

Topic: 20. Imaging

Title: Positron emission tomography imaging in multiple sclerosis highlights a diffuse inflammatory response in brain that appears normal on conventional magnetic resonance imaging

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Text: BACKGROUND

Multiple sclerosis (in all disease stages) is associated with a chronic, innate immune activation involving microglia and astrocytes. While this plays roles in repair, it may also contribute to neurodegeneration. Here we describe the use of positron emission tomography (PET) with [¹¹C] PBR28, a radioligand for the 18kDa translocator protein (TSPO), for the study of a group of multiple sclerosis (MS) patients as a marker of activated microglia/macrophages.

OBJECTIVES

To characterize the distribution of the inflammatory response in the brain and its relationship to magnetic resonance imaging (MRI) markers of pathology in people with MS.

METHODS

Twelve people with MS (10 women: 2 men; Expanded Disability Status Score (EDSS) range 1.0-7.0; aged 31-65; 9 relapsing remitting: 3 secondary progressive MS) underwent a PET scan with [¹¹C]PBR28 and correlative 3T MRI including magnetization transfer imaging. We stratified subjects based on the rs6971 polymorphism that determines TSPO binding affinity. T2 hyperintense white matter lesions (WML), and high and low magnetization transfer ratio (MTR) regions of T2-weighted normal appearing white matter (NAWM) were segmented on correlative MRI. A [¹¹C]PBR28 distribution volume ratio (DVR) was estimated using the Logan graphical method with the high MTR NAWM as a reference region.

RESULTS

DVR in WML (mean +/- SD, 0.83 +/- 0.06) was lower than in surrounding NAWM (1.02 +/- 0.02, $p < 1 \times 10^{-5}$). Low MTR NAWM had higher DVR (1.05 +/- 0.04) than whole NAWM (1.02 +/- 0.02, $p = 0.002$). The cortex had a higher mean DVR (1.13 +/- 0.09) than the NAWM ($p = 0.001$). Subcortical grey matter showed striking differences in DVR (thalamus, 1.21 +/- 0.15; caudate, 0.67 +/- 0.20, $p < 1 \times 10^{-6}$). There was a strong correlation between the NAWM MTR and the cortical grey matter (Spearman's rho = 0.74, $p = 0.006$) and thalamic (rho = 0.75, $p = 0.005$) DVR.

CONCLUSIONS

[¹¹C]PBR28 highlights *in vivo* that chronic T2 hyperintense lesions show little inflammatory response relative to NAWM. Low MTR NAWM shows evidence for an active inflammatory response. The strong correlations between MTR in NAWM and grey matter inflammation may reflect microglial responsiveness to neurodegeneration along the neuroaxonal unit.

Disclosure: ÖY has received honoraria for lectures from Teva (2011) and Bayer Schering (2012) (both paid to University Hospital Basel). ÖY received research funding from MAGNIMS / ECTRIMS, the University of Basel, the Swiss MS Society and Free Academy Basel, Switzerland.

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EAR holds stock in GSK, has received research funds from AbbVie, and consultancy/speaker fees (paid to King's College or Imanova) from GSK, BioTie, Gedeon Richter, Teva and Lighlake Therapeutics.

OC receives research grant support from the Multiple Sclerosis Society of Great Britain and Northern Ireland, the Department of Health Comprehensive Biomedical Centre, the International Spinal Cord Research Trust (ISRT) and the Engineering and Physical Sciences Research Council (EPSRC); she serves as a consultant for Novartis, Biogen and GE and payments are made to UCL Institute of Neurology.

RN has received honoraria for speaking from Bayer. Biogen - principal investigator, funds for staff, research, organising education, honorarium for speaking, advisory boards. Genzyme - honorarium for speaking, organising education, advisory boards. Merck Serono - honorarium for speaking, advisory boards. Novartis - principal investigator, honorarium for speaking, advisory boards. Roche - advisory boards. TEVA - principal investigator, funds for research

NDS has received honoraria from Schering, Biogen-Idec, Teva, Novartis, Genzyme, and Merck Serono S.A. for consulting services, speaking and travel support. He serves on advisory boards for Merck Serono S.A. and Novartis. He has received research grant support from the Italian MS Society.

PMM holds stock in GSK, has received research funds from Biogen and GSK, and consultancy/speaker fees (paid to Imperial College) from IXICO, GSK, Biogen, Novartis and Adelphi Communications.