Published in final edited form as:

Pediatr Neurol. 2009 November ; 41(5): 383–387. doi:10.1016/j.pediatrneurol.2009.06.007.

Magnetoencephalographic analysis in patients with vagus nerve stimulator

Naoaki Tanaka, MD, PhD^{*}, Elizabeth A. Thiele, MD, PhD[†], Joseph R. Madsen, MD[‡], Blaise F. Bourgeois, MD[§], and Steven M. Stuffelbeam, MD^{*}

^{*}Athinoula A. Martinos Center for Biomedical Imaging, Massachusetts General Hospital, Charlestown, MA, USA

[†]Pediatric Epilepsy Program, Department of Neurology, Massachusetts General Hospital, Boston, MA, USA

[‡]Department of Neurosurgery, Children's Hospital Boston, Boston, MA, USA

[§]Department of Neurology, Children's Hospital Boston, Boston, MA, USA

Abstract

The purpose of this study is to assess the feasibility of magnetoencephalography in epilepsy patients with vagus nerve stimulator. We performed magnetoencephalography in two patients (Patient 1 and 2) with medically intractable epilepsy who had a vagus nerve stimulator. Due to the artifacts caused by a vagus nerve stimulator, no spikes could be identified in the original magnetoencephalographic data in either patient. The temporally extended signal space separation method was used for removing artifacts. After processing by this method, left temporo-parietal spikes were clearly identified in Patient 1. Equivalent current dipoles calculated from these spikes were localized in the left posterior-temporal and parietal lobes. The location of the dipoles was consistent with the spike distribution on intracranial EEG. In Patient 2, bilateral, diffuse spikes were seen in the processed data. The contour maps demonstrated a bilateral pattern, not in agreement of single focal source. These findings supported the diagnosis of symptomatic generalized epilepsy in this patient. The present study demonstrates that magnetoencephalography may be a valuable option for evaluating intractable epilepsy patients with the vagus nerve stimulator.

Keywords

magnetoencephalography; epilepsy; vagus nerve stimulator; signal space separation; temporally extended signal space separation

Introduction

Vagus nerve stimulation is a non-pharmacologic therapy for patients with medically intractable epilepsy. Several studies have shown that vagus nerve stimulation is effective for reducing

© 2009 Elsevier Inc. All rights reserved.

Correspondence to: Naoaki Tanaka, Athinoula A. Martinos Center for Biomedical Imaging, 149 Thirteenth Street, Suite 2301, Charlestown, Massachusetts 02129, USA. Tel: 617-726-8517, Fax: 617-726-8626, naoro@nmr.mgh.harvard.edu.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

seizure frequency in patients with both partial and generalized epilepsy [1,2]. Typically, the stimulator is implanted under the skin in the chest.

Magnetoencephalography is a non-invasive method of recording magnetic signals in the brain used to characterize ictal and interictal epileptic activities. However, the neuromagnetic signals can easily be obscured by artifacts caused by any magnetic items inside and outside of human body [3]. The vagus nerve stimulators contain electronic circuitry that causes magnetic artifacts even when the stimulation is turned off. Due to these large artifacts, magnetoencephalography has not been performed in patients with vagus nerve stimulator.

The signal space separation method and its temporal extension have recently been introduced for removing the magnetic artifacts contaminating the brain signals on magnetoencephalography [4-6]. In signal space separation method, the recorded magnetic signals are decomposed into separate components representing the neuromagnetic signals arising from inside a volume enclosed by the sensor array and external interference signals arising from outside of the array. However, if the source of artifacts is close or inside the sensor array, which is the case for the vagus nerve stimulator, this division may not be sufficient for reducing the artifacts [5,6]. The temporally extended signal space separation method combines the signal space separation method with a temporal process capable of recognizing and removing any signals that do not strictly obey the basic signal space separation model [6]. By using this method, the neuromagnetic signals can be extracted from the magnetoencephalographic data without altering their field distribution.

In this report, we apply the temporally extended signal space separation method to magnetoencephalographic data obtained from two epilepsy patients with vagus nerve stimulator. We evaluate the magnetoencephalographic data prior and after application of the method.

Patients and methods

Patients

Magnetoencephalography was performed in two epilepsy patients at Athinoula A. Martinos Center for Biomedical Imaging. Written informed consent was obtained before data acquisition for the research, which was approved by the institutional review board.

Patient 1 was a 12-year-old boy who had frequent complex partial seizures with hemiconvulsions of the right side of his body since age 6. Cortical dysplasia was found in the left temporal lobe, and he underwent a left temporal lobectomy at age 7. At age 10, he was implanted with a vagus nerve stimulator due to the frequent seizures, however, he still had daily or weekly seizures. A second surgery was planned, considering a removal of the remaining left temporal lobe.

