LOCALIZATION OF INDEPENDENT COMPONENTS FROM MAGNETOENCEPHALOGRAPHY

Akaysha C. Tang,[123] *Dan Phung,*[12] *Barak A. Pearlmutter,*[23] *Robert Christner*[4]

Departments of [1]Psychology, [2]Computer Science, [3]Neurosciences,
University of New Mexico, Albuquerque, NM 87131, USA

[4]National Foundation for Functional Brain Imaging,
801 University Blvd, Suite 200, Albuquerque, NM 87106, USA

ABSTRACT

Blind source separation (BSS) decomposes a multidimensional time series into a set of sources, each with a one-dimensional time course and a fixed spatial distribution. For EEG and MEG, the former corresponds to the simultaneously separated and temporally overlapping signals for continuous non-averaged data; the latter corresponds to the set of attenuations from the sources to the sensors. These sensor projection vectors give information on the spatial locations of the sources. Here we use standard Neuromag dipole-fitting software to localize BSS-separated components of MEG data collected in several tasks in which visual, auditory, and somatosensory stimuli all play a role. We found that BSS-separated components with stimulus- or motor-locked responses can be localized to physiological and anatomically meaningful locations within the brain.

1. INTRODUCTION

Blind source separation (BSS) algorithms, such as Infomax (Bell and Sejnowski, 1995), second-order blind identification (SOBI) (Belouchrani et al., 1993), and fICA (Hyvarinen and Oja, 1997) have been applied successfully to electroencephalography (EEG) and magnetoencephalography (MEG) data resulting in several important technical and scientific advances. These algorithms can separate neuronal activity from various artifacts (Makeig et al., 1996; Vigário et al., 1998; Jung et al., 1998; Tang et al., 1999), such as eye-blinks, which often cause fairly large amounts of data to be discarded. In contrast with methods that rely on the use of a template, BSS removes these artifacts without any prior assumptions about the nature of the waveforms. Another technical improvement is that BSS-separated sources are sufficiently clean to show evoked responses in single trials (Jung et al., 1999; Tang et al., 2000). When coupled with the millisecond temporal precision of the EEG or MEG, this capability to perform single trial analysis permits the study of the precise timing of populational neuronal evoked responses (Tang et al., 2000) and allows one to distinguish between the absence of rhythmic activity and the absence of phase-locked rhythmic activity (Makeig et al., 1999a).

Since each of the BSS-separated components has a sensor projection, one can attempt to localize the generator(s) that give rise to the sensor projection by finding the best fitting dipole(s) using a forward model. Thus far, localization of BSS-separated components has not been attempted. Due to distortion and reduction of low spatial frequencies of the electric field signal by the skull, localization of generators from EEG data is ill posed. Consequently, it is difficult to relate the EEG independent components to specific neuronal populations in specific brain structures. In fact, researchers have carefully avoided making neuroanatomical interpretations of BSS-separated components (Makeig et al., 1996, 1997, 1999b). In magnetoencephalography, the magnetic field penetrates the skull with little distortion (Williamson and Kaufman, 1981). The precision of spatial localization of neural magnetic sources can be on the order of a few millimeters under optimal conditions and such localization has been performed routinely in both basic research and clinical studies (George et al., 1995). Given MEG's spatial resolution, it seems reasonable to map BSS-separated MEG components to neuronal populations within specific brain structures by localizing these components.

Associations between the BSS-separated components and underlying brain structures have been sug-

Supported in part by NSF CAREER award 97-02-311, the National Foundation for Functional Brain Imaging, an equipment grant from Intel corporation, the Albuquerque High Performance Computing Center, a gift from George Cowan, and a gift from the NEC Research Institute.

gested by the components' temporal profiles and the spatial patterns of their sensor projections (Tang et al., 2000). These associations are qualitative. In this paper, we use the standard Neuromag source modeling software to localize BSS-separated components as single ECDs, which provides a quantitative association between BSS-separation components and neuroanatomical areas.

2. METHODS

We tested four right-handed subjects (2 females and 2 males) in four visual reaction time tasks (90 or 270 trials per task). During these tasks, a pair of colored abstract forms were presented on each half of the display screen, one of which was the target. The subject was instructed to press either the left or right button when the target appeared on the left or right respectively. In all tasks, the target was never described to the subject prior to the experiment. The subject was to discover the target by trial and error using auditory feedback (low and high tones corresponded to correct and incorrect responses, respectively). All subjects discovered the rule within a few trials. The tasks differed in the difficulty with which the target could be determined and in their potential dependency on a particular brain structure. For the purpose of this paper, intra-task differences will not be discussed. The goal of this paper is to investigate whether BSS can separate components that correspond to focal neuronal populations during tasks that involve natural multi-modality sensory stimulation.

