Epilepsy Research (2013) **105**, 326—336

journal homepage: www.elsevier.com/locate/epilepsyres

Total intravenous anesthesia affecting spike sources of magnetoencephalography in pediatric epilepsy patients: Focal seizures vs. non-focal seizures

Ryosuke Hanaya[a], Hiroshi Okamoto[a], Ayataka Fujimoto[a], Ayako Ochi[a], Cristina Go[a], Carter O. Snead 3rd[a], Elysa Widjaja[b], Sylvester H. Chuang[b], Sheelagh M. Kemp[c], Hiroshi Otsubo[a,*]

[a] *Division of Neurology, The Hospital for Sick Children and The University of Toronto, Toronto, ON, Canada M5G 1X8*
[b] *Division of Neuroradiology, The Hospital for Sick Children and The University of Toronto, Toronto, ON, Canada M5G 1X8*
[c] *Division of Anesthesiology, The Hospital for Sick Children and The University of Toronto, Toronto, ON, Canada M5G 1X8*

Received 21 July 2012; received in revised form 29 December 2012; accepted 27 February 2013
Available online 4 April 2013

KEYWORDS
Focal seizure;
Epileptic spasm;
Generalized seizure;
Propofol;
MEG;
Thalamo-cortical network

Summary
Purpose: Magnetoencephalography (MEG) provides source localization of interictal spikes. This study evaluated the inhibitory effects of propofol on MEG spike sources (MEGSSs) among different types of seizures in patients who underwent two separate MEG studies with and without total intravenous anesthesia (TIVA) using propofol.
Methods: We studied 19 children (1—14 years; mean, 6.2 years) who had MEG with and without TIVA. TIVA was administered using propofol (0.03—0.06 mg/kg/min) to record MEG with simultaneous EEG. We analyzed number of spikes of MEG and MEGSSs comparing MEG studies done with and without TIVA.
Results: Seizures were divided into nine focal seizure (FS) with/without secondary generalization, five epileptic spasm (ES), and five generalized seizure (GS). TIVA significantly decreased the number of MEG spikes/min (from 4.5 to 2.0) in five FS without secondary generalization ($p < 0.05$). The number of MEG spikes/min was significantly lower (1.9) in FS than that in non-FS (ES + GS, 6.1) ($p < 0.01$). MEGSSs without TIVA were clustered in 15 patients (6FS; 4ES; 5GS), scattered in four (3FS; 1ES). MEG under TIVA showed clusters in 10 patients (1FS; 4ES; 5GS), scatters in three (2FS; 1ES) and no MEGSS in six patients with FS. Under TIVA, nine (90%) of ten patients with non-FS showed MEGSSs clusters compared to one (11%) of nine patients with FS ($p < 0.01$).

* Corresponding author at: Division of Neurology, Department of Pediatrics, The Hospital for Sick Children, 555 University Avenue, Toronto, ON, Canada M5G 1X8. Tel.: +1 416 813 6295; fax: +1 416 813 6334.
E-mail addresses: hiroshi.otsubo@sickkids.ca, hiotsubo@rogers.com (H. Otsubo).

0920-1211/$ — see front matter
http://dx.doi.org/10.1016/j.eplepsyres.2013.02.013

Conclusions: Reduction of MEGSSs occurred in patients with FS under TIVA. Diffuse/generalized spikes in non-FS are not affected by TIVA. Propofol may decrease focal spikes in the epileptic cortex in FS. Cortical hyperexcitability in non-FS group would be stronger or more extensive than that in the FS group of patients.

Introduction

Magnetoencephalography (MEG) is a useful tool to localize sources of interictal epileptiform discharges on magnetic resonance image (MRI). MEG recording requires patients to keep still for precise localization of intracranial epileptic and functional discharges. Excessive movement with respect to the MEG sensors, which are not directly attached to the patient, cause inaccurate co-registration of MEG and MRI which then provides unreliable data. A subset of pediatric patients with medically intractable epilepsy often has developmental and/or behavioral problems. For uncooperative pediatric patients, sedation is necessary to keep patients immobilized during MEG measurement for accurate source localization of brain activities. In our facility, we use total intravenous anesthesia (TIVA) with propofol and remifentanil to sedate these uncooperative pediatric patients for preoperative localization of somatosensory evoked fields and epileptic foci (Bercovici et al., 2008; Fujimoto et al., 2009).

