see Fig. 3a), the resulting activity maps of both methods correspond well with one

another. Both methods show bilateral occipital, left prefrontal and parietal, and midline superior frontal activity. In addition, the LORETA analysis shows a wider and higher distribution of activity of the right prefrontal cortex ($z = 1-22$), lower activity of the right pre- and postcentral gyrus ($z = 43$), and bilateral hemisphere activity of the temporo-occipital junction ($z = 8-15$), which was prominent in the individual fMRI data, but due to a wide dispersion of individual activity, was lost in the mean fMRI image. The mean nearest 3D distance between the local maxima of both methods was 17.8 mm for the grand-mean over subjects. According to the bootstrapping method, this correspondence is significant ($P < 0.048$). Figure 3b illustrates the correspondence method. The first row of Figure 3b displays local maxima (red) of the LORETA analysis of the grand mean ERP (see first row of Fig. 3a). The bottom row displays the nearest

TABLE I. Individual match: mean nearest distance between fMRI and ERP local maxima, and probability of correspondence for each individual subject

Subject no.	Distance (mm)	<i>p</i>
1	14.8	–
2	18.1	–
3	15.0	<0.03
4	13.2	–
5	14.4	–
6	14.3	<0.00
7	16.6	<0.01
8	14.9	<0.04
9	11.4	<0.02
10	12.3	–
<i>Average</i>	<i>14.5</i>	

found fMRI voxel (green) between the local maxima of both methods. This nearest distance is represented by the arrows.

Individual subjects

Of the 10 subjects, exactly half showed significantly corresponding activity within the common volume (summarized in Table I). The average distance over subjects between the local maxima of the microstate-weighted ERP current source densities and the nearest found BOLD contrast local maxima was 14.5 mm (see middle column of Table I for individual mean distances).

DISCUSSION

The results of this study verify that common neural networks are registered by event-related potential and BOLD-contrast data. Specifically, bilateral activity of the cuneus, middle occipital gyrus, lingual gyrus, precuneus and middle frontal gyrus, and left hemisphere activity of the inferior and superior parietal lobe, middle and superior temporal gyrus, cingulate gyrus, superior frontal gyrus and precentral gyrus were identified by both methods.

The mean correspondence between the integrated tomographic distributions of ERP current density and BOLD contrast was statistically significant without preselecting certain ERP components, without constraining number or locations of the ERP sources, and despite the fact that the 3D smoothness constraint in LORETA has no analogue in fMRI data. Visual inspection of the data indicate that most of the fMRI activation was within the solution space allowed in the

current LORETA implementation. The mean 3D distance from local ERP to local BOLD maxima was 17.8 mm (or ~2–3 LORETA voxels) for the mean data and ranged between 11.4 and 18.1 mm in individuals. Because the significant mean distance was determined on an individual level, the significant distance threshold was different for each subject. The local maxima correspondence of the mean data was significant, and half of the individual comparisons were significant according to the bootstrapping method, which is far better than the value expected by chance (5%, i.e., less than one subject). The lack of statistically significant correspondence in the other 50% of the subjects also indicate that there is no one-to-one relation between BOLD and ERP-derived tomographies. This lack of significant correspondence in all subjects could result from the multiple factors that lead to small differences or errors in temporal and spatial resolution. The difference is also reflected in the small common frequency range of the current ERP (0.1 Hz–30 Hz) and fMRI (0–0.31 Hz) data. In addition, spatial errors are to be expected from the distinct Talairach transformations of both methods (LORETA solutions are based on transformations from the 3D scalp, fMRI on the 3D brain) and finally, ERP current sources are estimated based on the smoothest 3D solution and constrained to an average gray matter volume. To overcome some of the above mentioned spatial limitations, LORETA source estimations could be computed on each subject's actual brain to better approximate the solution space and the spatial resolution of the fMRI methods; alternatively, artificially smoothing of fMRI tomographies might also improve statistical correspondence. The simultaneous measurement of both fMRI and brain electric methods, and event-related fMRI, which can also detect sequential activation patterns within a trial, could further optimize the correspondence, although hemodynamic “single-trial” responses have different shapes [Buckner et al., 1996] and different refractory periods [Huettel and McCarthy, 2000]. Further research must thus clarify if such limited correspondence also holds for other activation tests, designs, and analyses. Although unconstrained 3D tomographies are crucial to establish (rather than assume) correspondence, they may be followed by simpler dipole models to focus on the activation time course of specific corresponding sources.

CONCLUSION

In conclusion, the results of the current study suggest that the correspondence between both methods is not always accurate enough to justify constraining

ERP source solutions to spots of hemodynamic activation, as is currently suggested (and implemented in some programs). Correspondence at such an impoverished "common resolution" is clearly not the aim of multimodal imaging. It is a prerequisite, however, to characterize the same neural activation at the "full resolution" of both methods, and to detect critical differences in sensitivity between them. For those subjects with statistically significant correspondence, the combination of the high temporal and spatial resolution of both methodologies could help to further understand the neural basis of plasticity and information processing, and to detect various processing abnormalities such as processing delays or possible anatomical differences at different levels of information processing.

ACKNOWLEDGMENTS

This work represents a thesis accepted as doctoral dissertation by the faculty of arts of the University of Zurich in the Wintersemester 1999/00 on the recommendation of Prof. Dr. MC. Hepp-Reymond and Prof. F. Dr. Stoll. We would like to thank Drs. V. Marcar, F. Girard, and F. Hennel for their technical assistance.

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