Blind separation by SOBI (Belouchrani et al., 1993) was performed on 122-channel continuous data sampled at 300Hz band-filtered at 1–100Hz, (see Tang et al. (1999, 2000)). For all 122 recovered components, stimulus- or response-locked averages were calculated. Components with signal-to-noise ratios below a threshold value of 2.5 were not considered for this analysis. Typically, there are no more than 20 components in each experiment that had peaks in stimulus- or response-locked averages with S/N ratios above this threshold. For this small subset of components, dipole fitting was performed to localize a potential generator. We used the Neuromag bundled software for this single ECD fitting.

We expected visual, auditory, and somatosensory components to be separated because the tasks involve visual stimulus presentation, auditory feedback, and somatosensory stimulation due to a button press. Somatosensory sources were identified by a peak response between 20 and 50ms after the button press. Visual sources were identified by a peak response between 70 and 140ms. Auditory sources (auditory feedback triggered by button press) were identified by a peak response between 50 and 140ms after the button press. Although for each sensory modality multiple cortical areas supporting primary and secondary processing have been identified, and poly-sensory areas have also been detected using MEG, for the purpose of this paper we focused on neuronal populations within the primary visual, auditory, and somatosensory cortices rather than on secondary sources.

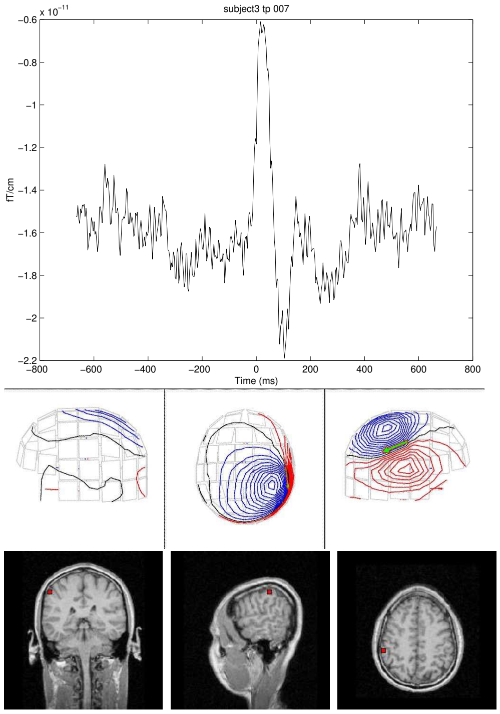

Figure 1: Localization of BSS-separated somatosensory component (Subject 3 Source 007). (top). Event-locked average for the component. Single trials (90)are aligned by the button press and then averaged. (middle) Contour plots of the field maps (left, dorsal, and right view). (bottom) component localized as a single ECD, superimposed on the MRIs. Radiologic convention: left on the right and right on the left.

3. RESULTS

SOBI-separated somatosensory, visual, and auditory components are shown in event-locked averages and contour plots along with fitted dipoles super-imposed on MRI images (3 of the 4 subjects had MRI). All components included in the analysis were first screened by their S/N ratio (> 2.5) and then by the confidence volumes of their dipole fits ($< 10mm^3$). *Somatosen-*

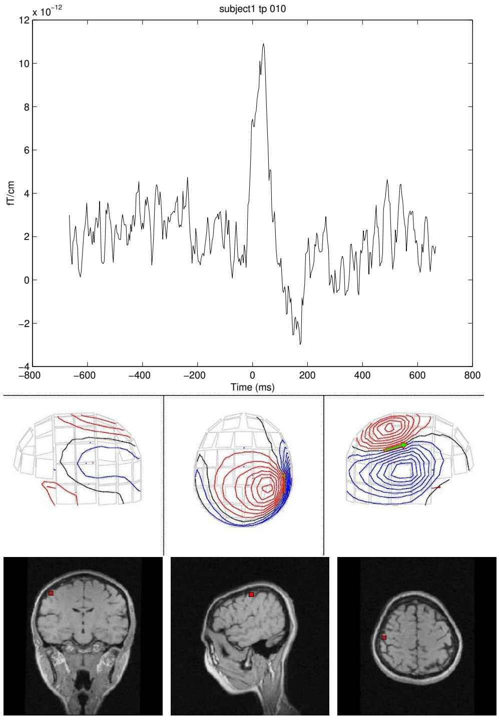

Figure 2: Localization of BSS-separated somatosensory component (Subject 1 Source 010).

