PK11195-PET Enhancement in Black Holes Correlates with Disability and Outcome in Progressive Multiple Sclerosis

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Introduction
Multiple sclerosis (MS) is characterized pathologically by focal areas of demyelination and variable axonal loss in the central nervous system. T2 and enhancing T1 MRI lesions have limited utility in predicting MS outcome. Literature on black holes (T1 hypointense MS lesions, BH) is inconsistent with regards to their pathological features and ultimate clinical role (Suhara et al., 2009). Activated microglia has a major role in the pathology of MS, for both neuroinflammation and degeneration. The PK11195 (PK) PET tracer has a high affinity for the translocator protein (TSPO), which is localised to and upregulated in activated microglia (Niehues et al., 2016). In vivo PK-PET has been used to study MS BHs, as an indicator of microglial activity and its correlation with disability.

Methods

STUDY POPULATION
• Nineteen MS patients
  • Relapsing: 10 subjects
  • Progressive: 9 subjects

INVESTIGATIONS
• Neurological examination (EDSS)
• Neuropsychological examination
• PK-PET scan
• Co-localising MRI scan

PK-PET QUANTIFICATION
• Binding potential relative to the non-specific volume (BPND)
• Reference tissue model (Guarn et al., 1997)
• Tissue reference input extraction: SUPERPK software (Immelmann, Turkheimer et al., 2007; Blockshaw et al., 2009)

BLACK HOLES
BHs were manually drawn, defined as hypointense regions > 3 mm² on T1-weighted MRI images corresponding to hypointense regions on T2-weighted images (Tuyen et al., 1996).

Table 1: Study population

Table 2: Black holes population

Table 3: Baseline demographic and clinical characteristics of progressive subjects. Subjects are grouped according to their clinical outcome at 2 year follow up

Table 4: Volume load and PK binding in progressive MS patients

CONCLUSIONS
In this study we used PK-PET heterogeneity within BHs as an in vivo marker of microglial/macrophage activation, to refine our understanding of the contribution of BHs to MS disability. We found that microglial/macrophage activation in MS BHs, determined by PKBPND, showed a high degree of heterogeneity and that only in progressive patients did the degree of activation correlate with disability and prognosis. In relapsing MS the level of PKBPND was higher in the smaller lesions and not associated with disability.