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Abstract Submission

Title: Examination of neuroinflammation in multiple sclerosis mouse models via quantification of cyclooxygenase-1 (COX-1) with the PET radioligand, [^{11}C]PS13.

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Abstract:

Purpose
To quantify cyclooxygenase-1 (COX-1) density using the radioligand [11C]PS13 in a mouse model of multiple sclerosis (MS), experimental autoimmune encephalomyelitis (EAE), as a potential biomarker for MS-related neuroinflammation.

Materials and Methods
Radiometabolite analysis of [11C]PS13 was performed in 3-month-old C57BL/6 mice (n=3M/3F) at 2, 5, 15, 30, and 60 minutes. EAE was induced in 10-week-

old C57BL/6 mice by subcutaneous injection of 200 µg of MOG35-55 antigen emulsion and 220 ng of pertussis toxin intraperitoneally. Autoradiography assessed COX-1 density in the cerebellum using [3H] PS13. Immunofluorescence staining was conducted in the cerebellum of EAE (n=4) and control mice (n=4) using IBA1, COX-1, and GFAP antibodies.

Results

Radiometabolite analysis showed 89.6% of [^{11}C]PS13 remained intact in the brain at 60 minutes, suggesting minimal metabolite penetration. Males showed a trend towards significance of higher intact [^{11}C]PS13 in blood ($p=0.061$) and brain retention ($p=0.050$) than females. Autoradiography revealed increased [3H]PS13 binding in EAE mice (mean=46.90) versus controls (mean=40.62). Immunofluorescence showed elevated colocalization of COX-1 with IBA1• microglia, and to a lesser extent, GFAP• astrocytes. EAE mice displayed higher COX-1 (mean=14.01), IBA1 (mean=18.23), and GFAP (mean=9.90) levels compared to controls (mean=8.03, 4.58, and 5.73, respectively), with greater colocalization of COX-1 with IBA1 than GFAP.

Conclusions

Our findings show that [^{11}C]PS13 is a suitable radiotracer for detecting increases in COX-1-related neuroinflammation in EAE mice. Next, we will perform PET imaging with [11C]PS13 in EAE mice and apply our radiometabolite data to pharmacokinetic analyses.