



Bedside functional brain imaging in critically-ill children using high-density EEG source modeling and multi-modal sensory stimulation

Danny Eytan^a, Elizabeth W. Pang^b, Sam M. Doesburg^c, Vera Nenadovic^b, Bojan Gavrilovic^d, Peter Laussen^e, Anne-Marie Guerguerian^{f,*}

^aDepartment of Critical Care Medicine, Neurosciences and Mental Health Program, Research Institute, The Hospital for Sick Children, University of Toronto, Toronto, Canada

^bDivision of Neurology, Department of Paediatrics, Neurosciences and Mental Health Program, Research Institute, The Hospital for Sick Children, University of Toronto, Toronto, Canada

^cDepartment of Biomedical Physiology and Kinesiology, Behavioural and Cognitive Neuroscience Institute, Simon Fraser University, Burnaby, Canada

^dInstitute of Biomaterials and Biomedical Engineering, Department of Critical Care Medicine, Neurosciences and Mental Health Program, Research Institute, The Hospital for Sick Children, University of Toronto, Toronto, Canada

^eDepartment of Critical Care, David and Stacey Cynamon Chair in Critical Care Medicine, The Hospital for Sick Children, Department of Anaesthesia, University of Toronto, Toronto, Canada

^fDepartment of Critical Care, Neuroscience and Mental Health Program, Research Institute, The Hospital for Sick Children, University of Toronto, Toronto, Canada

ARTICLE INFO

Article history:

Received 27 July 2015

Received in revised form 24 June 2016

Accepted 30 June 2016

Available online 04 July 2016

Keywords:

Bedside cerebral function

Children

Brain injury

Electroencephalography (EEG)

Evoked potentials

Neuroimaging

Pediatrics

ABSTRACT

Acute brain injury is a common cause of death and critical illness in children and young adults. Fundamental management focuses on early characterization of the extent of injury and optimizing recovery by preventing secondary damage during the days following the primary injury. Currently, bedside technology for measuring neurological function is mainly limited to using electroencephalography (EEG) for detection of seizures and encephalopathic features, and evoked potentials. We present a proof of concept study in patients with acute brain injury in the intensive care setting, featuring a bedside functional imaging set-up designed to map cortical brain activation patterns by combining high density EEG recordings, multi-modal sensory stimulation (auditory, visual, and somatosensory), and EEG source modeling. Use of source-modeling allows for examination of spatio-temporal activation patterns at the cortical region level as opposed to the traditional scalp potential maps. The application of this system in both healthy and brain-injured participants is demonstrated with modality-specific source-reconstructed cortical activation patterns. By combining stimulation obtained with different modalities, most of the cortical surface can be monitored for changes in functional activation without having to physically transport the subject to an imaging suite. The results in patients in an intensive care setting with anatomically well-defined brain lesions suggest a topographic association between their injuries and activation patterns. Moreover, we report the reproducible application of a protocol examining a higher-level cortical processing with an auditory oddball paradigm involving presentation of the patient's own name. This study reports the first successful application of a bedside functional brain mapping tool in the intensive care setting. This application has the potential to provide clinicians with an additional dimension of information to manage critically-ill children and adults, and potentially patients not suited for magnetic resonance imaging technologies.

© 2016 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

1. Introduction

Acute brain injury is a common cause for hospitalization in pediatric and adult intensive care units with traumatic brain injury being the leading cause of death in children and young adults (Moreau et al. 2013; Parslow et al. 2005). Common other causes of acquired brain

injury are strokes, intracranial hemorrhages, meningoencephalitis, tumors and hypoxic ischemic encephalopathy associated with cardiopulmonary arrest. All are associated with significant personal, social and economic burdens (Geocadin et al. 2008; Corso et al. 2006; Perkins et al. 2009). As these patients are often critically-ill and sometimes have associated metal hardware attached or implanted, routine brain imaging with modalities such as MRI or Computed Tomography (CT) are not feasible. Even when MRI is performed, it is usually in the later stages of the illness and is infrequently acquired. CT also has associated radiation exposure and a lower resolution. Critically, both clinical MRI and CT can detect anatomical but not functional alterations following brain injury and modalities such as PET and fMRI are not broadly available at such stages of the illness. A system that can be applied at the bedside

* Corresponding author.

