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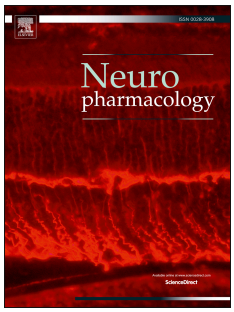

Cerebral ischemia: Celebrating successes, confronting challenges

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Editorial

Cerebral Ischemia: Celebrating Successes, Confronting Challenges

Notwithstanding declining death rates over the past decade, stroke continues to strike around 800,000 individuals per year in the US and remains the leading cause of long-term disability (AHA, 2017). This Special Issue devoted to cerebral ischemia follows upon a similar, highly cited issue on this theme published in this journal in 2008 (Frenguelli, 2008). In guest-editing the present issue, my goal has been to draw upon the most authoritative and accomplished investigative groups in the field so as to assemble a series of scholarly articles that embrace key topic-areas encompassing basic pathophysiology, advanced neuroimaging, recent clinical advances, and salient approaches that may hold future promise.

Understanding the complex pathophysiology of focal cerebral ischemia requires the use of reproducible experimental models to characterize the ischemic penumbra and to define the critical blood-flow thresholds that govern cellular energy depletion and electrical failure and set into motion injurious molecular and biochemical cascades. McCabe and colleagues introduce this topic, emphasizing widely used rodent models (McCabe, et al., 2018). Excitotoxicity, mediated principally by the neurotransmitter glutamate, is a principal mechanism of ischemic brain injury. Mayor and Tymianski offer a scholarly review of the roles of glutamate and other CNS neurotransmitters in this process (Mayor and Tymianski, 2018). Next, Dreier and colleagues provide a definitive exegesis of the phenomenon of spreading depolarization – a recurring pathological event associated with cytotoxic edema that over time may become a key mediator of ischemic neuronal death (Dreier, et al., 2018). Li and colleagues then review oxidative stress arising in the ischemic brain – an important injury-mechanism that leads to DNA damage to neurons, glia, and vascular elements (Li, et al., 2018). These authors emphasize that defective DNA repair in the ischemic brain worsens outcome while upregulation of DNA repair enzymes may facilitate recovery after stroke. Magaki and coworkers consider the multifaceted roles of neuroglial cells in the normal and diseased brain (Magaki, et al., 2018).

In addition to acute ischemic stroke, cerebrovascular dysfunction may also manifest itself in the form of vascular dementia – a common and often devastating form of cognitive impairment. Kalaria emphasizes the importance of cerebral small-vessel disease -- comprising arteriolosclerosis, lacunar infarction, microinfarcts, and diffuse perfusion-mediated white matter injury – as a principal cause of vascular cognitive impairment (Kalaria, 2018). In around 15% of patients with acute stroke, the mechanism of injury is hemorrhagic rather than ischemic. Wilkinson and colleagues provide a scholarly review of the pathophysiology of acute intracerebral hemorrhage (Wilkinson, et al., 2018).

Spectacular advances in neuroimaging have opened new vistas into the in vivo pathophysiology of cerebral ischemia and have transformed stroke diagnosis and management. Bahr Hosseini and Liebeskind survey the landscape of clinical neuroimaging (Bahr Hosseini and Liebeskind, 2018). Raja and colleagues follow upon this theme by describing how advanced magnetic resonance imaging may be