Early brain injury

“Acute brain injury” and “early brain injury” are related terms but are not synonymous. They are often used in the context of different phases or aspects of brain injury, particularly in the field of neuroscience and neurology.

Acute Brain Injury:

Definition: Acute brain injury refers to damage or trauma to the brain that occurs suddenly and often involves a rapid onset of symptoms. This can result from various causes, including traumatic events (such as head injuries or accidents), strokes, infections, or other medical conditions affecting the brain. Time Frame: The term “acute” generally implies the early stages of injury, but it does not specify a specific time frame. Acute brain injury can encompass the initial moments of injury and may extend into the early hours, days, or weeks following the event. Clinical Features: Acute brain injury is characterized by the immediate consequences of the injury, such as neurological symptoms, inflammation, and cellular damage. It may involve processes such as edema (swelling), bleeding, and changes in blood flow to the affected areas of the brain. Early Brain Injury:

Definition: Early brain injury refers to the initial damage to the brain that occurs shortly after the onset of a triggering event, such as trauma or a medical condition. It is a concept often used in the context of subarachnoid hemorrhage (bleeding in the space around the brain). Time Frame: The term “early” suggests a focus on the immediate aftermath of the triggering event, typically within the first 72 hours. However, the specific time frame may vary depending on the context of use. Clinical Features: Early brain injury involves pathological processes that occur shortly after the insult to the brain. This can include mechanisms such as oxidative stress, inflammation, and changes in cerebral blood flow that contribute to secondary brain damage. In summary, while acute brain injury refers more broadly to damage occurring in the early stages of an insult to the brain, early brain injury is a term often used in a more specific context, such as subarachnoid hemorrhage. Both terms highlight the importance of understanding and addressing the immediate consequences of brain injury to minimize secondary damage and optimize outcomes.

Over the last years, the focus of clinical and animal research in subarachnoid hemorrhage (SAH) shifted towards the early phase after the bleeding based on the association of the early injury pattern (first 72 h) with secondary complications and poor outcome. This phase is commonly referenced as early brain injury (EBI). In this clinical review, we intended to overview commonly used definitions of EBI, underlying mechanisms, and potential treatment implications.

Recent findings: We found large heterogeneity in the definition used for EBI comprising clinical symptoms, neuroimaging parameters, and advanced neuromonitoring techniques. Although specific treatments are currently not available, therapeutic interventions are aimed at ameliorating EBI by improving the energy/supply mismatch in the early phase after SAH. Future research integrating brain-derived biomarkers is warranted to improve our pathophysiologic understanding of EBI in order to ameliorate early injury patterns and improve patients' outcomes [1)]

The term early brain injury (EBI) has been coined and describes the immediate injury to the brain after SAH, before the onset of delayed vasospasm. During the EBI period, a ruptured aneurysm brings

on many physiological derangements such as increased intracranial pressure (ICP), decreased cerebral blood flow (CBF), and global cerebral ischemia. These events initiate secondary injuries such as blood-brain barrier disruption, inflammation, and oxidative cascades that all ultimately lead to cell death. Given the fact that the reversal of vasospasm does not appear to improve patient outcomes, it could be argued that the treatment of EBI may successfully attenuate some of the devastating secondary injuries and improve the outcome of patients with SAH [2)]

A study aimed to investigate the neuroprotective effect of ERRγ activation against early brain injury (EBI) after subarachnoid hemorrhage (SAH) and the potential underlying mechanisms. In a rat model of SAH, the time course of ERRs and SIRT3 and the effects of ERRγ activation were investigated. ERRγ agonist DY131, selective inhibitor GSK5182, or SIRT3 selective inhibitor 3-TYP were administered intracerebroventricularly (icv) in the rat model of SAH. The use of 3-TYP was for validating SIRT3 as the downstream signaling of ERRγ activation. Post-SAH assessments included SAH grade, neurological score, Western blot, Nissl staining, and immunofluorescence staining in rats. In an vitro study, the ERRγ agonist DY131 and ERRγ siRNA were administered to primary cortical neurons stimulated by Hb, after which cell viability and neuronal deaths were accessed. Lastly, the brain ERRγ levels and neuronal death were accessed in SAH patients. They found that brain ERRγ expressions were significantly increased, but the expression of SIRT3 dramatically decreased after SAH in rats. In the brains of SAH rats, ERRγ was expressed primarily in neurons, astrocytes, and microglia. The activation of ERRγ with DY131 significantly improved the short-term and long-term neurological deficits, accompanied by reductions in oxidative stress and neuronal apoptosis at 24 h after SAH in rats. DY131 treatment significantly increased the expressions of PGC-1α, SIRT3, and Bcl-2 while downregulating the expressions of 4-HNE and Bax. ERRγ antagonist GSK5182 and SIRT3 inhibitor 3-TYP abolished the neuroprotective effects of ERRγ activation in the SAH rats. An in vitro study showed that Hb stimulation significantly increased intracellular oxidative stress in primary cortical neurons, and DY131 reduced such elevations. Primary cortical neurons transfected with the ERRγ siRNA exhibited notable apoptosis and abolished the protective effect of DY131. The examination of SAH patients' brain samples revealed increases in ERRγ expressions and neuronal apoptosis marker CC3. We concluded that ERRγ activation with DY131 ameliorated oxidative stress and neuronal apoptosis after the experimental SAH. The effects were, at least in part, through the ERRγ/PGC-1α/SIRT3 signaling pathway. ERRγ may serve as a novel therapeutic target to ameliorate EBI after SAH [3)].

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