POSTER ABSTRACTS

Thursday | 5 November

11:00 - 11:30 Group 5 - Basic science

Chair: Christopher Reid

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Metabolomics profiling of the brain revealed potential mechanisms associating Alzheimer's disease to higher seizure susceptibility in mice

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Patients with Alzheimer's disease (AD) have up to 10-fold increased risk of epilepsy, compared to healthy age-matched controls. The underlying mechanisms leading to this increased risk are unclear.

Objectives

The aim of this study was to identify metabolic pathways that are altered in the early stage of amyloid precursor protein (APP) pathology to generate hypotheses regarding mechanisms associated with increased epilepsy risk in AD. The highly seizure-prone Tg2576 mouse model of AD is an appropriate tool for investigating changes in the brain associated to mutant APP over-expression.

Methods

Metabolomics data was collected from the cortex and hippocampus of 6-month old Tg2576 mice (n=7) along with their wild-type (WT) littermate (n=7) via liquid chromatography-mass spectrometry. Univariate, multivariate and pathway enrichment analyses were performed on MetaboAnalyst and the weighted correlation network analysis was performed using R.

Results

We identified 11 metabolites (adjusted-$p < 0.05$, variable importance in projection score > 1) significantly affected by APP over-expression in the cortex. Pathway enrichment analysis yielded 4 significantly enriched metabolic pathways from the cortex and 1 from the hippocampus (adjusted-$p < 0.05$, pathway impact > 0.2). Network analyses identified 5 pathways that were significantly correlated (adjusted-$p < 0.05$) with AD genotype. Our analyses suggest that oxidative stress, lipid and amino acid metabolism pathways could be affected early by the APP pathology.

Conclusion

This study identified changes in metabolite levels and metabolic pathways that are linked to the early stage of the APP pathology in AD. These findings provide new insights into the early disruption to the metabolic processes in the CNS caused by the APP pathology, which might increase the seizure susceptibility of the brain.