Objective:
To determine the relationship between microglial activation in the deep grey matter (DGM) and both regional atrophy and physical disability in multiple sclerosis (MS).

Background:
DGM atrophy is a proposed biomarker for neurodegeneration in MS but its pathogenesis is not clear. [F-18]PBR06 is a novel, long half-life PET tracer for assessing microglial activation. The relationship between DGM microglial activation and atrophy in MS is unknown.

Design/Methods:
Fourteen MS patients [age 42.2±12.8 years, 8 relapsing-remitting (RR), 6 secondary progressive (SP), Expanded Disability Status Scale (EDSS) score 3.9±2.3 (range 1-7.5); timed 25 foot walk (T25FW) 8.0±3.9 (range 4-19.4) seconds] and 8 healthy controls (HC) (age 42.5±16.3 years) underwent [F-18]PBR06 PET and 3T MRI for assessing DGM (thalamus, caudate, putamen, globus pallidus (GP)) microglial activation and atrophy, respectively. Standardized Uptake Value (SUV) PET maps were co-registered to MRI. SUV ratios (SUVRs) were global brain-normalized. The FSL-FIRST pipeline determined DGM volumes (Vols). Independent samples t-tests and Pearson's correlations were performed.

Results:
Thalamic SUVR was higher in SPMS vs. HC (+9.8%, p=0.03) and thalamic, putaminal and GP SUVRs were higher in SPMS vs. RRMS (+14.8%, +12.9%, +14.0%, p=0.001, 0.005, 0.01, respectively). Thalamic, putaminal and GP Vols were lower in MS vs. HC (-17.1%, -18.4%, -19.4%, p=0.003, 0.001, 0.0001, respectively), SPMS vs. HC (-16.5%, -19.1%, -20.7%, p=0.01, 0.005, 0.002, respectively) and RRMS vs. HC (-17.5%, -18.0%, -18.4%, p=0.002, 0.02, 0.002, respectively). Among MS patients, bivariate (r=-0.56, p=0.03) and age-adjusted partial (r=-0.57, p=0.04) correlations indicated that the link between structure-specific DGM microglial activation and atrophy was strongest in the GP. Thalamic (r=0.89, p=0.00002; r=0.87, p=0.00005) and putaminal (r=0.63, p=0.01; r=0.68, p=0.007) SUVRs showed significant correlations with EDSS score and T25FW.

Conclusions: Increased DGM microglial activation can be detected in patients with MS and is associated with regional atrophy and physical disability.