

Face activated neurodynamic cortical networks

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Abstract Previous neuroimaging studies have shown that complex visual stimuli, such as faces, activate multiple brain regions, yet little is known on the dynamics and complexity of the activated cortical networks during the entire measurable evoked response. In this study, we used simulated and face-evoked empirical MEG data from an oddball study to investigate the feasibility of accurate, efficient, and reliable spatio-temporal tracking of cortical pathways over prolonged time intervals. We applied a data-driven, semiautomated approach to spatio-temporal source localization with no prior assumptions on active cortical regions to explore non-invasively face-processing dynamics and their modulation by task. Simulations demonstrated that the use of multi-start downhill simplex and data-driven selections of time intervals submitted to the Calibrated Start Spatio-Temporal (CSST) algorithm resulted in improved accuracy of the source localization and the estimation of the onset of their activity. Locations and dynamics of the identified sources indicated a distributed cortical network involved in face processing whose

complexity was task dependent. This MEG study provided the first non-invasive demonstration, agreeing with intracranial recordings, of an early onset of the activity in the fusiform face gyrus (FFG), and that frontal activation preceded parietal for responses elicited by target faces.

Keywords Magnetoencephalography · Spatio-temporal source localization · Face processing · Oddball paradigm · Fusiform face gyrus

1 Introduction

Functional magnetic resonance imaging (fMRI) studies have revealed a distributed face-processing network in the ventral visual pathway (e.g., [23]). Three regions in the occipito-temporal cortex are usually found to respond preferentially to faces: fusiform face gyrus (FFG), superior temporal sulcus (STS), and occipital face area (OFA) around the inferior occipital gyrus (e.g., [9, 18, 26, 39]). Recently, intracranial recordings in epileptic patients confirmed that up to six regions along the ventral visual pathway are involved in face recognition [6].

Scalp EEG (electroencephalography) and MEG (magnetoencephalography) studies typically report an N170/M170 component over occipito-temporal cortex that is larger to faces than control, non-face stimuli (e.g., [8, 30, 43]). Quite a few MEG studies on face processing used source analysis, mostly to locate the M170 generators [10, 16, 24, 27–29, 32, 43, 45, 59–61, 64–66]. These were found in the inferior-temporal cortex around fusiform face area, in agreement with fMRI and PET studies (e.g., [26, 39, 47]). A number of studies have reported the source(s) of the M100 component in the occipital cortex [16, 24, 45, 60, 61, 66]. We have shown that these early visual responses are related

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to face processing and they are sensitive to changes in face stimuli including face inversion [56–58]. Recent MEG study reported an early face inversion effect in the right fusiform gyrus [35].

Halgren et al. [16] modeled cortical activity during the first 270 ms with three equivalent current dipoles (ECDs). They demonstrated that a midline occipital source at 110 ms showed distinct activity for faces and control stimuli, and it was sensitive to low-level stimulus features and emotional content. Left and right occipito-temporal sources were active at around 170 ms and were larger to true than randomized faces, were strongest to face photographs, and did not change significantly for different emotional expressions. At 256 ms, these occipito-temporal sources distinguished true from randomized faces, but were not sensitive to emotional expressions. Watanabe et al. [66] modeled MEG responses to upright and inverted images by three ECDs located in the occipital lobe around the midline, in the inferior-temporal cortex and in the lateral temporal cortex, separately for the two hemispheres. They suggested that the locations of sources activated by upright and inverted faces were the same, but their dynamics were modulated by the inversion. Itier et al. [24] used the beamformer technique to identify sources of M100, M170, and M220 to upright, inverted, and contrast-reversed faces, respectively. The sources of M100 and M220 were found bilaterally in the occipital lobe medially and around the middle occipital region, respectively. For the M170, they identified a bilateral posterior source and an unilateral, right-hemisphere source, more anteriorly around the fusiform gyrus. Source locations or intensity were not different for upright, inverted, and contrast-reversed images. Itier and colleagues also suggested that M220 is the reactivation of the bilateral M170 source as their locations were not significantly different. Schweinberger et al. [45] fitted pairs of symmetric sources for each component; both M100 and M170 were modeled with two sources located in the occipito-temporal cortex, while two pairs of sources for the repetition-sensitive M250 response were localized around FFA and cingulate gyrus, respectively.

To explore face activated neurodynamic cortical networks, we used a semiautomated approach to spatio-temporal source localization with no a priori assumptions on active cortical regions. For multiple current-dipole models, inverse-problem solutions are often very sensitive to the starting parameters (dipole locations and orientations). Selection of the starting parameters can easily lead the search to a local minimum [51–53]. To avoid this problem, semi-automated multi-start algorithms have been developed [21, 41], which for a given time interval and number of dipoles randomly select hundreds or thousands of initial starting locations from a variable resolution grid in the brain volume to help in finding the global minimum. Compared to the standard localization methods, the multi-

start approach offers distinct advantages: the selection of the initial starting parameters without user bias, the calculation of thousands of unconstrained independent fits in the search for a global minimum, the use of the data from all sensors and no constraints for the best-fitting parameters. Multi-start downhill simplex minimization increases the probability of finding the best model fit to the measured data and consequently an adequate and accurate source dynamics estimate. This multi-start spatio-temporal modeling technique was evaluated on simulated and empirical data, and has been shown to represent a significant improvement over traditional inverse methods in terms of source localization accuracy and ability to model previously unknown and/or weak sources (e.g., [3, 21, 49]).

Numerical simulations demonstrated that statistical measures of goodness of fit such as reduced chi-square value and, for empirical data in particular, its saturation can be effective in determining model order which may be equal or smaller than the number of the active sources [51–53]. Simulations also indicated that the evaluation of several model orders is necessary. Physiological plausibility of results should also be evaluated whenever possible (e.g., [3]). Singular-value decomposition may be used to narrow down the range of model orders to be evaluated as it gives a minimum number of independent sources, i.e., the minimum model order [21].