Propofol has antiepileptic effects against status epilepticus (Marik, 2004), experimental focal seizures (Drummond et al., 1992; Rampil et al., 1993) and interictal epileptiform activities in vitro (Ohmori et al., 2004; Rasmussen et al., 1996). Because, propofol acts as a gamma-aminobutyric acid (GABA) agonist by increasing $GABA_A$ mediated inhibition and by inhibiting other membrane currents mediated by N-methyl-D-aspartate receptor (NMDA)/glycine receptors, sodium channels and voltage-gated calcium channels (Kotani et al., 2008), it has similar effects as those of intravenous diazepam (Laguna and Korein, 1972) and clonazepam (Browne, 1976).

MEG studies of adult populations with intractable focal epilepsy found no spikes in 10—30% of patients examined without anesthesia (Iwasaki et al., 2005; Paulini et al., 2007; Stefan et al., 2003). A retrospective analysis of MEG testing performed with and without anesthesia, found no difference in spikes between patients who had MEG with TIVA (74%) and those without anesthesia TIVA (80%) (Balakrishnan et al., 2007). Although propofol did not alter the likelihood of interictal spikes compared to recording MEG without propofol (Balakrishnan et al., 2007; Szmuk et al., 2003), we previously reported TIVA using propofol reduced interictal spikes on EEG and MEG, and affected MEG spike sources (MEGSSs) especially for the patients without lesion (Fujimoto et al., 2009).

Subset of generalized seizure (GS) were in fact secondarily generalized seizures (2GS), therefore the seizures classified as GS were possible 2GSs with unclear/undetected focal seizure onset and rapid early propagation. Chugani et al. reported infantile spasms as one of the 2GS with focal seizure onset for resective surgery (Chugani et al., 1992) We have applied MEG for pediatric patients with focal seizure (FS), epileptic spasm (ES) and GS to localize the epileptic focus for epilepsy surgery (Snead, 2001) MEG revealed the localization of early ictal EEG onset and epileptogenic zone of 2GS in some patients with ES, which was proved by epilepsy surgery (Otsubo and Imai, 2007; Ramachandrannair et al., 2008; Inage et al., 2012).

There has been no report on the effect of propofol for different seizure types. We hypothesize that the effect of propofol is different among the seizure types in the pediatric epilepsy population. Furthermore, by analyzing the effects of TIVA on MEGSSs in different types of seizures, we can postulate that cortical hyperexcitability in non-FS group would be stronger or more extensive than that in the FS group of patients.

Methods

Patients

We selected patients who underwent two separate MEG studies, with and without TIVA between 2000 and 2010 as part of their presurgical evaluation. As we knew the effect of TIVA in decreasing MEG spikes (Fujimoto et al., 2009), we repeated MEG studies without TIVA to ensure the similar location of the epileptic foci even in the long interval from the first MEG study with TIVA and even with changes in seizure characteristics.

Before MEG study, we captured habitual seizures with scalp video-EEG (VEEG) after partial withdrawal of anticonvulsant medications. Our presurgical evaluation using scalp VEEG, MRI and MEG were described elsewhere (Ochi and Otsubo, 2008). According to the information of scalp VEEG monitoring close to the time of MEG with TIVA, we divided the patients into two groups: (1) focal seizure (FS) group, patients were diagnosed with partial epilepsy who presented with FS with and without secondarily generalized seizure (2GS); (2) non-FS group, patients with symptomatic generalized epilepsy, who presented epileptic spasm (ES) and generalized seizure (GS). GSs included myoclonic seizures, tonic seizures, generalized tonic-clonic seizures. The GS in this study did not imply any seizures from primary generalized epilepsy. The myoclonic seizures were suspected to have focal onset with 2GS in symptomatic generalized epilepsy. Cases where patients had both focal epilepsy and generalized epilepsy were classified in the non-FS group. In non-FS group, MEG studies were planned for possible surgical treatment, because of suspected focal onset on scalp VEEG. We divided ES from FS and GS because the ILAE Classification Core Group classified ES under focal onset or no classified seizures (Berg et al., 2010).

Parents or guardians gave informed consent for all procedures, and the protocols received prior approval from our institutional review board and the Research Ethics Board at The Hospital for Sick Children.