Patient 2 was a 16-year-old boy who had daily drop attacks since early infancy. Anticonvulsant medications were not effective. He was implanted with a vagus nerve stimulator, but he continued to have daily seizures. His magnetic resonance imaging (MRI) showed no structural lesions. Previous electroencephalography (EEG) showed diffuse spikes or spike-and-slow-wave complexes predominantly in the left or bilateral frontal area. The possibility of the frontal origin of these discharges was investigated, although he was considered to have symptomatic generalized epilepsy.

Magnetoencephalography and data processing

Magnetoencephalography was performed with a 306-channel, whole-head system (Elekta-Neuromag Oy, Helsinki, Finland) in a magnetically shielded room. Scalp EEG was

simultaneously recorded according to the 10-10 system. The details of the recordings have previously been described [7].

In processing with the temporally extended signal space separation method, the data was divided into non-overlapping temporal (4s) segments. The signal space was divided into two linearly independent subspaces; one for the neuromagnetic signals inside a spherical volume encompassed by the sensor array and one for interference signals outside the array [4,5]. By using these subspaces, a unique decomposition of the measured signal vector with separate components for the internal and external signals was obtained within each segment. Then the temporally correlated signals between the internal and external parts were removed using a temporal orthogonal projection [6]. Assuming that the brain signals were temporally uncorrelated with the artifacts, those signals were interpreted as artifacts. A correlation limit of 0.80 was used in this study.

The original and the processed magnetoencephalographic data were visually examined by two experienced interpreters (NT and SMS) for detecting epileptic spikes. Clinical information of each patient, such as medical history, the findings of the previous EEG and MRI, was available during interpretation of the data, if necessary. At time instants when the spikes showed contour maps consistent with a dipolar source, equivalent current dipoles were fitted to the data. Equivalent current dipoles with a goodness-of-fit better than 70% were superimposed on the MRI of the patients.

Results

Patient 1 (Fig. 1)

Sporadic spikes were seen in the left posterior temporal and parietal electrodes (P3, P7) on EEG. The original magnetoencephalographic data contained large artifacts, and no spikes could be clearly identified by the two interpreters. The contour map of magnetic fields showed complicated field distribution contaminated with the artifacts. After processing with the temporally extended signal space separation method, the data showed clear spikes in the left posterior temporal sensors, and the contour map showed a single-dipole pattern. Equivalent current dipoles calculated from these spikes were localized in the left posterior-temporal and parietal lobes.

The patient also underwent an intracranial EEG monitoring, with the coverage of the left frontal, temporal and parietal lobes. The interictal spikes on intracranial EEG were mainly seen in the left posterior-temporal and parietal lobes, consistent with the dipole distribution. The posterior temporal lobe and a part of the parietal lobe were surgically removed, and the seizure frequency of the patient has been significantly reduced for 14 months after surgery.

Patient 2 (Fig. 2)

Frequent spikes or spike-and-slow-wave complex bursts were seen predominantly in the bilateral fronto-temporal electrodes on EEG. No epileptic activity could be identified in the original magnetoencephalographic data by the two interpreters due to large artifacts. The contour maps of the original data were contaminated with the artifacts. After processing with the temporally extended signal space separation method, magnetoencephalographic spikes were seen bilaterally and diffusely, corresponding to the EEG spikes. The contour maps suggested no single cortical source.

These findings were consistent with the assumed diagnosis of symptomatic generalized epilepsy in this patient. An anterior corpus callosotomy was performed for reducing his seizure frequency.

Discussion

In this study, the temporally extended signal space separation method substantially reduced the magnetic artifacts caused by the vagus nerve stimulator. In both patients, epileptic spikes were clearly identified in the processed data. In Patient 1, the dipole source localization of magnetoencephalographic spikes was consistent with the spike distribution observed on intracranial EEG. In patient 2, the widespread spikes observed in the processed data confirmed the previous diagnosis.

Our results are in accordance with previous reports of the temporally extended signal space separation method being able to successfully remove artifacts from magnetic sources that are relatively close to the brain [5,6]. However, the quality of the data can be affected by the choice of the threshold parameter for the correlation limit used in the method [8]. Lowering the threshold will result in better removal of the artifacts, but may also distort the signal from the brain. In our case, the consistency of the dipole source localization with the intracranial EEG data in Patient 1 suggests that the threshold used (0.8) was appropriate.

The present study suggests that patients with vagus nerve stimulator can be successfully studied with magnetoencephalography. Previously, the temporally extended signal space separation method has been demonstrated to suppress magnetic artifacts caused by a deep brain stimulator in a patient with Parkinson's disease [9]. This method may enable magnetoencephalographic studies in patients with various kinds of medical devices, such as cardiac pacemakers, metal plates and surgical clips, that otherwise disturb the neuromagnetic signals.