Typically, the entire interval of transient evoked neuromagnetic response is submitted to the inverse procedure (e.g., [3, 21, 49]). Time-course estimation accuracy, however, is critically dependent on the resolution of all active regions [52]. Consequently, we explored the effects of the time-interval selections submitted to the spatio-temporal source localization procedure on the source resolution and accuracy in the estimation of the best-fitting location and time-course parameters. In this study, we also searched for the optimal number of starting points for selected data-driven choices of time intervals for the multi-start downhill simplex search to improve its efficiency and the reliability of its results. All simulations were driven by our rather challenging set of MEG data evoked by faces in an oddball paradigm. Results from simulation studies helped us to adopt more efficient strategies for following dynamics of complex cortical pathways with an improved accuracy of location and, in particular, onset of cortical activations.

Overall, neuroimaging studies have reported distributed cortical networks involved in face processing, but neither their dynamics nor complexity is still fully understood. As fMRI has a poor temporal resolution and intracranial recordings are invasive, MEG is the method of choice to investigate both dynamics and complexity of face-activated cortical networks and their task-related modifications. Previous MEG studies mostly concentrated on finding the sources of some components such as M100 and M170,

often using a priori assumptions on cortical regions involved. Using an effective strategy in spatio-temporal source localization, we wanted to estimate the sequence of activation of sources during the entire transient evoked neuromagnetic response to a face, with no a priori assumptions. As we analyzed empirical data from an oddball study, we were also able to examine task-related modulations by target detection.

2 Methods

2.1 Spatio-temporal source localization

Neuromagnetic activity was modeled assuming multiple rotating current dipoles in a spherical head model using the Calibrated Start Spatio-Temporal (CSST) inverse procedure incorporated in MRIVIEW [41]. An automated segmentation tool was used to label each subject's cortical surface volume. The starting points were randomly selected mostly from the segmented cortex but also from the brain volume close to it. The simplex search volume and the best-fitting dipole locations were, however, not constrained to any preselected volume. The segmented cortical surface was used to estimate the best-fitting sphere for the head model. Dipole location parameters (x , y , z coordinates) were fitted first and kept constant for the selected time window while dipole strength and orientation (Q_x , Q_y , Q_z) were estimated for each time instance. The CSST inverse procedure involved a two-stage multi-start simplex minimization of the reduced chi-square (χ_r^2). Singular-value decomposition was performed on the data to estimate the minimum model order, which was used to start the model-order search. The best-fitting model parameters were obtained by minimizing the reduced chi-square (χ_r^2) [51, 52] for each model order assumed. Since best-fitting solutions for an adequate model of the data tend to form clusters [21, 51], adequate solution estimates were evaluated for that criterion as well, in addition to evaluate residual field waveforms and the saturation of the reduced chi-square value [51]. To estimate the effects of measurement noise on the best-fitting location parameters, we performed 100 Monte Carlo simulations by adding Gaussian noise from the baseline time window to the modeled MEG fields created by the best-fitting solution. The locations of the identified sources were shown superimposed on individual MRIs for all subjects.

To explore the effect of time-interval length on the accuracy of source localization and the onset of the identified sources, we considered the entire time interval of evoked response, and selections of shorter time intervals. Visual inspection of waveforms and isofield contour maps were used to estimate the duration of activity of assumed

sources and, accordingly, initial short-time intervals were selected to involve most of the activity of individual sources. Our previous simulations [55] have demonstrated that a data-driven choice of time windows for the analysis is as efficient as an optimized regular time window scanning across the entire spatio-temporal data matrix whose length was found to depend on source configuration. The selection of the time windows was guided by visual inspection of isofield contour maps; the width of the time window was determined by the field minima. Because of the complexity of face-evoked MEG data, we varied the width and the start of time interval (e.g., for 10–30 ms) to determine how these affect the locations and dynamics of the identified sources.

For longer time intervals and a larger number of active sources, thousands of initial starting locations were needed to get the best-fitting solutions tightly clustered, whereas for shorter time intervals and two or three active dipoles, hundreds of initial starting locations were sufficient to obtain stable best-fitting solutions. Using simulation results and varying the number of starting locations in the empirical data sets, we optimized that number for each particular choice of time intervals considered; the main criteria were saturation of χ_r^2 and tight clustering of solutions. The number of initial starting locations depended on the length of the analyzed time window and assumed number of dipoles, and ranged between 100 and 15000 in our analyses of empirical data.

2.2 Simulated data

The simulated data sets were generated using the Forward Simulator within MRIVIEW. A segmented cortical surface from a subject's MRI was used to determine the local cortical geometry. Locations, strengths, and dynamics of the simulated point-dipole sources were defined to correspond to the typical findings from the empirical data; the source orientation was assumed to be perpendicular to the local cortical geometry. We modeled 5–8 sources in occipital, temporal, and parietal regions with minimal distance between sources of 25 mm. The forward fields were computed using a spherical head model and the Sarvas formula [44], with a sensor configuration derived from an empirical data set. Gaussian white noise was added to the simulated MEG activity to calculate forward fields, which were then submitted to the CSST inverse procedure. The standard deviation of the noise was variable across channels, and it was chosen to correspond to the noise level from our empirical data.

2.3 Empirical data from a face oddball study

Gray-scale face stimuli were presented centrally with a visual angle of $2.7^\circ \times 2.2^\circ$ for 150 ms by the Presentation

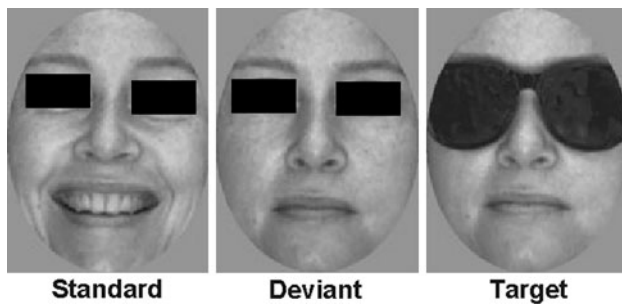


Fig. 1 The face stimuli used in an oddball paradigm

software (Neurobehavioral Systems Inc, Albany, CA). During the inter-stimulus interval of 450 ms, the subjects fixated on a dark gray cross at the center of the screen. Face stimuli (Fig. 1) were presented in an oddball paradigm ($P_{\text{standard}} = 0.8$, $P_{\text{deviant}} = P_{\text{target}} = 0.1$). The task was silent counting of the target face. The subjects were presented with 100 deviants, approximately 800 standards, and 100 targets.

