Nonconvulsive Seizures after Subarachnoid Hemorrhage: Multimodal Detection and Outcomes.


OBJECTIVE: Seizures have been implicated as a cause of secondary brain injury, but the systemic and cerebral physiologic effects of seizures after acute brain injury are poorly understood. METHODS: We analyzed intracortical electroencephalographic (EEG) and multimodality physiological recordings in 48 comatose subarachnoid hemorrhage patients to better characterize the physiological response to seizures after acute brain injury. RESULTS: Intracortical seizures were seen in 38% of patients, and 8% had surface seizures. Intracortical seizures were accompanied by elevated heart rate (p = 0.001), blood pressure (p < 0.001), and respiratory rate (p < 0.001). There were trends for rising cerebral perfusion pressure (p = 0.03) and intracranial pressure (p = 0.06) seen after seizure onset. Intracortical seizure-associated increases in global brain metabolism, partial brain tissue oxygenation, and regional cerebral blood flow (rCBF) did not reach significance, but a trend for a pronounced delayed rCBF rise was seen for surface seizures (p = 0.08). Functional outcome was very poor for patients with severe background attenuation without seizures and best for those without severe attenuation or seizures (77% vs 0% dead or severely disabled, respectively). Outcome was intermediate for those with seizures independent of the background EEG and worse for those with intracortical only seizures when compared to those with intracortical and scalp seizures (50% and 25% death or severe disability, respectively). INTERPRETATION: We replicated in humans complex physiologic processes associated with seizures after acute brain injury previously described in laboratory experiments and illustrated differences such as the delayed increase in rCBF. These real world physiologic observations may permit more successful translation of laboratory research to the bedside.

Complex Detection, Complex Decisions: More Detail on Subclinical Seizures in the Acutely Sick Brain

Commentary

Nonconvulsive seizures and nonconvulsive status epilepticus occurring in sick hospitalized patients represent a major challenge. Neurologists are frequently asked to see and advise on the management of patients who are unwell and encephalopathic, usually in an intensive care setting. These patients may or may not have a history of established epilepsy, may have a number of pre-existing comorbidities, may be on multiple medications, and are acutely unwell due to either systemic, neurological, or surgical disease. The immediate clinical questions that arise in such patients are the following:

1. What is the cause, or causes, of the encephalopathy?
2. Are convulsive or nonconvulsive seizures clinically apparent?
3. Is it possible that subtle or subclinical nonconvulsive seizures are contributing to the clinical picture?
4. What immediate appropriate neurological investigations are indicated (and available) at the particular center?
5. Are suspected or proven nonconvulsive seizures causing homeostatic and neurological harm, thus contributing to secondary brain injury?
6. How aggressive should anti-epileptic drug therapy be in suppressing nonconvulsive seizures, and what difference does this make to long-term outcomes?

Translational clinical research attempting to answer some of these highly relevant and common clinical dilemmas is welcomed. The ongoing work of the Critical Care Neurology and Epilepsy Divisions at Columbia University in New York is at the vanguard of this research. In the current paper, the authors attempt to measure aberrant cerebral physiology associated with non-convulsive seizures in 48 comatose (Glasgow Coma Scale ≤ 8) patients following subarachnoid hemorrhage. Patients with clinically obvious seizures were excluded from this study. As part of their “routine clinical care,” patients were monitored with intracortical electroencephalography using mini-depth electrodes, and multimodal physiological recordings. The latter included measurement of intracranial pressure, interstitial cerebral microdialysis (assaying lactate, pyruvate, and glucose), partial brain tissue oxygenation, and brain temperature. All patients were on prophylactic phenytoin for 1 week after subarachnoid hemorrhage, which was then discon-
tinued unless seizures had been recorded on scalp EEG. In the 48 patients analyzed in this study, 8% had scalp seizures and 38% had intracortical seizures recorded. Intracortical seizures had associated statistically significant elevations in heart and respiratory rates, and in blood pressure, and a trend toward elevations in increasing cerebral perfusion and intracranial pressure after seizure onset. Interestingly, functional outcome was poorest for those with severe background EEG attenuation without seizures, and outcome was also worse for those with intracortical seizures only compared to those with both intracortical and scalp seizures.

The optimum management of encephalopathic patients in ICU remains a significant clinical and resource challenge. In many centers, continuous EEG monitoring and neurocritical care expertise are not available, or certainly less readily available than at Columbia University Medical Center, where the investigations outlined are described as being a component of “routine clinical care.” However, I suspect there is a wide disparity worldwide in the monitoring and treatment of nonconvulsive seizures in the intensive care unit environment. In addition, of course, if subclinical seizures are not routinely screened for, they will not be detected, and thus won’t be treated. In centers where continuous EEG is not available, routine EEG is used, but obviously with much less sensitivity. In an Irish general adult ICU setting, where routine continuous EEG is not available, in a study of 52 patients with single or repeated EEG evaluations, epileptiform abnormalities were seen in only 15% of patients, and just one patient had an electrographic seizure recorded (1).

The study outlined here is of significant clinical and physiologic interest. The authors continue to investigate the incidence, pathophysiology, and clinical implications of subclinical nonconvulsive seizures in critically ill patients in ICU. Subclinical seizures are common in adult ICUs, reported to occur in approximately 20% of patients (2). Subclinical seizures are also common in critically ill neonates (3) but may be less common in older pediatric patients (4). The most important dual clinical question remains: how meticulously should subclinical nonconvulsive seizures be searched for, and when found how aggressively should they be treated? We know that the most important factor determining the prognosis following the occurrence of clinically apparent status epilepticus occurring de novo in sick hospitalized patients is underlying etiology (5); the same is likely to be true for patients with subclinical seizures detected on continuous EEG monitoring only. Thus, does the occurrence and treatment of nonconvulsive seizures alter long-term prognosis? We need to answer this question with a prospective placebo-controlled interventional trial that examines not just the abolition of subclinical seizures but also important long-term outcomes, such as survival and functional status several months and longer after ICU treatment. Such a study would be challenging, not least because neurologists and neurophysiologists would most probably be inherently resistant to the idea of not treating seizures, and implicitly the community likely accepts the intuitive notion that all seizures (like Orwell’s two legs) are bad and must be suppressed. However, the history of evidence-based medicine should teach us that some of our accepted dogmas may be founded on quicksand (6).

by Norman Delanty, MD

References
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Disclosure of Potential Conflicts of Interest

Instructions

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