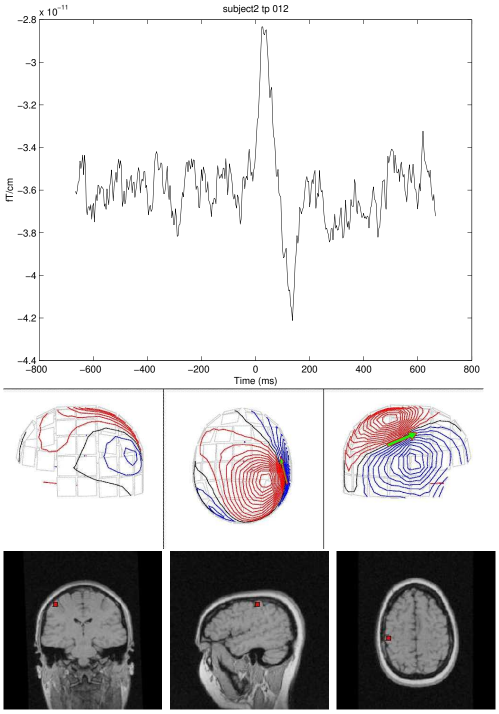

Figure 3: Localization of BSS-separated somatosensory component (Subject 2 Source 012).

sory Sources. We were able to identify components with button-press-locked responses having latencies of 38.3 ± 4.8ms, and with dipoles localized to the hand region of the somatosensory cortex (Fig. 1, 2, and 3), which indicates their somatosensory origin. In all three subjects, we show a fitted dipole in the right hemisphere (bottom panels). Because a thumb button press was required and thumb movement should stimulate the median nerve, it was expected that these putative somatosensory components would be localized in the same region that is normally activated by median nerve stimulation (Hari and Forss, 1999).

The goodness of fits for these BSS-separated components were $73.6 \pm 8.36\%$. These fits are far superior to the $40.7 \pm 5.4\%$ of somatosensory sources modeled using the event-locked average from the best sensor, the conventional method. Compared to the goodness of fits reported in the literature for median nerve stimulation, these numbers may appear to be low. However this is to be expected, because, unlike the precisely controlled median nerve stimulation, the somatosensory sources modeled here reflect the more natural and more variable stimulation of the larger somatosensory area involved during the thumb button-press.

Visual Sources. Early visual responses to colored arbitrary forms with a latency of 109.47 ± 10.4ms were identified. Fig. 4 shows one such component localized to the occipital lobe, consistent with the literature (Aine et al., 1995; Hashimoto et al., 1999; Portin et al., 1999). Across subjects, the precise location of this source within the occipital lobe differs: some are more medial and some more dorsal. The goodness of fits are $76.0 \pm 3.1\%$, much better than the goodness of fits of $65.8 \pm 5.02\%$ for the same type of sources modeled using the conventional procedure.

Auditory Sources. Auditory responses to the low/high tone feedback with peak latencies of 101.5 ± 18.0ms were found for a subset of tasks. This auditory component can be localized to the primary auditory cortex in the lateral fissure. Fig. 5 shows one such localized auditory source. The goodness of fit is $59.3 \pm 5.7\%$, which is poorer than the somatosensory and visual sources. This is reasonable given the relative insignificance of auditory processing during a large portion of the task. The goodness of fit is also poor when compared to the literature (over 90%). The small number of trials (90) and lack of explicit attention could both contribute to this difference. Using conventional methods, we failed to identify any auditory responses at all in the event-locked average from the best sensor. Therefore, using BSS, we can identify and localize sources that are not identifiable at all using previous