The MEG signals were recorded in a magnetically shielded room (Euroshield Ltd, Finland) at the BioMag Laboratory, HUCH, with a 306-channel whole-head system (Elekta Neuromag Oy, Helsinki, Finland) comprising 204 planar gradiometers and 102 magnetometers. Horizontal and vertical eye movements were monitored with electro-oculogram (EOG) electrodes placed above and below the left eye and lateral to each eye. The MEG data were recorded with a bandwidth of 0.1–200 Hz and sampled at 600 Hz.

To remove external noise from the data, we used the spatio-temporal Signal Space Separation method (tSSS) [62, 63]. Signals were averaged offline separately for standard, deviant, and target stimuli over a time interval starting 100 ms before and ending 550 ms after the stimulus onset. Epochs with EOG or MEG values exceeding 150 μV or 3000 fT/cm, respectively, were excluded from averaging. The averaged MEG data were preprocessed using MEGAN, an MEG data visualization tool developed by Elaine Best from the Biophysics Group, Los Alamos National Laboratory. The averaged data were digitally low-pass-filtered at 40 Hz; the mean signal value between 100 and 0 ms before stimulus onset served as the baseline.

3 Results

3.1 Simulations

We conducted a number of simulations to examine the impact of time interval width on the accuracy of the inverse solutions. Here, we show two sets of simulated data to illustrate our main findings.

Figure 2a shows locations and dynamics of five simulated sources during 100 ms, similar to the previous empirical study which has identified five sources in the time interval 80–165 ms [2]. The distance between sources was quite small (the closest sources were set 25 mm apart) as it is often found in visual MEG studies (e.g., [2]). Several sources were simultaneously active, which poses a particular challenge for the spatio-temporal source localization (e.g., [48, 52, 53]). In addition, some dipoles had unequal strength, which also reduces the separability [51]. It was not possible to identify dipole 1 when the whole-time interval was submitted to the inverse procedure (Fig. 2b) although the correct model order was used. However, for the 50-ms time intervals all five sources were identified (Fig. 2c). The initial locations and time courses of each of the identified dipoles were rather accurately estimated. The largest error in location and dynamics was found for the closest simultaneously active sources of unequal strength (dipoles 3 and 4). As our previous study [55] has shown, data-driven choice of time windows submitted to the analysis yielded to more accurate source locations and time course estimates.

Figure 3 shows the dynamics of the identified sources for an example fit to the six-source simulated data (panel c), for the whole time interval (panel d), and shorter time intervals (panel e). Visual inspection of the MEG waveform (Fig. 3b) advocated for division to three shorter time intervals. Evaluation of several model orders suggested that roughly two dipoles are active in each of these shorter time intervals. In order to determine the onset of dipole 3, several time windows were analyzed and one of them (120–160 ms) is shown in Fig. 3e. For the whole time interval, the best-fitting solution was calculated with 10000 initial starting locations, while best-fitting solutions for the smaller time intervals clustered already for 50 initial starting locations.

Simulations again showed an improvement in source localization accuracy for shorter time intervals (Fig. 3f). For example, dipole 4 was 14 mm from the simulated source when fitted for the whole time interval (80–300 ms), and only 2.6 mm when fitted for the time interval 160–200 ms. The dynamics of the estimated sources were also more accurate for the short-time intervals. For example, for the whole-interval fit, the onset of dipole 3 seemed to be at about 100 ms, not at 130 ms as set up in the simulations. These problems with accuracy of estimated sources usually occurred for the nearby sources (e.g., sources 2 and 4 were only 25 mm apart), even when they were not synchronously active. However, they were easily resolved by considering shorter intervals, and thus separating their activity in time. The analysis of shorter time intervals was not more time-consuming than the analysis of the whole-time interval because a rather small number of

Fig. 2 **a** Locations and dynamics of five simulated sources. Locations and dynamics of ten best-fitting solutions obtained for **b** the whole-time interval, and **c** time intervals 80–130 and 130–180 ms

