Poster #19

Research Study

Title: "Investigating the effects of the ketogenic diet on axonal regeneration and RGC survival after optic nerve injury"

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Category: Neurology; Basic Science

Keywords: optic nerve regeneration; retinal ganglion cells; ketogenic diet; wnt signaling; neuroinflammation

Introduction and Objective. Optic nerve injury and pathologies such as glaucoma lead to RGC death and as a consequence, irreversible blindness. Therapeutics such as intravitreally injected Wnt3a have been shown to induce axonal regrowth and improved RGC survival after optic nerve crush (ONC). There is also interest in developing non-pharmacologic neuroprotectants such as the high fat-low carbohydrate ketogenic diet (KD), which has been shown to be neuroprotective in the context of various neurologic diseases. However, the effect of the KD on optic nerve regeneration in the setting of traumatic optic injury has not been investigated.

Methods. This study uses the ONC model in mice placed the KD for two weeks prior to ONC and for the remainder of the experiment. Mice were injected intravitreally with Wnt3a or saline. Nutritional ketosis was confirmed by measuring beta-hydroxybutyrate (BHB) levels. Axonal regeneration was quantified by counting the number of axons at 500 μm intervals past the crush site. Pattern electroretinogram (PERG) was used to assess RGC functional response and immunohistochemistry (IHC) was used to assess RGC counts.

Results. Mice fed the KD were found to have improved RGC survival ($p=0.037$) but did not have improved RGC function ($p=0.065$) or axonal regeneration. Furthermore, mice fed the KD prior to ONC were found to have less inflammatory IBA-1-positive microglia/macrophage cells compared to mice on the control diet ($p=0.0279$). In contrast, mice fed the KD in the presence of intravitreally injected Wnt3a had improved RGC function ($p=0.0049$), decreased axonal regeneration (p<0.05), and no effect on RGC survival.

Conclusions-Implications. These results demonstrate that KD may improve RGC survival after traumatic optic nerve injury under certain conditions but does not induce axonal regeneration. Additionally, the KD is likely to reduce inflammation after ONC as demonstrated by decreased microglia/macrophage counts.