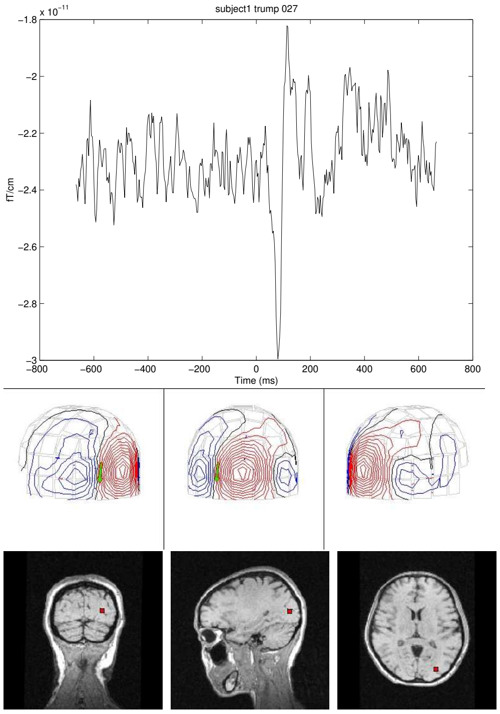

Figure 4: Localization of BSS-separated visual component. Same as Fig.1 through Fig. 3 but responses were locked onto visual stimulus onset (Subject 1 Source 027.)

methods.

4. DISCUSSION

We analyzed a data set from four tasks originally designed for a memory study. Each of the tasks involves sensory stimulation from visual, auditory, and somatosensory modalities which interact in a "natural" context. In contrast to isolated stimulation of each sensory modality using extremely well controlled stimuli, such as visual forms with very small visual angle, median nerve stimulation, and pure tones delivered monaurally, the visual stimuli used in this study have large visual angles, the somatosensory stimuli to the thumb and the associated muscles and nerves were generated by the subject's own button presses, and the auditory stimuli were provided binaurally as a consequence of (and as feedback for) the button-press motor action. The responses to these sensory stimuli were strongly modulated by task demands, such as differential attention to different sensory modalities. Initially attention was directed to visual stimulation, but as soon as a button press response was made the subject needed to direct attention to the auditory stimulus

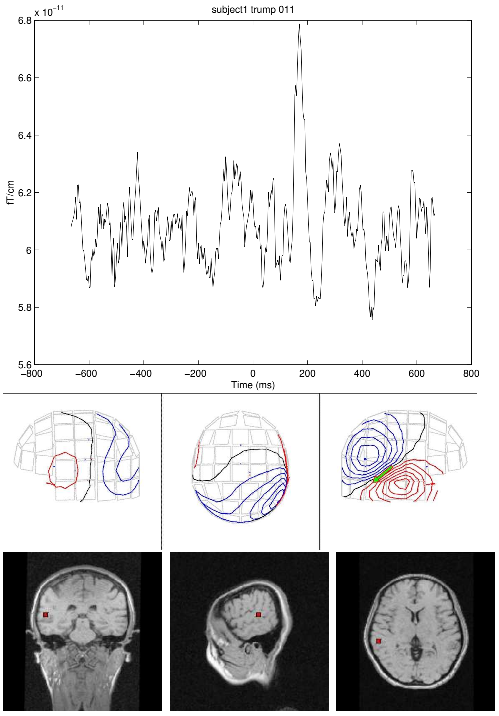

Figure 5: Localization of BSS-separated auditory component. (Subject 1 Source 011.)

to determine whether the response was correct. Attention to auditory feedback became unnecessary after the subject discovered which stimulus was the target using the auditory feedback (low versus high frequency tones). Processing of somatosensory stimulation due to button-presses was never an explicit part of the task and received no explicit attention. This type of attentional shift from one sensory modality to another embodies another aspect of natural sensory information processing.

One difficulty in studying sensory processing in such complex "natural" tasks is that stimulation to each modality was embedded in the context of the stimulation of another modality and also in the context of motor action. The close temporal proximity among neuronal responses associated with these multiple sensory modalities and the motor response make the separation and identification of signals arising from distinct neuronal populations difficult to accomplish. Event-related field generators are typically modeled by first selecting single response peaks in single channel waveforms. Using this method, if two generators have overlapping peaks, separation becomes impossible. Another difficulty in studying these types of tasks is the variability in the focus of attention throughout the task and across modalities, and variability in the states of processing associated with each modality which may serve to prime the subsequent processing. These variabilities reduce the S/N ratio, therefore requiring averaging over a large number of trials. These difficulties may have contributed to the fact that to date most studies of sensory processing with MEG have been conducted under either more controlled or single modality stimulation.