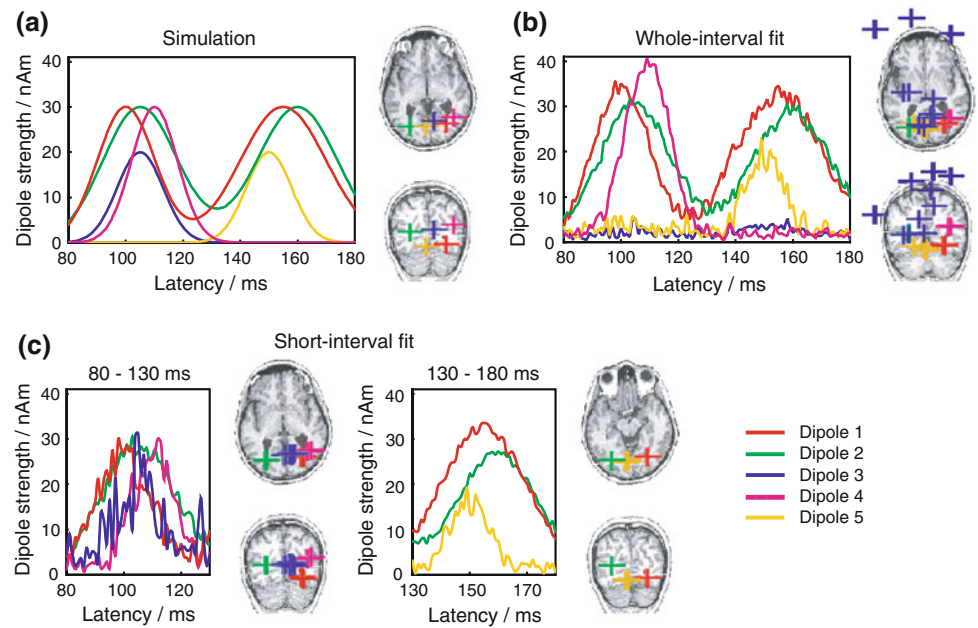
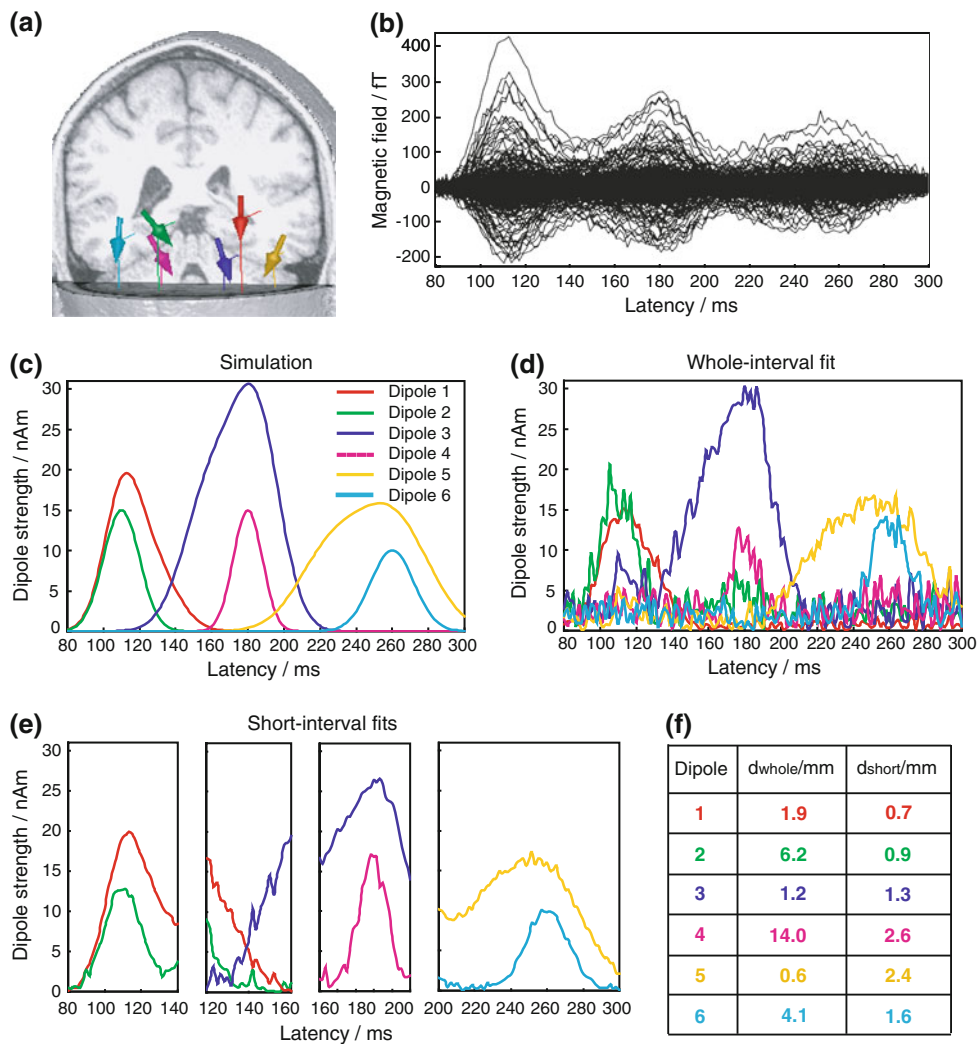


Fig. 3 **a** Simulated sources were located in the right and left occipital cortex (dipoles 1 and 2), around right and left fusiform gyrus (dipoles 3 and 4), and in the right inferior-temporal and left occipito-temporal regions (dipoles 5 and 6). **b** Simulated field values were calculated at all sensor locations and Gaussian noise with standard deviation of 10 fT was added. **c** Dynamics of six simulated sources. **d** One of the best-fitting time course estimates for the whole-time interval calculated with 10000 initial starting locations and adequate model order. **e** The whole-time interval is divided in shorter intervals and submitted to the inverse procedure with 50 initial starting locations. Time course estimates for characteristic time windows are displayed. **f** Displacement from simulated (i.e., actual) locations of dipole location estimates calculated by considering the entire time interval and short, selected time intervals, respectively



initial starting locations were sufficient for short-time intervals to obtain good clustering of the best-fitting solutions.

3.2 Empirical data from a face oddball study

3.2.1 Face-processing cortical pathways

Figure 4 and Table 1 show anatomical locations and the sequence of activation of the estimated sources during 400 ms of the transient evoked response for three subjects with best signal-to-noise ratio. The MEG response to the happy standard face was modeled with ECDs fitted in the indicated time intervals. In all three subjects, early occipital sources were identified, followed by occipito-temporal and inferior-temporal sources in both hemispheres. In addition, for two subjects, we found activation of parietal sources and reactivation of occipital areas at later latencies.

