chronic-branched-chain amino acid ingestion aggravates hilar neuron loss in a rodent model of temporal lobe epilepsy

Shau Evan Gruenbaum, Roni Dhaher, Amedeo Rapuano and Tore Eid

OBJECTIVES/SPECIFIC AIMS: We previously developed a translationally relevant model of temporal lobe epilepsy (TLE) in which glutamine synthetase is irreversibly inhibited by methionine sulfoximine (MSO), resulting in spontaneous seizures and dentate hilar neuron loss. The objective of this study was to determine the effects of chronic BCAA ingestion on neuronal viability in the dentate hilus in MSO model of TLE. METHODS/STUDY POPULATION: Sixteen rats were randomly divided into 2 groups: 8 rats drank a 4% aqueous solution of all 3 BCAAs (BCAA group) ad libitum for 31 days, and the other 8 rats drank regular water (control group) for the same period. After 10 days of drinking, a microinjection cannula (Alzet osmotic pump, model 2004) was surgically implanted in the right dentate gyrus to continuously infuse MSO at a rate of 0.64 μg/g per hour for 28 days. After 31 days of drinking, rats were perfused transcardially with 0.9% NaCl followed by 4% paraformaldehyde in phosphate buffer. The brains were removed and fixed, sectioned, and stained with NeuN. Neuron counts in the hilar region were performed (lateral and contralateral to the infusion site using a stereological technique. RESULTS/ANTICIPATED RESULTS: BCAA treatment did not produce an increase in hilar neuron loss compared to controls. However, we did observe an increase in the number of NeuN+ neurons in the BCAA group compared to controls. DISCUSSION: Our findings suggest that BCAA supplementation may have a protective effect on hilar neuron loss in a model of temporal lobe epilepsy. These results have important implications for the development of therapeutic strategies to prevent neuronal loss in epilepsy.