E-mail address: anne-marie.guerguerian@sickkids.ca (A.-M. Guerguerian).

¹ Laboratory address: Peter Gilgan Centre for Research and Learning, 686 Bay Street, 8th Floor South, 08.9709, Toronto, Ontario, Canada, M5G 0 A4.

² Administrative and mailing address: The Hospital for Sick Children, Department of Critical Care, Second Floor Atrium, Room 2830-A, 555 University Avenue, Toronto, Ontario, Canada, M5X 1G8.

of critically-ill patients and provide functional mapping and continued neuromonitoring, may offer opportunities for earlier detection of neurological injury, aid in guiding therapy and improve outcomes (Vidjeon and Strong 2011).

Electroencephalography (EEG) is a noninvasive modality with bedside availability that measures voltage fluctuations resulting from ionic current flows within the neurons of the brain, mostly as a result of synchronized synaptic activation to pyramidal cortical neurons (Niedermeyer and da Silva 2005). EEG waveforms recorded at the scalp reflect cortical activity through the summation of excitatory postsynaptic action potentials arising mainly from the pyramidal neurons in cortical layers III, V and VI with contribution from glial cells (Buzsáki et al. 2003; Ebersole 2003). There are associations between the EEG signal and other functional recording modalities such as fMRI and magnetoencephalography (MEG) (Singh et al. 2003). EEG use in intensive care settings in the context of acute brain injury is often limited to the detection of subclinical seizures and of encephalopathic features. Some studies have shown the utility of EEG signals to assist in the prediction of outcomes and to follow recovery after traumatic brain injuries (Duncan et al. 2011; Nenadovic et al. 2008; Ramachandran Nair et al. 2005), and in hypoxic ischemic encephalopathy (Wijdicks et al. 2006; Nishisaki et al. 2007).

Evoked Potentials (EPs) are electrical signals triggered by various sensory or cognitive stimuli that reflect the time course of information processing in the brain, thereby allowing for assessment of somatosensory, auditory, visual, cognitive and emotional processing pathways in healthy and brain-injured patients (Lehembre et al. 2012; Picton et al. 2000; Fernandez-Espejo and Owen 2013; Fischer et al. 2008; Daltrozzo et al. 2007). There are some reports on the use of EPs in the context of severe head injuries (Robinson et al. 2003; Folmer et al. 2011; Lew et al. 2006; Kane et al. 1996) mainly the somatosensory evoked potential (SEP) with only a few studies reporting the use of continuous SEP in the context of traumatic brain injury (Amantini et al. 2009).

In the present study, we implemented a bedside functional neuromonitoring system that combined high-density EEG monitoring with multi-modal sensory stimulation and EP recordings. The electrical signals captured with such a system allows for the generation of functional brain images by source modeling, as is commonly done in cognitive neuroscience (Lee et al. 2014), as has been reviewed previously (Murray et al. 2004). Use of EEG and EPs are becoming more prevalent in studies of patients with decreased levels of consciousness (Harrison and Connolly 2013). Some researchers have also suggested that in traumatic brain injuries it may be useful to combine these electrophysiological measures with imaging modalities such as CT and MRI (Duncan et al. 2011; Irimia et al. 2013a; Irimia et al. 2013b).

Such a bedside system as described in this proof of concept study may prove valuable for early diagnosis and detection of cerebral dysfunction in order to guide therapy in injured patients and to facilitate understanding of the functional brain state in subjects with a decreased level of responsiveness. Having a portable system that can be deployed at bedside presents many advantages over MEG and fMRI which require moving patients into the scanner and restricts recording durations (e.g., over several days and nights).