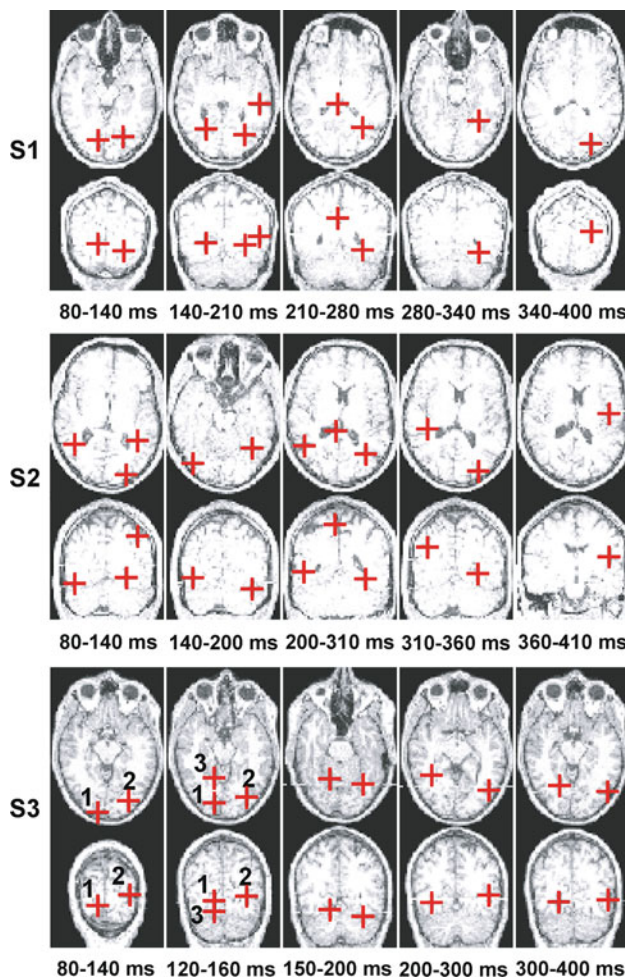


Fig. 4 Locations of the estimated current dipoles identified from MEG responses to happy standard face for three subjects

Figure 5a shows locations and dynamics of eight ECDs fitted in the time interval 80–400 ms for subject S1. A singular-value decomposition and saturation of statistical measures of goodness of fit suggested an 8-dipole model. Further analysis using shorter time intervals showed, however, that this solution should be reconsidered. The isofield contour maps for MEG response at 110 and 170 ms (Fig. 5b) and singular-value decomposition of corresponding time windows suggested the activity of two pairs of nearby sources with opposite directions. Inverse solutions obtained for the time intervals 80–140 and 140–210 ms confirmed this presumption (Fig. 5b). Different orientations of the identified sources clearly indicated an activation of distinct parts of the cortical surface. The distances between the two left and the two right posterior sources identified in these two subsequent time intervals were 18 and 11 mm, respectively. However, when the entire time interval was analyzed, these close sources could not be separated. Similar results were obtained for a 9-dipole model. As our simulation suggested, we had to analyze shorter time intervals to identify adjacent sources.

Furthermore, it is likely that the source dynamics obtained for the whole time interval were not accurate. For example, there were eight active sources in the time interval 140–210 ms for the whole-interval fit (Fig. 5a), which did not seem plausible from the isofield contour maps and singular-value decomposition. When an 8-dipole model was fitted to the 140–210 ms interval, some sources were outside the head, suggesting over modeling. A 3-dipole solution obtained for the same interval indicated activation of left and right occipito-temporal sources and a right temporal source (Fig. 5b). Analysis for the time interval 80–140 ms showed corresponding results; it is not likely that eight distinguishable sources were active in that time interval. As our simulation implied, analysis of shorter time intervals and lower model order brought a more plausible solution and consequently more accurate dynamics.

3.2.2 Onset of the activity in the FFG

Table 2 shows estimated onsets of activity in the left and right inferior-temporal cortical regions around fusiform gyrus for the happy standard face. Estimated onsets varied a lot, even for subjects whose data had a very good signal-to-noise ratio, such as subjects S1, S2, and S3. Namely, we identified only the right FFG source, with an onset at 210 ms, for S1. The onset times for S2 were 80 ms for left FFG source and 150 ms for right FFG source. For S3, left FFG became active at 120 ms and right FFG at 160 ms. For S8, we did not identify any sources in the inferior-temporal cortex around fusiform gyrus.

Table 1 Order of activation of the identified sources for subjects S1, S2, and S3. Sometimes identified sources were localized in adjacent cortical patches but they had distinct locations and orientations during indicated time intervals

S1		S2		S3	
Time interval	Identified sources	Time interval	Identified sources	Time interval	Identified sources
80–140 ms	Left occipital Right occipital	80–140 ms	Right occipital Left inferior-temporal Right parietal	80–140 ms	Left occipital Right occipital
140–210 ms	Right temporal Left occipito-temporal Right occipito-temporal	140–200 ms	Left occipito-temporal Right inferior-temporal	120–160 ms	Left inferior-temporal Right occipito-temporal
210–280 ms	Mid-parietal Right inferior-temporal	200–310 ms	Left near parieto-occipito-temporal border Mid-parietal Right occipito-temporal	150–200 ms	Left inferior-temporal Right occipito-temporal
280–340 ms	Right inferior-temporal	310–360 ms	Left parietal Right occipital	200–300 ms	Left inferior-temporal Right occipito-temporal
340–400 ms	Occipito-parietal	360–410 ms	Right frontal	300–400 ms	Left inferior-temporal Right occipito-temporal

Approximate onset times were determined by varying the number of dipoles and time windows around selected time points identified by visual inspection of contour maps. This was not always straightforward because of other simultaneously active sources. For example, for S3, visual inspection of contour maps, singular-value decomposition and source localization in various time intervals suggested early activation of two occipital sources (dipoles 1 and 2 in Fig. 4) followed by left inferior-temporal source with onset around 120 ms (dipole 3 in Fig. 4). However, when three dipoles were fitted in the time window 80–160 ms, their time courses failed to show that the activity of the left inferior-temporal source had started at 120 ms (Fig. 6a); it seemed that dipole 3 was continuously active. Nevertheless, when three dipoles were fitted in the time interval 80–120 ms, no source was found in the left inferior-temporal region (Fig. 6b). We simulated an analogous situation and demonstrated that it can be resolved by analyzing shorter time intervals and by varying their starting time (Fig. 3).

3.2.3 Target detection

Source localization suggested activation of the frontal cortical areas for targets at time intervals around 260–320 ms, usually in the right hemisphere, followed by the distributed activity in the parietal cortex. This observation was consistent across all subjects. Figure 7 shows locations of identified frontal and parietal sources for the target face. Arrows in Fig. 8 schematically show the time

flow of standard and target processing for subject S1. Target faces activated a larger cortical network than standard faces, which involved frontal cortical regions.

