

Identification of an Intracranial Pressure (ICP) Response Function from Continuously Acquired Electroencephalographic and ICP Signals in Burst-Suppressed Patients

Mark Connolly, Raymond Liou, Paul Vespa, and Xiao Hu

Abstract Continuous intracranial pressure (ICP) and electroencephalographic (EEG) monitoring are used in the management of patients with brain injury. It is possible that these two signals could be related through neurovascular coupling. To explore this mechanism, we modeled the ICP response to brain activity by treating spontaneous burst activity in burst-suppressed patients as an impulse, and identified the ICP response function (ICPRF) as the subsequent change in ICP.

Segments of ICP were filtered, classified as elevating or stable, and suitable ICPRFs were identified. After calibration, each ICPRF was convolved with the EEG to produce the estimated ICP. The mean error (ME) versus distance from the selected ICPRF was calculated and the elevating and stable ICP segments compared.

Eighty-four ICPRFs were identified from 15 data segments. The ME of the elevating segments increased at an average rate of 57 mmHg/min, whereas the average ME of the stable segments increased at a rate of 0.05 mmHg/min.

These findings demonstrate that deriving an ICPRF from a burst-suppressed patient is a suitable approach for stable segments. To completely model the ICP response to EEG activity, a more robust model should be developed.

Keywords Intracranial pressure • Burst suppression

M. Connolly • R. Liou • P. Vespa
Department of Neurosurgery, David Geffen School of Medicine,
University of California-Los Angeles, Los Angeles, CA, USA

X. Hu, PhD (✉)
Departments of Physiological Nursing/Neurosurgery, University
of California-San Francisco, San Francisco, CA, USA

Institute for Computational Health Sciences, University
of California-San Francisco, San Francisco, CA, USA

Affiliate, UCB/UCSF Graduate Group in Bioengineering,
University of California-San Francisco, San Francisco, CA, USA
e-mail: xhu@mednet.ucla.edu

Introduction

Patients who suffer insults to the brain, such as traumatic brain injuries (TBIs) or subarachnoid hemorrhages (SAHs), are susceptible to secondary complications, which can cause further damage. One such complication is intracranial hypertension, resulting in ischemia and herniation [2, 7]. To detect the intracranial hypertension, the patients' intracranial pressure (ICP) is continuously monitored. Other secondary complications such as non-convulsive seizures and cortical spreading depressions can be detected using continuous scalp or depth electroencephalography (EEG) [8].

As ICP is an indirect measure of cerebral blood flow and EEG detects neural activity, the integration of these two monitoring modalities presents a unique opportunity to measure neurovascular coupling in patients during the acute phase following their injury. Our preliminary studies of burst-suppressed patients with continuous ICP and depth EEG monitoring found a relationship between the characteristics of the EEG burst and the subsequent changes in ICP [5].

The burst of activity in the EEG signal followed by a transient change in the ICP is analogous to what is known as an impulse response function (IRF) in systems engineering. An IRF is based on the idea that a linear and time-invariant system can be defined by its response to an impulse input (an input with infinite magnitude, zero duration, and integrates to 1.0). Based on our previous results, we hypothesized that an ICP response following a burst could act as an IRF, and convolution between this ICP segment and the EEG would model the ICP response for different bursts. Because the IRF assumes that the system is time-invariant, the ICP estimation would be more accurate during time periods when the cerebral circulatory dynamics were stable and less accurate during periods of ICP elevation.

Materials and Methods

This study used ICP and depth EEG segments collected from two patients admitted to the ICU at UCLA Ronald Reagan Hospital, who were burst-suppressed with pentobarbital for the management of refractory intracranial hypertension. To maximize the time between bursts and minimize the overlap of the ICP responses, data segments were selected from when the pentobarbital dosage was highest and the patient was most burst-suppressed. The ICP was low pass filtered at 0.2 Hz to remove cardiac effects. The frequency component caused by respiration between 0.15 and 0.4 Hz was programmatically selected and removed using a band-stop filter. The onset and termination of each EEG burst was segmented using an adaptive thresholding algorithm.

