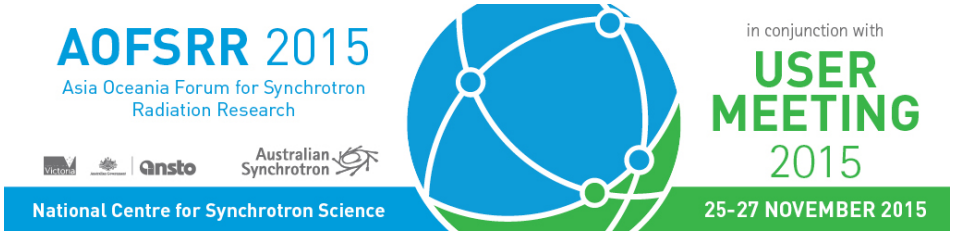

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Development of a synchrotron FTIR microspectroscopy approach to evaluate the efficacy of candidate multiple sclerosis therapeutics

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The sphingosine-1-phosphate receptor 1 (S1PR1) is a target for the multiple sclerosis drug FTY720, a functional antagonist causing sequestration of autoreactive immune cells. Conventional approaches with the experimental autoimmune encephalomyelitis (EAE) model do not provide an overall index of drug efficacy, hence the use of FTIR microspectroscopy. Experimental groups included vehicle-only, EAE+placebo (EAE+P) and EAE+FTY720 (EAE+FTY). Spinal cord grey (gm) and white matter (wm) changes were evaluated and compared with data from conventional techniques. Different profiles of tissue destruction and FTY720-mediated damage prevention were documented. In gm, spectra showed significantly increased protein and lipid content in the EAE+P group relative to controls, in agreement with cellular infiltration. However the EAE+FTY group showed significantly higher protein but lower lipid content relative to the EAE+P group, suggesting reduced infiltration, but combined with upregulation of repair pathways. In wm, spectra showed significantly lower protein, but higher lipid content, suggesting that protein and lipid increases associated with cellular infiltration are exceeded by tissue destruction. The EAE+FTY group showed significantly higher lipid content, but no significant protein difference with controls, in agreement with both reduced infiltration and tissue destruction. The complexity and size of the acquired spectral data set warrants a multivariate approach to the analysis. We are currently applying principal component analysis (PCA) with the aim of building a model capable of further discriminating biochemical differences between the experimental groups for application to second-generation S1PR1-targeted drugs.

Keywords

FTIR microspectroscopy, GPCR, S1PR, candidate drugs, multiple sclerosis, EAE model

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