We take advantage of one particular blind source separation algorithm which utilizes information available in the fine temporal structures of the signals associated with different underlying field generators. The process of identifying or separating neuronal sources does not involve signal averaging across trials, nor does it require the subsequent identification of a peak response from potentially overlapping peaks in the averaged sensor signals. Instead, continuous non-averaged data are provided as input to the algorithm which generates multiple one-dimensional time series (*i.e.* components.) Each component potentially corresponds to some magnetic field generator(s). The algorithm outputs as many such components as there are sensors in the data acquisition system. Those with stimulus- or motor-locked responses are candidates for being neuronal generators. Those with responses locked onto other external events, such as eye-blinks or heart beats detected using EOG and EKG, are considered known noise sources. The rest remain as generators from unknown noise sources that are not task related. Along with the time series for each component, the algorithm also generates a field map for each component, which shows how strongly the putative generator can influence each sensor. When the pattern of the field map agrees with known neuronal generators and when the time course of the component matches that of the same generator based on past MEG studies and other neuroanatomical constraints, the components are considered to reflect the activity of a neuronal generator (Tang et al., 2000). Following such a procedure, neuronal and non-neuronal generators with temporally overlapping responses have been separated and identified (Tang et al., 1999, 2000). Because the algorithm simultaneously separates noise from neuronal components, the time series of the neuronal components is much cleaner than the *sensor* time series. When performing event-locked averages using the separated components, fewer trials should be needed than when using the sensor time series.

We obtained MRIs for each individual subject and used standard Neuromag software to model the components with single equivalent current dipole (ECD). The input to the software is the field pattern and the output is the location of the ECD projected onto the subject's MRI. From the earlier discussed complex tasks, we were able to separate and identify visual, auditory, and somatosensory components that show appropriate event-locked responses with response latencies consistent with past literature. Despite the large variability associated with stimulation induced by the subjects' self-directed button presses, somatosensory components with an average peak latency of approximately 40ms were identified. Since this somatosensory stimulation was caused by a thumb button-press, the components are localized to the same region where sources for median nerve stimulation have been found (Hari and Forss, 1999). Despite the lack of strong attentional demand and the rapidly reducing attentional demand for auditory stimuli during the course of the experiments, auditory components were identified with an average peak latency of approximately 100ms and were localized to the vicinity of the lateral fissure, consistent with previous studies (Cansino et al., 1994). Finally, despite the large visual angles of the visual stimuli, early visual components were localized to regions within the occipital lobe with an average peak latency of approximately 110ms across four subjects, which is also consistent with previous studies (Aine et al., 1995; Hashimoto et al., 1999; Portin et al., 1999).

Establishing that BSS-separated components are not simply an arbitrary combination of multiple discontiguous neuronal sources but can in fact be localized to meaningful brain regions is only the first step in demonstrating the usefulness of BSS algorithms. The next question is whether BSS provides any advantages in source localization. In principle, one could expect improved source localization because BSS simultaneously separates known and unknown sources of noise from neuronal components. The BSS-separated neuronal components are cleaner than the raw sensor data, and therefore should have better S/N ratios and better precision of localization in terms of goodness of fit. We compared localized sources from BSS-separated components and from original sensor data. Our results showed that (1) while for some sensory modalities, such as the auditory system, the conventional analysis procedure completely failed to identify any dipole sources at all due to a failure to detect peaks in the averaged sensor signal, BSS-separated components correspond clearly to neuronal activity originating in primary auditory cortex in terms of their response latencies and their source locations; (2) When the conventional analysis method does result in localization of dipole sources, the BSS-separated sources always have fitted dipoles with greater goodness of fit than dipoles fitted to the averaged sensor data. These observations suggest that BSS can serve to improve source localization by improving goodness of fit and in identifying dipoles under challenging experimental conditions (low sensor S/N ratios). BSS can be viewed as a pre-processor to any existing source localization method. The next step is to systematically study the effect of BSS on source localization when combined with more sophisticated source localization algorithms than single ECD modeling.

Through the application of a BSS algorithm to MEG data, we have previously shown that (1) BSS is capable of separating various artifacts from neuronal sources (Tang et al., 1999); (2) BSS is capable of separating neuronal sources at different processing stages along the visual pathways; and (3) BSS is capable of supporting single-trial analysis (Tang et al., 2000). In this paper, we show that BSS-separated components can be further localized to meaningful spatial locations within the brain. Localization of BSS-separated components provides the critical link between the independent components and their corresponding generators in the brain. This link allows us to relate functions, revealed by responses in time, to structures specified in space.

5. REFERENCES

Aine, C. J., Supek, S., and George, J. S. (1995). Temporal dynamics of visual-evoked neuromagnetic sources: effects of stimulus parameters and selective attention. *Intern. J. Neuroscience*, 80:79–104.

