Imaging of Neuroinflammation in GFAP-IL6 Mice utilising 125I-CLINDE and 18F-PBR111

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Using a known radiotracer designed to express microglial activation presented in the brain during neuorinflammation, this combined *in vitro* and preclinical imaging study is aimed to further examine mechanisms underlying the neuroinflammation found in the heterozygous mouse model (GFAP-IL6)

Background

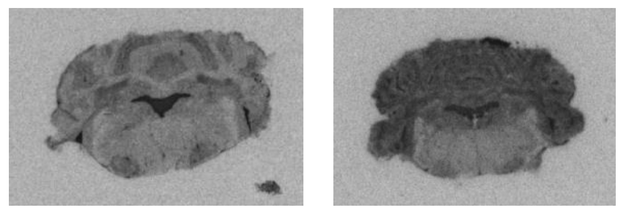
Neuroinflammation is a promising therapeutic target for many degenerative and age-related brain diseases, ranging from benign forms such as cognitive decline in the elderly, to neurodegenerative diseases including Alzheimer's (AD) and Parkinson's disease and even depression [1]. Currently, there is a strong need for well-validated preclinical models to study neuroinflammatory pathophysiology and *in vivo* drug screening for neuroinflammation related diseases.

In this study, the feasibility of the heterozygous neuroinflammation mouse model (GFAP-IL6; GFAP-Glial fibrillary acidic protein; IL6-Interleukin 6) [2] was explored by utilising the neuroinflammatiory marker, translocator protein (TSPO) radiotracers; firstly using in vitro autoradiography, followed by in vivo PET/CT imaging.

Autoradiography

Brain tissues from 5-month-old mice fed with ad-libitum lab chow diet (GFAP-IL6 (n=6) and C57Bl/6 wild type (n=4)) were extracted, sliced and exposed to 125I-CLINDE, a known TSPO marker in an autoradiography assay [3].

There was a statistically significant increase of 125I-CLINDE binding in the cerebellum of the GFAP-IL6 mice group compared to the wild type mice group.

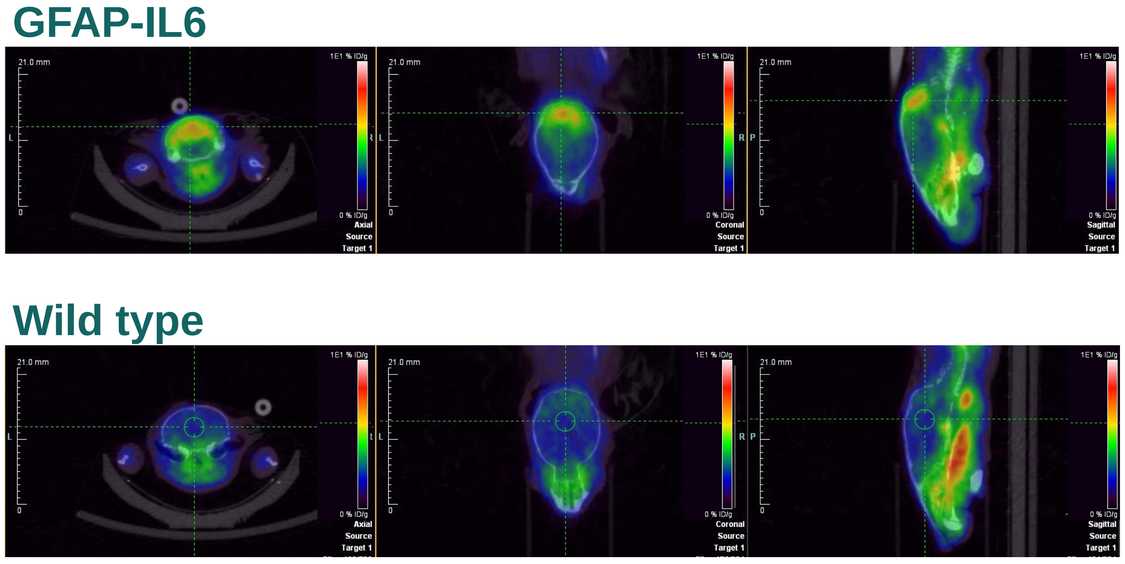


Result 1. Autoradiography derived images of 125I-CLINDE binding in the cerebellum of the GFAP-IL in comparison to wild type mice

