Exploring a non-invasive stimulation as a novel treatment for epilepsy

Jennifer Tinston[1], Anna Harutyunyan[1], Juliana Silva[1], Matthew Hudson[1], Nigel Jones[1]

1. Department of Neuroscience, Central Clinical School, Monash University, Melbourne, VIC, Australia

Introduction

Patients with Alzheimer's disease (AD) have a higher propensity to develop epilepsy than age-matched controls. However, the mechanisms underlying this increased risk are unknown, and specific seizure treatments for this group do not exist. Recent work has developed a novel light and sound stimulation paradigm consisting of 40Hz light flicker and synchronous audio stimulation which entrains gamma rhythms in neural networks, increases microglial phagocytic clearance of amyloid-beta (Aβ) peptide and improves cognition in 5xFAD mice. Here, we tested the therapeutic potential of the sensory-evoked gamma entrainment to improve the epilepsy phenotype of 5xFAD mice, an AD model with an increased propensity for seizures.

Methods

5xFAD mice (n=16) received sensory-stimulation of 1hr per day, which began for two weeks before Y-maze behavioural testing, and is continuous through the subsequent electrical amygdala kindling protocol. Kindling protocol consists of electrical stimulation at the after-discharge threshold current, once per day, until five fully generalised class V, or fifteen seizures are experienced. MRI was conducted before and after to observe in vivo changes in Aβ plaques, and histopathological analysis examined phenotypic changes in microglia and Aβ plaques.

Results

There was no difference in the number of stimulations required to reach the 1st class V seizure or to reach the endpoint of five class V seizures ($p=0.56$; $p=0.67$, unpaired t-test) between control and sensory-stimulation treated groups. Further, no improvements to cognitive performance was observed ($p=0.63$, unpaired t-test). To conclude, we have validated a new strategy for treating the underlying pathologies of microglia and Aβ accumulation in an AD model which may contribute to epileptogenic processes. However, in this paradigm, no improvements in the rate of seizure development or severity of seizure type are seen. Therefore, our data suggests that the reduction of Aβ plaques may not successfully mitigate seizure outcomes in models of epilepsy.