Neuroprotection for Traumatic Brain Injury

Treatments and neuroprotection following Traumatic brain injury (TBI) are limited because secondary injury cascades are poorly understood.

Neuroprotective treatments that limit secondary tissue loss and/or improve behavioral outcomes have been well established in multiple animal models of TBI. However, the translation of such neuroprotective strategies to human injury has been disappointing, with the failure of more than thirty controlled clinical trials. Both conceptual issues and methodological differences between preclinical and clinical injury have undoubtedly contributed to these translational difficulties [1].

Evaluating novel compounds for neuroprotective effects in animal models of traumatic brain injury (TBI) is a protracted, labor-intensive, and costly effort. However, the present lack of effective options for traumatic brain injury treatment, despite decades of traumatic brain injury research, shows the critical need for alternative methods for screening new drug candidates with neuroprotective properties. Because natural products have been a leading source of new therapeutic agents for human diseases, Weisz et al. used an in vitro model of stretch injury to rapidly assess the pro-survival effects of three bioactive compounds, two isolated from natural products (clovanemagnolol [CM], vinaxanthone [VX]) and the third, a dietary compound (pterostilbene [PT]) found in blueberry. The stretch injury experiments were not used to validate drug efficacy in a comprehensive manner but used primarily, as proof-of-principle, to demonstrate that the neuroprotective potential of each bioactive agent can be quickly assessed in an immortalized hippocampal cell line in lieu of comprehensive testing in animal models of TBI. To gain mechanistic insights into potential molecular mechanisms of neuroprotective effects, they performed a pathway-specific PCR array analysis of the effects of CM on the rat hippocampus and microRNA sequencing analysis of the effects of VX and PT on cultured hippocampal neural progenitor cells. They showed that the neuroprotective properties of these natural compounds are associated with the altered expression of several genes or microRNAs that have functional roles in neurodegeneration or cell survival. The approach could help in quickly assessing multiple natural products for neuroprotective properties and expedite the process of new drug discovery for traumatic brain injury treatment [2].

Management is based on weak evidence, with little attempt to personalize treatment. A need exists for new precision medicine and stratified management approaches that incorporate emerging technologies.

Some drugs such as corticosteroids and progesterone have already been investigated in TBI neuroprotection but failed to demonstrate clinical applicability in advanced phases of the studies. Dietary antioxidants, such as curcumin, resveratrol, and sulforaphane, have been shown to attenuate traumatic brain injury-induced damage in preclinical studies. These dietary antioxidants can increase antioxidant defenses via transcriptional activation of NRF2 and are also known as carbonyl scavengers, two potential mechanisms for neuroprotection [3].

Hypothermia

see Hypothermia.

Valproate

Several studies have indicated that 300 mg/kg or 400 mg/kg of valproate (VPA) exhibits neuroprotective effects in animal models. However, humans cannot tolerate high doses of VPA.

A study found that 30 mg/kg of VPA assists in treating TBIs in rat models [4].

1)
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