2. Materials and methods

2.1. Participants

Ten healthy volunteers (six males and four females) and five critically-ill patients (three males and two females) participated in this study. The healthy volunteers ranged in age from 7 to 16 years (median 12 years) and nine were right-handed. The patients were aged from 2.5 to 16 years (median 8.5 years); all with acute brain injury of various etiologies (traumatic brain injury, hemorrhagic stroke, necrotizing encephalitis or ischemic stroke). In these patients, all recordings were

done in the critical care unit while subjects were in the acute phase of their illness (less than one week of admission to hospital). All participants' guardians provided informed written consent and when applicable participants provided assent. This study was approved by Research Ethics Board of The Hospital for Sick Children's in Toronto, Ontario, Canada.

2.2. Experimental set-up, procedure and recording

The set-up consisted of a high-density EEG coupled with three multi-modal sensory stimulation generators: visual, auditory and somatosensory. This set-up was mounted on a small mobile cart to enable bedside recordings within the critical care unit (for either private or multiple patient rooms). The set-up was tested and approved by the Biomedical Engineering Department of The Hospital for Sick Children.

2.2.1. EEG recordings

The QuikCap electrode cap (Compumedics Neuroscan, El Paso, TX) was used for EEG electrode placement. The stretchable electrode cap contained 64 Ag–AgCl electrodes arranged according to the modified 10–20 system of electrode placement (Guideline 5 2006). The advantages of electrode caps are two-fold: they can be applied quickly and easily, which is essential in the critical care unit, and electrode positions can be reliably calculated by referencing common anatomical landmarks. The reference electrode was positioned near the vertex between the Cz and CPz electrodes and the ground electrode was located over the frontal area of the scalp, between the Fz and FPz electrodes. Electrode impedances were <10 k Ω .

An average reference montage was used for visualization and analysis (Cuffin 2001; Michel et al. 2004). Continuous EEG data from 64 channels were recorded throughout each stimulation session using a Neuroscan RT system (Compumedics Neuroscan, El Paso, TX) with exact time stamping of the sensory stimuli. Data were digitized at 1000 Hz and low-pass filtered at DC–200 Hz for visual and auditory stimulation and digitized at 5000 Hz and low-pass filtered at DC–1000 Hz for somatosensory stimulation.

2.2.2. Sensory stimulation

Multi-modal sensory stimuli were provided using standard equipment and driven by a laptop running custom-made software using Matlab (The Mathworks, Natick, MA, USA) and the Psychophysics Toolbox (Brainard 1997) according to standard clinical guidelines (International Federation of Clinical Neurophysiology). The stimulation computer and software was used to control the sensory modality, stimulus parameters (timing, duration, amplitude, pitch etc.) and was paired with an EEG recording computer via a serial port, to allow exact time stamping of stimuli delivery, and to the stimulation equipment using an Arduino UNO controller. Each recording session lasted approximately 1 h and included both multi-modal stimulation and baseline resting state EEG recordings.

Visual stimuli were presented using a standard xenon flash lamp (XLTEK XLPS-1 Photostimulator, Stellate, Montreal, Canada) and consisted of 300 stroboscopic light flashes (23 W/m²) at a rate of 2 Hz.

Somatosensory stimulation was presented via median nerve stimulation using a Grass S12 biphasic stimulator (Grass instruments, Quincy, MA, USA). Stimuli consisted of 300 stimuli (square wave, 200 μ sec duration) for each arm at a rate of 2 Hz. Stimuli were delivered to the median nerve at the wrist, at an intensity just above each individual's motor threshold.

Auditory stimuli were delivered using headphones at an intensity of 80 dB using two different oddball paradigms. A tone-based paradigm consisted of “rare”-deviant (probability of 0.2, 1100 Hz, duration 75 msec, rise and fall times of 5 msec) and “common”-standard (probability 0.8, 1000 Hz, duration 75 msec, rise and fall times of 5 msec) tones to induce a mismatch negativity (see citations (36–38)). Deviant stimuli were interspersed randomly between the standard tones.

Download English Version:

<https://daneshyari.com/en/article/3074805>

Download Persian Version:

<https://daneshyari.com/article/3074805>

[Daneshyari.com](https://daneshyari.com)