

Session/Poster#

Presenter

B22

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Anti-epileptogenic effects of early administration of brivaracetam in rats after severe traumatic brain injury

Posttraumatic epilepsy (PTE) can occur in up to 40% of patients who sustain a severe traumatic brain injury (TBI). Despite decades of research, there are no therapeutic interventions to prevent PTE. Moreover, in many cases of PTE, seizures cannot be controlled with standard antiseizure medications (ASMs). Early intervention with ASMs may be one strategy to prevent PTE by interdicting the posttraumatic epileptogenic cascade. Using the controlled cortical impact (CCI) injury model of severe TBI, we have assessed the efficacy of brivaracetam (BRV) to prevent PTE. BRV is an FDA approved ASM that targets the synaptic vesicle protein 2A (SV2A) and appears to exert its anti-seizure actions by modulating synaptic glutamate release. We predict that BRV can prevent or mitigate the TBI-induced epileptogenic process and consequent cortical hyperexcitation. Sprague Dawley rats (P26-30) were subjected to a severe CCI injury (2mm depth, 4m/s) in the somatosensory cortex and given a single BRV dose (21 mg/kg, i.p.) immediately after injury. Due to the low incidence of spontaneous seizure activity in rodent TBI models, chemical-challenge with a low dose of the pro-convulsant drug, 4-aminopyridine (4-AP), was used to assess seizure susceptibility as a metric for post-traumatic epileptogenesis. At 3 - 4 weeks after injury, rats were given a single dose of 4-AP (3.5mg/kg, i.p.), and then monitored for the development of stage 4/5 behavioral seizures up to 70 minutes after injection. CCI injured animals treated with BRV (CCI-BRV) demonstrated a ~50% reduction in 4-AP-induced behavioral seizures compared to un-treated CCI animals. These results suggest that early, post-injury administration of a single dose of BRV may be anti-epileptogenic by interfering with the posttraumatic epileptogenic progress and thus reduce susceptibility to PTE.