4 Discussion

Although MEG and neuromagnetic source localization have millisecond temporal resolution, information on the source dynamics (e.g., onset of the activity) often cannot be easily retrieved from the data. Previous simulation studies have shown larger errors for the dynamics than for the location of the identified sources [51, 52]. The analysis of long-time intervals of MEG data to complex visual stimuli such as faces poses a particular challenge. In this study, we used simulated data to show that analysis of data-driven choices of shorter time intervals leads to more accurate neuromagnetic source localization and time-course estimates. We applied these findings in the analysis of MEG data to faces in an oddball paradigm to explore face-processing pathways and task-related modulations. The nature of our study was iterative; we performed empirical data-driven simulations which led to the simulation-driven optimization of the spatio-temporal analysis of face data.

4.1 Simulations

Our simulation results suggested that it is advantageous to submit shorter time windows than the whole-time interval to the inverse procedure, especially in two cases: (1) when

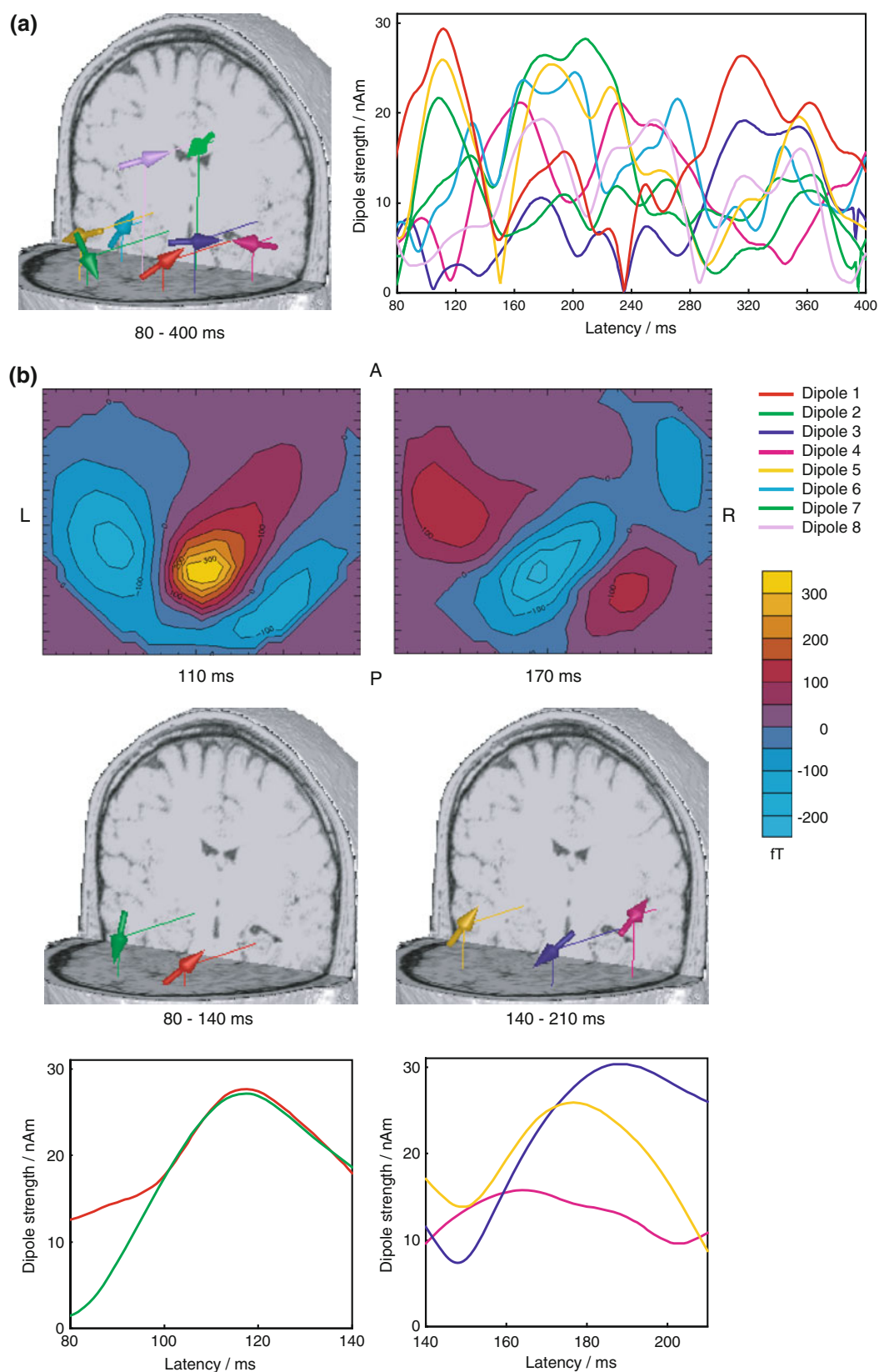
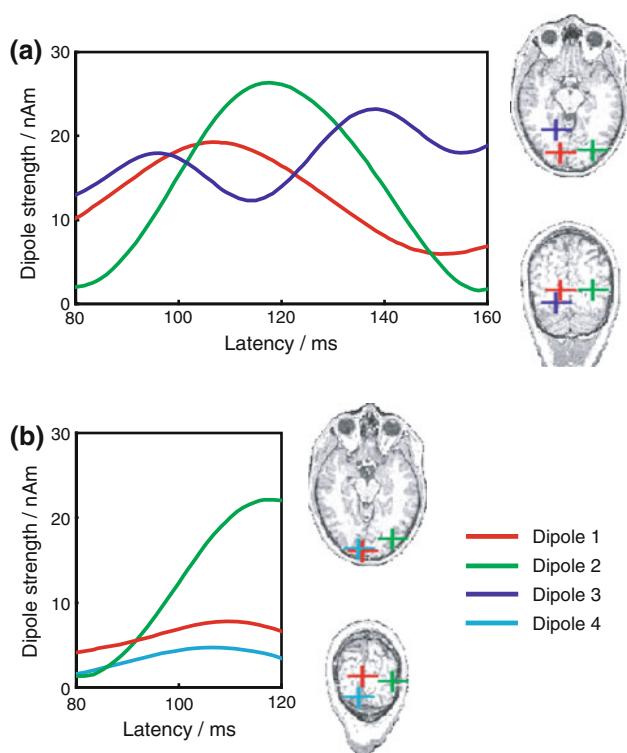