Acknowledgments

We thank Seppo P Ahlfors, Ph.D., Matti S. Hämäläinen, Ph.D., and Samu Taulu, Ph.D. for the helpful comments on the manuscript. This work was supported by National Institutes of Health (P41RR14075, RO1NS037462-07), Mental Illness and Neuroscience Discovery Institute, NARSAD Young Investigators Award.

References

1. Ben-Menachem E, Mañon-Espaillet R, Ristanovic R, Wilder BJ, Stefan H, Mirza W, Tarver WB, Wernicke JF. Vagus nerve stimulation for treatment of partial seizures: 1. A controlled study of effect on seizures. First International Vagus Nerve Stimulation Study Group. *Epilepsia* 1994;35:616–26. [PubMed: 8026408]
2. Labar D, Murphy J, Tecoma E. Vagus nerve stimulation for medication-resistant generalized epilepsy. E04 VNS Study Group. *Neurology* 1999;52:1510–2. [PubMed: 10227649]
3. Hämäläinen M, Hari R, Ilmoniemi RJ, Knuutila J, Lounasmaa OV. Magnetoencephalography—theory, instrumentation, and applications to noninvasive studies of the working human brain. *Rev Mod Phys* 1993;65:413–97.
4. Taulu S, Kajola M, Simola J. Suppression of interference and artifacts by the Signal Space Separation Method. *Brain Topogr* 2004;16:269–75. [PubMed: 15379226]
5. Taulu S, Simola J. Spatiotemporal signal space separation method for rejecting nearby interference in MEG measurements. *Phys Med Biol* 2006;51:1759–68. [PubMed: 16552102]
6. Taulu, S.; Hari, R. Removal of magnetoencephalographic artifacts with temporal signal-space separation: Demonstration with single-trial auditory-evoked responses. *Hum Brain Mapp* [serial on the Internet]. 2008 Jul. [cited 2009 Mar 24]. Available from: <http://www3.interscience.wiley.com>
7. Knake S, Halgren E, Shiraishi H, Hara K, Hamer HM, Grant PE, Carr VA, Foxe D, Camposano S, Busa E, Witzel T, Hämäläinen MS, Ahlfors SP, Bromfield EB, Black PM, Bourgeois BF, Cole AJ, Cosgrove GR, Dworetzky BA, Madsen JR, Larsson PG, Schomer DL, Thiele EA, Dale AM, Rosen BR, Stufflebeam SM. The value of multichannel MEG and EEG in the presurgical evaluation of 70 epilepsy patients. *Epilepsy Res* 2006;69:80–6. [PubMed: 16516443]

8. Medvedovsky M, Taulu S, Bikmullina R, Ahonen A, Paetau R. Fine tuning the correlation limit of spatio-temporal signal space separation for magnetoencephalography. *J Neurosci Methods* 2009;177:203–11. [PubMed: 18996412]
9. Mäkelä JP, Taulu S, Pohjola J, Ahonen A, Pekkonen E. Effects of subthalamic nucleus stimulation on spontaneous sensorimotor MEG activity in Parkinsonian patient. *International Congress Series* 2007;1300:345–348.

Fig. 1.

A. EEG shows a sharp wave in the left posterior temporal and parietal areas (P3, P7). The original magnetoencephalographic waveforms in the left parietal sensors are shown, containing large artifacts caused by a vagus nerve stimulator. The data processed with the temporally extended signal space separation method shows a clear spike in the same area.

B. At the time point shown by an arrow in A, the contour map of the original magnetic fields showed complicated field distribution contaminated with the artifacts. The contour map of the data processed with the temporally extended signal space separation method shows a single-dipole pattern at the same latency. Lines and dotted lines indicate outflux and influx of magnetic fields. The arrow indicates calculated the equivalent current dipole.

C. Equivalent current dipoles calculated at the peak of the spikes are localized in the left posterior-temporal and parietal lobes.

D. (Top) The reconstructed CT images show the location of the intracranial EEG electrodes (Gray circle). White circles show the electrodes in which interictal spikes are frequently seen. (Bottom) A typical interictal spike appears in the electrodes of numbered circles, which are shown on the CT images.

Fig. 2.

A. EEG shows a diffuse spike dominant in the bilateral fronto-temporal areas. The original magnetoencephalographic waveforms contain large artifacts caused by a vagus nerve stimulator. The data processed with the temporally extended signal space separation method shows a clear diffuse spike.

B. At the time point shown by an arrow in A, the contour map of the original data is contaminated with the artifacts. The contour map of the data processed with the temporally extended signal space separation method shows a bilateral pattern at the same latency. Lines and dotted lines indicate outflux and influx of magnetic fields.