B17

Anika Sanjana Advisor(s): Douglas S.F. Ling

Early intervention with SV2A-ligand antiseizure drugs prevents injury-induced changes in AMPA receptor expression after traumatic brain injury in rats

A pathologic sequelae of traumatic brain injury (TBI) is the development of epilepsy. In the controlled cortical impact (CCI) model of TBI in rats, severe cortical trauma leads to posttraumatic epileptogenesis (PTE) characterized by evoked and spontaneous ictal-like discharges. We have found that timely, post-injury administration of the pyrrolidone, SV2A ligand antiseizure drugs (ASDs), levetiracetam (LEV) or brivaracetam (BRV), can prevent PTE after CCI injury. In this study, we examined the effects of post-injury administration of BRV and LEV on injury-induced changes of glutamatergic AMPA receptor subunit expression. Rats were subjected to severe CCI trauma (2.0 mm depth) at post-natal day 25 – 30. Randomly selected CCI-injured rats were given a single dose of LEV (150 mg/kg, IP) or BRV (21 mg/kg, IP) immediately after injury, while drug-control subjects received only the saline vehicle. Sham-injured control rats were not subjected to CCI injury. Three weeks after injury, rats were euthanized and their brains snap- frozen which later underwent western blot analysis to evaluate GluA1 and GluA2 expression levels. We found that the ratio of GluA1 to GluA2 levels in CCI-injured rats were significantly higher in the ipsilateral hippocampus compared to the contralateral hemisphere as well as those in sham-injured subjects ($p < 0.05$), which would be consistent with an increase in synaptic excitation due to a potential shift towards calcium-permeable AMPA receptor expression. Analysis of tissue from CCI-injured rats treated with LEV or BRV showed significantly lowered GluA1/GluA2 ratio, that were not significantly different from those in sham-injured subjects. This suggests that early intervention with these ASDs prevented the injury-induced changes in the GluA1/GluA2 ratio. These findings may provide insights to the pathogenic mechanisms of TBI that give rise to neural circuit hyperexcitation and epileptogenesis, and to the antiepileptogenic mechanisms of LEV and BRV.