Fig. 5 **a** Locations and time-courses for an eight-dipole model applied to the whole-time interval (80–400 ms) for subject S1. **b** The isosurface maps for the measured MEG responses to

standard face stimulus at 110 and 170 ms, and locations of the corresponding sources identified for the time intervals 80–140 and 140–210 ms

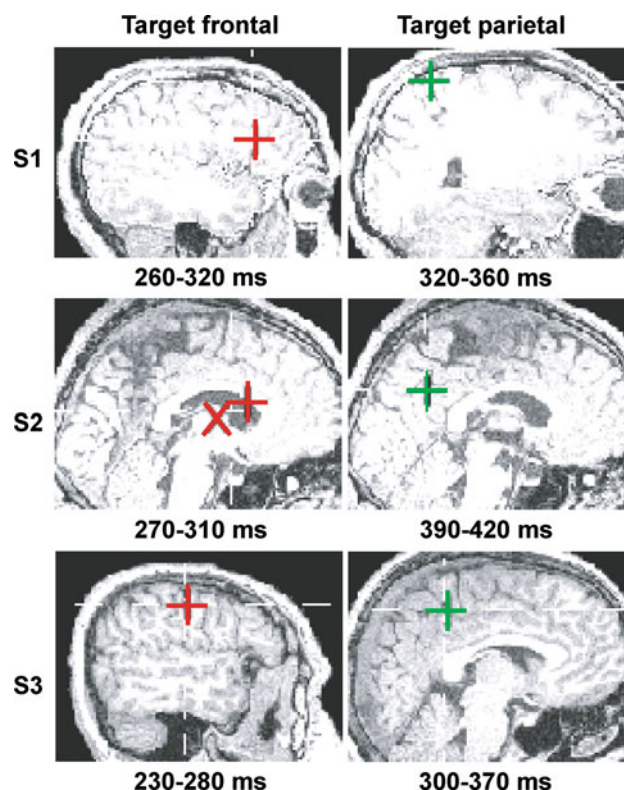
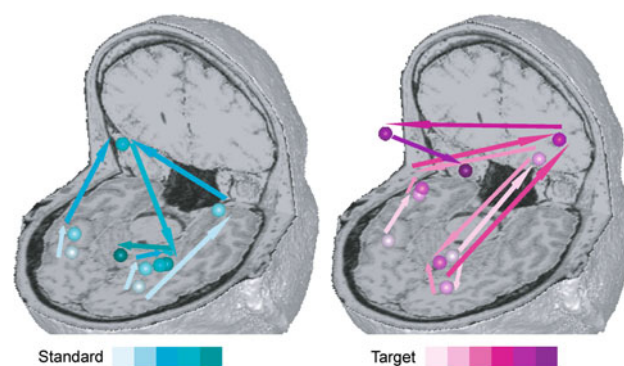
Table 2 Estimated onsets of the activation of the inferior-temporal cortex around the left and right fusiform face areas

Subject	Latency/ms	
	Left FFA	Right FFA
S1	–	210
S2	80	150
S3	120	160
S4	80	90
S5	135	120
S6	–	100
S7	120	180
S8	–	–

**Fig. 6** Locations and time-courses for a three-dipole model applied to time intervals 80–160 and 80–120 ms. Two sources were identified for both time windows (*red* and *green*). Left inferior-temporal source (*dark blue*), which was identified at 80–160 ms and appeared to be active all the time could not be localized at 80–120 ms. Instead, another left occipital source (*light blue*) was identified quite close to another source with the opposite orientation, suggesting over-modeling situation (Color figure online)

sources are rather close, which is often the case within the visual modality; (2) when the onset of a particular source is explored.

Division of the whole time interval helps in localization of rather close cortical sources which are not separable otherwise. Usually simultaneously active sources are most

**Fig. 7** Locations of frontal (*red*) and parietal (*green*) estimated current dipoles identified in the indicated time intervals for MEG responses to targets for three subjects. For S2, two frontal sources were identified (marked by + and x) (Color figure online)**Fig. 8** Locations of estimated current sources for standard and target face for S1 at time interval 80–400 ms. Arrows schematically show temporal sequence of cortical activations; time is shown by monochromatic color bars (*light colors* for earlier time intervals) (Color figure online)

difficult to estimate accurately (e.g., [48, 52]). Even non-simultaneous sources can be problematic for source localization if they are close and have similar orientation (e.g., [33, 52]). Segmentation of the evoked response in shorter time intervals enables separation of their activity in time. This results in better location accuracy, and consequently, allows a more accurate estimate of source dynamics. Analysis of shorter time intervals is also helpful when

some of the sources are simultaneously active (Fig. 2). Usually, in a shorter time interval fewer sources are active, thus lower model orders are used. A decrease in the number of fitted parameters in the inverse calculation leads to better estimation accuracy because of the smaller number of local minima.

Analysis of data-driven choices of shorter time intervals is also needed to obtain a good estimate of the onset of certain simulated sources. Sometimes, in the analysis of the whole time interval a “ghost” activity appears before the actual source onset because the model assumption “forces” sources to be active all the time. It is advisable to apply a number of time intervals of different lengths at different start latency to examine if the source was actually active or just “forced” to be active.