Bell, A. J. and Sejnowski, T. J. (1995). An information-maximization approach to blind separation and blind deconvolution. *Neural Computation*, 7(6):1129–1159.

Belouchrani, A., Meraim, K. A., Cardoso, J.-F., and Moulines, E. (1993). Second-order blind separation of correlated sources. In *Proc. Int. Conf. on Digital Sig. Proc.*, pages 346–351, Cyprus.

Cansino, S., Williamson, S., and Karron, D. (1994). Tonopotic organization of human auditory association cortex. *Brain Res.*, 663:38–50.

George, J. S., Aine, C. J., Mosher, J. C., Schmidt, D. M., Ranken, D. M., Schlitt, H. A., Wood, C. C., Lewine, J. D., Sanders, J. A., and Belliveau, J. W. (1995). Mapping function in the human brain with magnetoencephalography, anatomical magnetic resonance imaging, and functional magnetic resonance imaging. *J. Clin. Neurophysiol.*, 12:406–431.

Hari, R. and Forss, N. (1999). Magnetoencephalography in the study of human somatosensory cortical processing. *Phil. Trans. R. Soc. Lond. B*, 354:1145–1154.

Hashimoto, T., Kashii, S., Kikuchi, M., Honda, Y., Nagamine, T., and Shibasaki, H. (1999). Temporal profile of visual evoked responses to pattern-reversal stimulation analyzed with a whole-head magnetometer. *Exp. Brain Res.*, 125(3):375–382.

Hyvarinen, A. and Oja, E. (1997). A fast fixed-point algorithm for independent component analysis. *Neural Computation*, 9(7).

Jung, T.-P., Humphries, C., Lee, T.-W., Makeig, S., McKeown, M. J., Iragui, V., and Sejnowski, T. (1998). Extended ica removes artifacts from electroencephalographic recordings. In NIPS*97 (1998).

Jung, T.-P., Makeig, S., Westerfield, M., Townsend, J., Courchesne, E., and Sejnowski, T. J. (1999). Analyzing and visualizing single-trial event-related potentials. In *Advances in Neural Information Processing Systems 11*, pages 118–124. MIT Press.

Makeig, S., Bell, A. J., Jung, T.-P., and Sejnowski, T. J. (1996). Independent component analysis of electroencephalographic data. In *Advances in Neural Information Processing Systems 8*, pages 145–151. MIT Press.

Makeig, S., Jung, T. P., Bell, A. J., Ghahremani, D., and Sejnowski, T. J. (1997). Blind separation of auditory event-related brain responses into independent components. *Proc. Natl. Acad. Sci. USA*, 94(20):10979–10984.

Makeig, S., Townsend, J., Jung, T.-P., Enghoff, S., Gibson, C., Sejnwoski, T. J., and Courchesne, E. (1999a). Early visual evoked response peaks apper to be sums of activity in multiple alpha sources. *Soc. Neurosci. Abstr.*, 25(652.8).

Makeig, S., Westerfield, M., Jung, T.-P., Covington, J., Townsend, J., Sejnwoski, T. J., and Courchesne, E. (1999b). Functionally independent components of the late positive event-related potential during visual spatial attention. *J. Neurosci.*, 19(7):2665–2680.

NIPS*97 (1998). *Advances in Neural Information Processing Systems 10*. MIT Press.

Portin, K., Vanni, S., Virsu, V., and Hari, R. (1999). Stronger occipital cortical activation to lower than upper visual field stimuli. *Exp. Brain Res.*, 124:287–294.

Tang, A. C., Pearlmutter, B. A., Zibulevsky, M., Hely, T. A., and Weisend, M. P. (2000). An MEG study of response latency and variability in the human visual system during a visual-motor integration task. In *Advances in Neural Information Processing Systems 12*, pages 185–191. MIT Press. To appear.

Tang, A. C., Pearlmutter, B. A., Zibulevsky, M., and Loring, R. (1999). Blind separation of neuromagnetic responses. In *Computational Neuroscience*. To appear as a special issue of *Neurocomputing*.

Vigário, R., Jousmäki, V., Hämäläinen, M., Hari, R., and Oja, E. (1998). Independent component analysis for identification of artifacts in magnetoencephalographic recordings. In NIPS*97 (1998).

Williamson, S. and Kaufman, L. (1981). Magnetic fields of the cerebral cortex. In Erne, S., Hahlbohm, H., and Lubbig, editors, *Neuromagnetism*, pages 353–402. Walter de Gruyter, Berlin.