The ICP segments were each fit to a least squares line and the slopes for each segment were arranged into a histogram. The slope threshold that best separated the slopes into two groups was identified. Those segments with a slope less than the threshold were classified as stable, and those with a higher slope were classified as elevating.

The ICP response functions (ICPRFs) were defined as a filtered ICP increase from the onset to its return to the initial value before the onset of the following EEG burst (Fig. 1a). ICPRF amplitudes were shifted to 0.0 mmHg. The corresponding impulse was the analytic amplitude of

the preceding EEG burst calibrated so that it integrated to 1.0 (Fig. 1b).

For each ICPRF of a given data segment, the EEG of the entire segment was calibrated as above and then convolved with the ICPRF to produce the estimated ICP (Fig. 1c). The number of estimates produced for each data segment was equal to the number of valid ICPRFs. The mean error vs distance from the selected ICPRF was calculated and compared between the elevating and stable ICP segments.

Results

Fifteen data segments were collected from two patients: a 38-year-old woman with a TBI (7 segments), and a 53-year-old woman with an aneurysmal SAH (8 segments). A threshold of 0.3 mmHg/min was sufficient to divide the slopes of the segments into two clusters, 5 of which were classified as elevating and 10 were classified as stable. From these segments, 84 ICPRFs were identified; 21 from elevating segments and 63 from stable segments.

Computing the mean error vs the distance from the ICPRF showed that the mean error of the elevating segments increased at an average rate of 0.57 mmHg/min, while the average mean error of the stable segments increased at a rate of 0.05 mmHg/min (Fig. 2).

