Dexmedetomidine In in vivo Murine Traumatic Brain Injury Model

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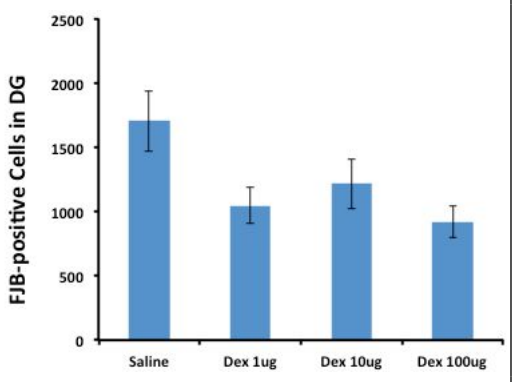
Introduction

Traumatic brain injury has been shown to involve secondary injury pathways including autonomic dysregulation, ischemia, and excitotoxicity leading to neuronal death(1,2,3). Dexmedetomidine is an alpha-2 agonist that has demonstrated neuroprotection in ischemic animal models(4,5). There have been no published reports of dexmedetomidine's effectiveness in neuroprotection following traumatic brain injury.

Methods

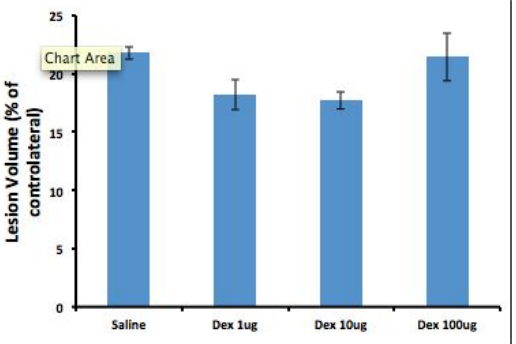
Controlled cortical impact through a pneumatic device was used to create a moderate head injury in 8 week-old mice as previously described (6). The mice were randomized to receive either saline or dexmedetomidine at 1ug/kg, 10ug/kg, or 100ug/kg doses at 1 hour and 12 hours after injury. Mice were sacrificed at 24 hours after injury. Histopathological analysis was carried out using Fluoro Jade-B and cresyl violet staining. Fluoro Jade-B staining was used to mark neuronal death in the dentate gyrus. Cresyl violet staining allowed for quantification of ischemic damage to the cortex.

Fluoro-Jade B staining for neuronal cell death



1ug/kg and 100ug/kg dexmedetomidine demonstrated significantly less neuronal death when compared to saliine.

Cresyl violet staining demonstrating ischemic damage to all cells in the cortex



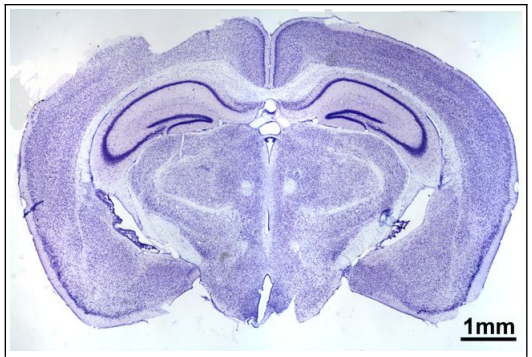
There was significantly less ischemic damage in the cortex at 10ug/kg compared to saline ($p<0.05$)

Results

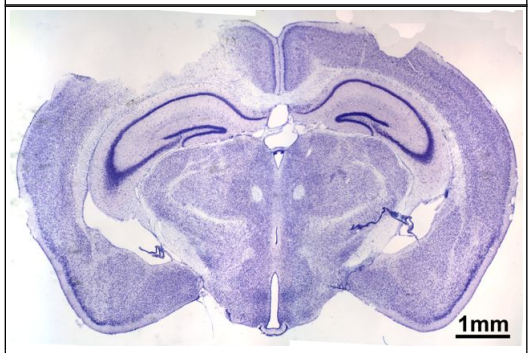
There was significantly less neuronal death at 1ug/kg and 100ug/kg dexmedetomidine compared to saline ($p < 0.05$). There was significantly less ischemic damage in the cortex at 10ug/kg, but not at 1ug/kg or 100ug/kg doses ($p < 0.05$).

Conclusions

Dexmedetomidine demonstrated neuroprotection in a in vivo murine model for TBI. Dexmedetomidine deserves further research to determine if these results can be duplicated in other animal models and possibly applied to humans.



10 ug/kg Dexmedetomidine treated mouse with cresyl violet staining



Saline control mouse with cresyl violet staining

Learning Objectives

At the end of the presentation, participants will understand the potential role for dexmedetomidine in traumatic brain injury.

References

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4. Hoffman WE et al. Dexmedetomidine improves neurologic outcome from incomplete ischemia in the rat. Reversal by the alpha 2-adrenergic antagonist atipamezole. Anesthesiology 1991:75;328-32.
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6. Gao, X. and J. Chen, Conditional knockout of brain-derived neurotrophic factor in the hippocampus increases death of adult-born immature neurons following traumatic brain injury. J Neurotrauma, 2009. 26(8): p. 1325-35.