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NEUROCRITICAL CARE SOCIETY

EDITORIAL

Introduction to Spreading Depolarizations Special Edition Volume 2

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The clinical applications and scientific understanding of spreading depolarizations (SDs) continue to evolve and expand. Once considered a physiological curiosity, multiple studies in both human patients and experimental animal models show not only that SDs occur commonly after brain injury but also that they are both critical markers and mediators of secondary damage, clinical worsening, and poor outcome. The growing importance of SDs in neurology and critical care medicine is highlighted by the enthusiastic reception to the first volume of the special edition of *Neurocritical Care* on SDs. Articles published in the first volume were downloaded at a high rate and discussed enthusiastically on social media, in journal clubs, and on bedside teaching rounds in the intensive care unit. We are now happy to follow up this well received first volume with a second volume of work that further advances the clinical science of SDs. Articles in this second volume run the gamut from experimental work in model systems to clinical studies to topical reviews.

Multiple preclinical studies provide experimental evidence solidifying the link between brain injury, SDs, and secondary worsening. Menyhárt et al. clarify the link between disordered cerebral autoregulation and SDs by showing that anoxia-related hypotension events that occur in the setting of disrupted cerebral autoregulation can be an important trigger of SDs [1]. Similarly, Mosley et al. demonstrate that mice subjected to closed head injury showed increased SD susceptibility with lower baseline cerebral blood flow [2]. This study also shows that SDs occurring at the time of initial acute brain injury appear to be associated with worse cognitive outcomes. Another study by the same research group characterizes SDs in a mouse model of acute subarachnoid hemorrhage [3]. Such models will be instrumental in further clarifying the effects of SDs on delayed deterioration after subarachnoid hemorrhage. Finally, a study by Han et al. explores the link between anoxic SDs that occur after cardiac arrest and systemic hemodynamic status [4, 5].

Among clinical studies, Foreman et al. provide evidence that SDs are twice as common as seizures after traumatic brain injury and clarify the relationship between these two important neurophysiological events [6, 7]. Major et al. highlight challenges in bedside detection of SDs, however, by describing nonspreading depolarizing shifts that mimic SDs during hyperoxygenation episodes (which commonly occur in mechanically ventilated patients in the intensive care unit) [8]. Finally, multiple studies explore the potential for SD identification using noninvasive electrophysiological methods. Robinson et al. provide evidence from a case report that quantitative scalp electroencephalography can identify SDs confirmed with invasive depth electrode recordings [9]. In contrast, a study by Sivakumar et al. shows that ictal–interictal continuum findings seen on conventional scalp electroencephalography appear to be poorly associated with SDs [10]. A computational study by Hund et al. clarifies the voltage changes on scalp recordings that may unambiguously identify true SDs [11].

Several reviews provide perspectives on the mechanisms of SD initiation and propagation as well as pathophysiological pathways by which SDs induce secondary brain injury. Kearns et al. investigate the links between microglial activation and SDs [12]. Finally, a set of perspectives explore our assumptions regarding the links between SDs and excitotoxicity and identify areas of

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contention in SD research that should inform future studies [13, 14].

We wish to extend heartfelt gratitude to all of the reviewers who donated their time and intellectual effort to provide critical feedback for the submissions. We have thoroughly enjoyed collating these studies and have learned a great deal through the process. We hope the readers of *Neurocritical Care* will find similar enjoyment from reading this issue.

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