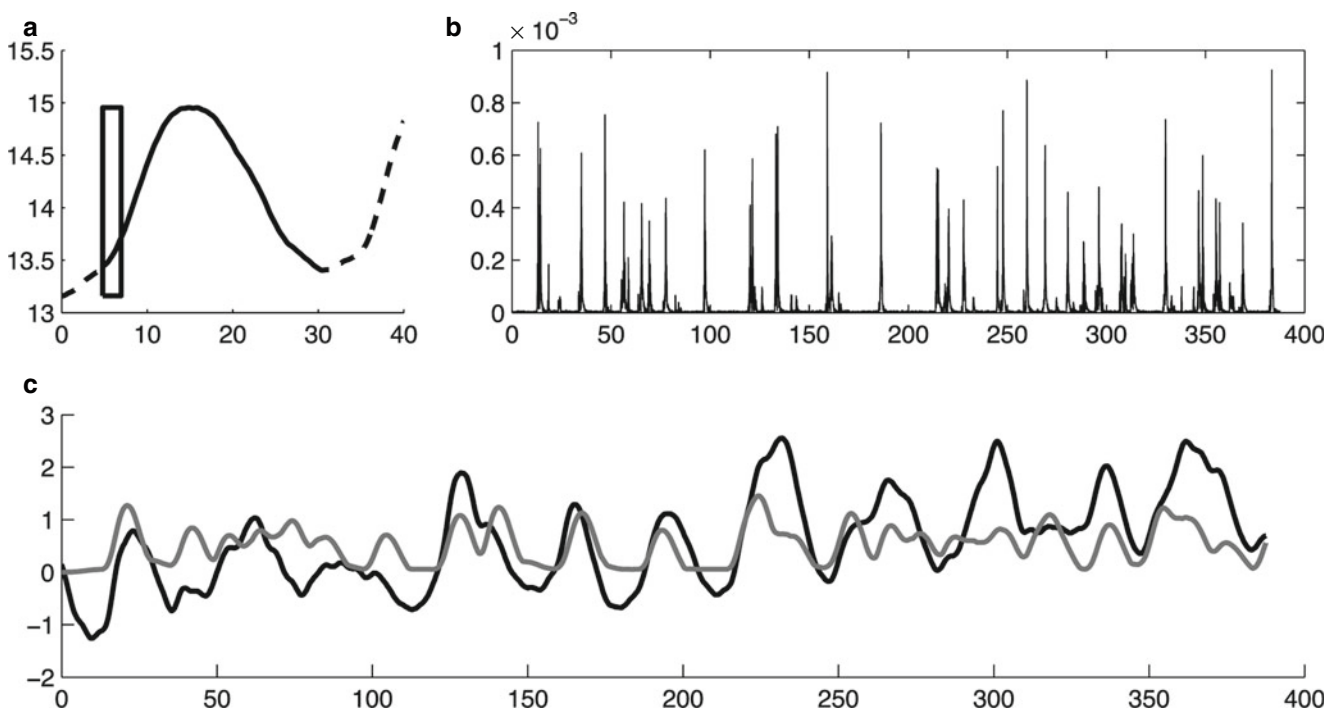


Fig. 1 (a) The timing of the electroencephalographic (EEG) burst (black box) and the subsequent intracranial pressure response function (ICPRF; solid black line). (b) The analytic amplitude of the EEG signal

calibrated so that the burst from (a) integrates to 1.0. (c) The measured filtered ICP (black line) compared with the estimate produced from the convolution of the ICPRF and the calibrated EEG

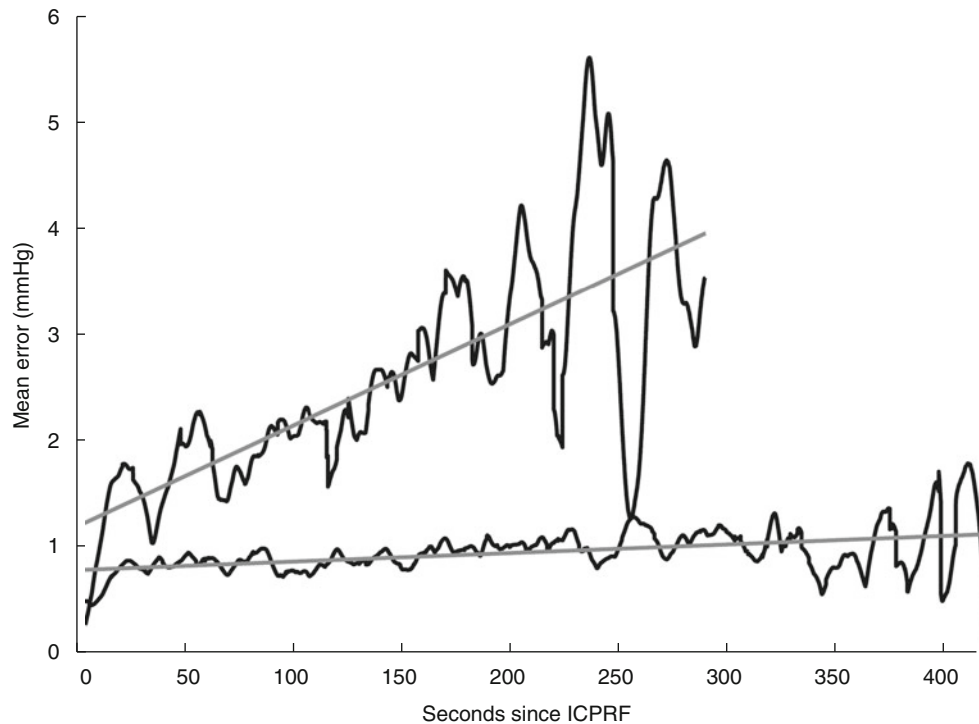


Fig. 2 The mean error of the ICP estimate as a function of the time difference between the ICPRF and the ICP it is used to estimate. The *top line* is the error vs time for the data segments classified as elevating

and the *lower line* is the error vs time for the segments classified as stable. The *gray line* through each is the linear fit used to calculate the rate of error increase

Conclusions

Neurovascular coupling is a well-defined mechanism whereby an increase in local brain activity creates a metabolic demand, and subsequently induces vasodilation, increasing blood flow to the active region. However, injury to the brain can induce abnormal patterns of neurovascular coupling, such as hyperemia and oligemia, in response to epileptic activity or cortical spreading depression [1, 3].

While pathological neurovascular coupling has been observed in humans, much of our information comes from animal models [4, 6]. Collection of these data is limited as the traditional techniques for assessing neurovascular coupling are noncontinuous, expensive, require moving the patient, and are generally not feasible in the acute period following a trauma, when events such as epileptic activity and CSDs are more likely to occur.