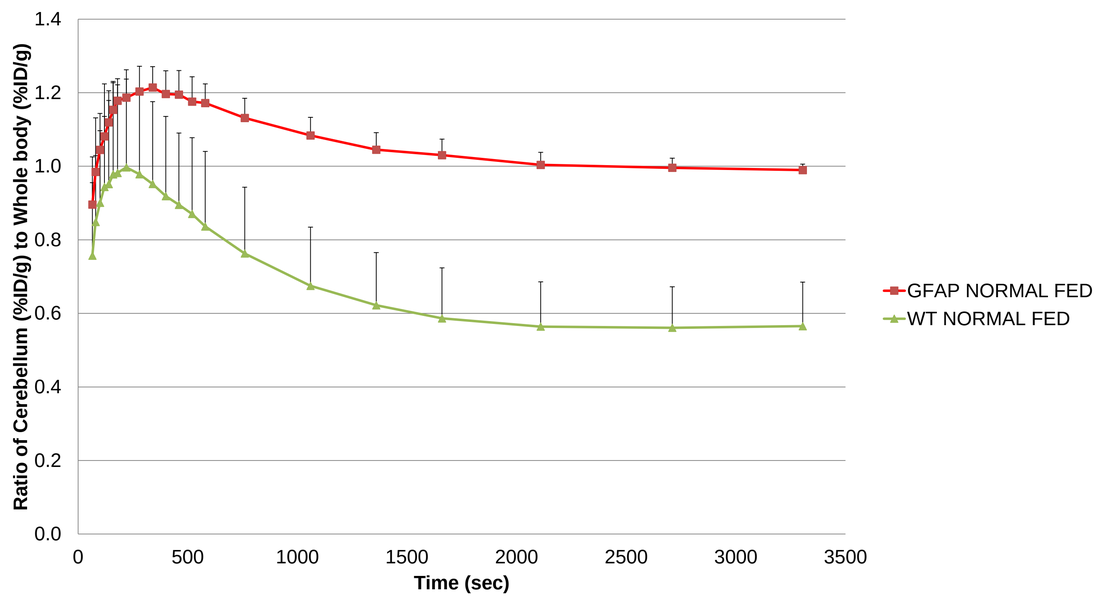
PET/CT imaging

The PET/CT study was then performed in another subset of 5-month-old mice (GFAP-IL6 (n=5) and C57Bl/6 wild type (n=5)). 1 hour dynamic PET/CT scan was performed using 18F-PBR111, a known PET radiotracer for TSPO for neuroinflammation [3,4].

Results from the PET/CT imaging study are in line with the autoradiography finding where there is a statistically significant increase in the 18F-PBR111 uptake in the cerebellum throughout the duration of the PET scan of the GFAP-IL6 mice compared with the wild type mice.



Result 2a. PET/CT derived image of 18F-PBR111 distribution in the cerebellum of the GFAP-IL versus wild type mice.



Result 2b. Activity in Cerebellum in comparison to whole body in GFAP-IL mice after 18F-PBR111 injection

Conclusion

Result from both autoradiography and PET/CT scans suggests increased neuroinflammation in the cerebellum in GFAP-IL6 mice.

This study has further validated that this heterozygous mouse model is a potential candidate to study neuroinflammation.

Furthermore, PET/CT imaging using 18F-PBR111 can also be utilised to study the effect of potential drug candidates to treat or possibly prevent neuroinflammation in this mouse model.

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Reference

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