TRAUMATIC BRAIN INJURY

Spreading depolarization can cause secondary injury after TBI

After acute injury to the brain, neurons at the damage epicentre depolarize, and this depression of activity spreads outward in waves through the cortex. A recently published study sheds light on how spreading depolarization can produce secondary damage after traumatic brain injury (TBI), and a second study presents a technique for the noninvasive monitoring of this phenomenon in patients with brain injury.

In a healthy brain, neuronal activity and cerebral blood flow are closely coupled: when neuronal depolarization increases in a given area, blood flow to that region also increases to restore intercellular concentrations of the ions necessary for neural function. After brain injury, however, the neurovascular response to depolarization can change. Jason Hinzman, who led the first study, explains: “in injured tissue these depolarizing waves can cause a reduction in cerebral blood flow, which produces a mismatch between the tissue’s energy demand and supply. The resulting metabolic stress could lead to neuronal injury.”

Inverse neurovascular coupling has been observed after subarachnoid haemorrhage and stroke in patients and in animal experiments, so Hinzman and colleagues wondered if it also occurred in patients with TBI. The investigators enrolled 24 patients due to undergo craniotomies after TBI. Spreading depolarization was measured via intracranial EEG electrodes placed on the exposed brain surface, while changes in cerebral blood flow were measured with a probe placed near the electrodes.

“We found that a decrease in blood flow was more prevalent than the physiological increase in cerebral flow following these electrical depolarizing waves,” reports Hinzman. Decreases in blood flow were only observed when the probes were placed in injured or deteriorating tissue, which suggests that inverse neurovascular coupling is a mechanism of secondary injury after acute trauma.

These results underscore the importance of monitoring patients’ brain activity after TBI, but the invasive approach limits the clinical relevance of this methodology. In a second study, Jed Hartings and co-workers investigated whether the spreading depolarization seen on intracranial EEG recordings could also be measured using scalp EEG electrodes.

Hartings *et al.* conducted simultaneous intracranial and scalp EEG recordings in 17 patients with TBI. “The current standard for assessment of EEG recordings is to review individual waveforms, on a scale of seconds,” says Hartings, “but we examined the EEG in a very different way, by zooming out so that trends could be seen over several hours.”

The intracranial EEG revealed slow depolarization events—lasting from 10 min to several hours—in 13 patients, and more than 80% of these events could be detected via scalp EEG. Furthermore, by measuring differences in the onset of electrical depression between EEG channels, Hartings and colleagues were able to chart the spread of depolarization. “We saw individual waves spread from frontal to parietal, and all the way to occipital and temporal regions,” says Hartings.

Although the results from both studies require further validation, these data provide important insight into the aftermath of acute brain injury. Spreading depolarizations and neurovascular coupling might also represent novel therapeutic targets for minimizing the effects of TBI.

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PhotoDisc/Getty Images/Don Farrall

Original articles Hinzman, J. M. *et al.* Inverse neurovascular coupling to cortical spreading depolarizations in severe brain trauma. *Brain* doi:10.1093/brain/awu241 | Hartings, J. A. *et al.* Spreading depression in continuous electroencephalography of brain trauma. *Ann. Neurol.* doi:10.1002/ana.24256