Neuroprotection

Neuroprotection refers to the relative preservation of neuronal structure and/or function.

When treating acute ischemic stroke patients in our daily clinical practice, we strive to achieve recanalization of the occluded blood vessel as fast as possible using pharmacological thrombolysis and mechanical clot removal. However, successful recanalization does not equal successful reperfusion of the ischemic tissue due to mechanisms such as microvascular obstruction. Even if successful reperfusion is achieved, numerous other post-recanalization tissue damage mechanisms may impair patient outcomes, namely blood-brain barrier breakdown, reperfusion injury and excitotoxicity, late secondary changes, and post-infarction local and global brain atrophy. Several cerebroprotectants are currently evaluated as adjunctive treatments to pharmacological thrombolysis and mechanical clot removal, many of which interfere with post-recanalization tissue damage pathways. However, our current lack of knowledge about the prevalence and importance of the various post-recanalization tissue damage mechanisms makes it difficult to reliably identify the most promising cerebroprotectants and design appropriate clinical trials to evaluate them. Serial human MRI studies with complementary animal studies in higher-order primates could provide answers to these critical questions and should be first conducted to allow for adequate neuroprotection trial design, which could accelerate the translation of cerebroprotective agents from bench to bedside to further improve patient outcomes [1)].

Evidence provides insufficient evidence of neuroprotective strategies to guide clinical management, and more randomized clinical trials are needed to optimize patient care [2)].

In the case of an ongoing insult (a neurodegenerative insult) the relative preservation of neuronal integrity implies a reduction in the rate of neuronal loss over time, which can be expressed as a differential equation.

It is a widely explored treatment option for many central nervous system (CNS) disorders including neurodegenerative diseases, stroke, traumatic brain injury, and spinal cord injury. Neuroprotection aims to prevent or slow disease progression and secondary injuries by halting or at least slowing the loss of neurons.

Despite differences in symptoms or injuries associated with CNS disorders, many of the mechanisms behind neurodegeneration are the same. Common mechanisms include increased levels in oxidative stress, mitochondrial dysfunction, excitotoxicity, inflammatory changes, iron accumulation, and protein aggregation.

Of these mechanisms, neuroprotective treatments often target oxidative stress and excitotoxicity—both of which are highly associated with CNS disorders. Not only can oxidative stress and excitotoxicity trigger neuron cell death but when combined they have synergistic effects that cause even more degradation than on their own.

Thus limiting excitotoxicity and oxidative stress is a very important aspect of neuroprotection. Common neuroprotective treatments are glutamate antagonists and antioxidants, which aim to limit excitotoxicity and oxidative stress respectively.

Great expectations have been raised about neuroprotection of therapeutic hypothermia in patients with traumatic brain injury (TBI) by analogy with its effects after heart arrest, neonatal asphyxia, and drowning in cold water.

Traumatic Brain Injury

Neuroprotection for Traumatic Brain Injury.

Spinal Cord

Neuroprotection of the spinal cord during the early phase of injury is an important goal to determine a favorable outcome by prevention of delayed pathological events, including excitotoxicity, which otherwise extend the primary damage and amplify the often irreversible loss of motor function. While intensive care and neurosurgical intervention are important treatments, effective neuroprotection requires further experimental studies focused to target vulnerable neurons, particularly motoneurons.

Neuroprotective Agent

Neuroprotective Agent

1)
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2)
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