Defining the relationship between ICP and EEG takes advantage of two clinically indicated monitoring modalities to produce a surrogate measure of neurovascular coupling that can be used to investigate changes during this acute period. In this study we looked at data from burst-suppressed patients and used the transient changes in ICP after an EEG burst to describe the system underlying neurovascular coupling.

We found that using the ICP response as an IRF and convolving it with a calibrated EEG could accurately reproduce the measured ICP. However, the estimation was less accurate for the segments of data where there was a distinct elevation in the ICP. Specifically, we found that for these elevating segments, the time difference between the EEG burst-ICPRF pair and the estimation correlated negatively with the accuracy. In other words when a specific ICPRF was convolved with the EEG from much earlier or later in the segment, the estimation was less accurate than when convolved with the EEG near the same time as the ICPRF, especially when the ICP was rapidly increasing.

This loss of accuracy during elevations in ICP is likely due to the earlier assumption that the underlying system is both linear and time-invariant. As the ICP increases throughout the duration of a data segment, the relationship between blood flow and pressure changes. If the shape of the pressure-volume curve changes with time, this would mean that the system is not time-invariant. Alternatively, if the system moves to a significantly different point in the pressure-volume curve, the assumption of linearity would be violated.

While the ICPRF approach to modeling the relationship between ICP and EEG waveforms does not capture the entirety of the system underlying neurovascular coupling, it provides a starting point for developing more sophisticated

models. The identification of these models will offer insight into the relationship between these two signals and neurovascular coupling during the acute period following a brain injury.

This study was limited by the small cohort of patients with continuous depth EEG and ICP monitoring, and the narrow criteria for data selection (high burst suppression). The inclusion of patients with surface EEG in future studies will increase the volume of data, and allow the investigation of ICP and EEG when the patients are not burst-suppressed.

Acknowledgments The present work is partially supported by NS066008, NS076738, and the UCLA Brain Injury Research Center.

Conflicts of Interest There are no conflicts of interest to disclose.

References

1. Ayata C (2013) Spreading depression and neurovascular coupling. *Stroke* 44(6 suppl 1):S87–S89. doi:10.1161/strokeaha.112.680264
2. Bouma GJ, Muizelaar JP, Choi SC, Newlon PG, Young HF (1991) Cerebral circulation and metabolism after severe traumatic brain injury: the elusive role of ischemia. *J Neurosurg* 75(5):685–693. doi:10.3171/jns.1991.75.5.0685
3. Dreier JP (2011) The role of spreading depression, spreading depolarization and spreading ischemia in neurological disease. *Nat Med* 17(4):439–447
4. Füchtmeier M, Leithner C, Offenhauser N et al (2010) Elevating intracranial pressure reverses the decrease in deoxygenated hemoglobin and abolishes the post-stimulus overshoot upon somatosensory activation in rats. *Neuroimage* 52(2):445–454, Available at: <http://www.sciencedirect.com/science/article/pii/S105381191000649X>
5. Hu X, Vespa PM, Connolly M (2013) Neurovascular coupling explains transient response of intracranial pressure increase to EEG burst. In: *IEEE EMBC Short Papers*. Osaka. No. 0188.
6. Lauritzen M, Jørgensen MB, Diemer NH, Gjedde A, Hansen AJ (1982) Persistent oligemia of rat cerebral cortex in the wake of spreading depression. *Ann Neurol* 12(5):469–474. doi:10.1002/ana.410120510
7. Miller JD, Becker DP, Ward JD, Sullivan HG, Adams WE, Rosner MJ (1977) Significance of intracranial hypertension in severe head injury. *J Neurosurg* 47(4):503–516. doi:10.3171/jns.1977.47.4.0503
8. Vespa PM, Nenov V, Nuwer MR (1999) Continuous EEG monitoring in the intensive care unit: early findings and clinical efficacy. *J Clin Neurophysiol* 16(1):1–13, Available at: <http://www.ncbi.nlm.nih.gov/pubmed/10082088>. Accessed 14 Dec 2013