Weaker sources (with smaller amplitude and briefly active) cannot always be localized using the whole-time interval because other nearby stronger sources “take over” their activity. Using a shorter time interval facilitates localization of such sources, again because activity of different sources may be separable in time and/or because lower model order may be applied. In general, submission of shorter time intervals to the inverse calculation circumvents some weak points in the multi-start downhill simplex method such as “forcing” sources to be active during the entire interval of the evoked response.

4.2 Empirical data from a face oddball study

4.2.1 Face-processing cortical pathways

Using advanced multi-start source localization of neuro-magnetic responses to standard faces from an oddball paradigm, we investigated spatio-temporal dynamics of the face-processing pathways during the entire 400 ms of the transient evoked response. We identified 8–11 sources that were mostly located in occipital, occipito-temporal, inferior-temporal, parietal, and temporal cortex. Here, we showed results for three subjects with best signal-to-noise ratio; similar results were obtained for other subjects, too. Locations of identified sources are in agreement with direct evidence from intracranial ERP recordings in humans (e.g., [4, 6, 7, 11–14, 34, 40]) and single-neuron studies in monkeys (e.g., [36–38, 50]). Our findings also corroborate PET and fMRI reports on a distributed face-processing network, especially in the ventral visual pathway (e.g., [23, 26, 39, 47]).

Previous studies mostly modeled MEG responses to faces by sources in the occipital and occipito-temporal cortex (e.g., [16, 24, 29, 43, 45, 59–61, 64–66]). Lu et al. [32] found three areas outside the occipital visual cortex involved in face processing: an area around the occipito-temporal junction, the inferior parietal lobe, and the middle temporal lobe. There are at least three reasons why we

were able to locate face-related activity in more brain regions than previous studies. First, our data had a very good signal-to-noise ratio, since about 800 responses were averaged for standards. Second, we used rather short-time intervals, which enabled us to identify weaker sources that were not likely to be found in the longer time intervals usually used in previous studies (e.g., [16, 65, 66]). Our simulation results argued for the analysis of shorter time intervals, in accordance with previous simulation and empirical results [53] as well as the present results of our empirical data analysis. Third, we used a multi-start localization approach with no assumptions about source localization, which was not the case in the previous studies [24, 45, 65, 66].

Depth-recorded potentials found the earliest response to faces in the occipital lobe followed by activation of basal occipito-temporal cortex (fusiform gyrus) and many other structures in the occipital, temporal, and parietal lobes [11]. For all subjects, we found the initial activation in the occipital cortex. The subsequent sequence of activation was subject-dependent. For example, for subject S2 we identified a left inferior-temporal source at 80–140 ms and a right parietal source at 110–150 ms after the stimulus onset, while for S3 we did not identify a parietal source at all. Also, for S3 a left inferior-temporal source was activated around 120 ms. These inter-individual differences are partially due to variability in functional neuroanatomy. As MEG measures mainly activity from the cortical fissures [17], different folding of the cortical surface yields different magnetic fields on the head surface. The large inter-individual differences found in this study are likely to be related both to differences in individual functional geometries well documented for V1 [2, 5, 46] and the central presentation of the visual stimuli that cause cancellation of the magnetic fields on the head surface as shown by simulation [20] and empirical studies [25], which prevents localization of all active sources. Some MEG studies have already discussed the origin of the inter-individual differences in visual MEG data (e.g., [1, 2]). Inter-subject differences in a sequence of activations of brain regions to the same stimulus have been reported as well [54]. The inter-individual variability is also found in intracranial recordings, though they might be partly explained by different electrode placements in each patient to define the epileptogenic zone. Our results showed that our neurodynamics estimation approach allows us to non-invasively follow the activity of face-processing networks in space and time.

4.2.2 Onset of the activity in the FFG

Our results on the early onset of the MEG response to faces in the inferior-temporal regions around FFG are in

agreement with a previous MEG study, which reported a face inversion effect in the FFG between 70 and 100 ms after stimulus onset [35]. Localization of early differences in the EEG response to faces and buildings also revealed that FFG is involved in a very early stage of face processing [19]. These results are in agreement with intracranial recordings [6, 11]. They suggest a rapid propagation of visual information on faces from the primary areas to extrastriate visual areas related to face processing.

Many studies have localized the M170 response around FFG (e.g., [10, 16, 24, 29–32, 43, 45, 59–61, 65, 66]). Although we had a very good signal-to-noise ratio for the standards, we did not find activation of the FFG around 170 ms for one subject; for subject S1, we identified a source around the right FFG just at the time interval 210–280 ms and later. Some previous MEG studies also did not find activity around 170 ms around FFG for all subjects (e.g., [43]). Intracranial ERP studies suggested activation of multiple areas in the occipito-temporal and the inferior-temporal cortex by face stimuli around 170 ms [4, 6, 11]; it is possible that some MEG studies as well as this study were not able to separate distinct multiple nearby foci for all subjects. Consequently, the location of the right posterior source identified during the time interval of 140–210 ms for S1 might correspond to an equivalent center of gravity of multiple activated areas.

4.2.3 Target detection

At later time intervals, in the range of 260–320 ms, a strong target-related activity was evident, and frontal sources were localized for all subjects despite rather large intersubject differences in cortical activations in other regions. The activity in the anterior regions was followed by the activation in the parietal cortex during the time windows in the range of 300–420 ms. Many studies have reported activation of a distributed parieto-frontal neuronal network during an oddball task in different modalities (e.g., [7, 13–15, 22]). We are the first to observe non-invasively that frontal activation precedes parietal, which is in line with results of intracranial recordings [7, 13]. The identified cortical pathway was selectively activated by the attentional switch to the target and consequently might represent a neural correlate of the target detection. Activation of the frontal and the parietal sources might have been related to the silent counting task [42, 67].

To summarize, we conducted a number of simulations to optimize our analysis approach. Results of our simulation studies showed that it is advantageous to use a shorter time interval in semi-automated multi-start spatio-temporal localization of close sources and in the estimation of source onset. We employed this strategy on our empirical data

from an oddball study with faces. Our approach enabled us to identify many regions involved in the face processing and the early onset of the FFG activity, both of which have not been reported in previous MEG studies.

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