Glutamate is elevated in presupplementary motor area in Parkinson's disease
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Introduction
Parkinsons’ disease (PD) is a relentlessly progressive neurodegenerative disorder. Evidence suggests that PD-associated neuronal dysfunction occurs years before symptoms appear and clinical diagnosis is possible. Enlarged substantia nigra ultrasound hyperechogenicity (SN+), present in 90% of PD patients, is showing promise as a method of identifying neurologically asymptomatic persons at risk of PD [1]. It is also apparent that compensatory changes in brain motor circuitry, including increased activation or novel area recruitment may help to mask symptom development. Here, we studied the pre-supplementary motor area (preSMA) of subjects with mild to moderate PD, neurologically normal SN+ controls and neurologically normal (SN-) controls using magnetic resonance spectroscopy to detect possible biomarkers of early disease or neural compensation.

Methods
Subjects (8 SN-, 55-62 y; 4 SN+ 51-61 y; 8 PD 56-63 y) were scanned at 3T (Philips Achieva TX) using an 8 channel head coil. A 2cm3 VOI was positioned in the left preSMA and a 1H MR spectrum acquired using the PRESS sequence (TR = 2s, TE = 32 ms, 32 scans) along with a water reference. Spectra were processed in the time domain using the AMARES and QUEST algorithms of jMRUI (vs 3 and 4 (build 162), respectively) and compared to the water resonance. Subjects also underwent ultrasound to determine SN hyperechogenicity and motor and neurological assessment. Statistical significance was tested using Kruskal Wallis non-parametric ANOVA followed by a Mann-Whitney U test where significance was indicated. Correlations were tested using the Spearman rank test in Graphpad Prism (v 5).

Results
Levels of glutamate were significantly elevated in PD (Fig. 2) compared to SN- controls (P = 0.0007) but not compared to SN+ (P = 0.054). There were no significant differences in NAA, choline and creatine peaks, nor myo-inositol although some involvement of NAA in motor ability was indicated by the correlation of NAA with the Parkinson’s motor severity scale UPDRS (P = 0.011). Accordingly, a more robust correlation (Fig. 3) was found between Glu/NAA and UPDRS (P = 0.0081; ρs = 0.60) and between Glu/Cr and UPDRS (P = 0.038; ρs = 0.48). Additionally, Cre and NAA correlated (P = 0.032, ρs = 0.48) but neither showed any correlation with Cho.

Discussion
We detected a significant increase in glutamate levels in the PreSMA, which, along with Cre and NAA levels, was related to decreased motor function. Previously lower NA/Cr has been reported in preSMA in an older PD cohort (70 y) at 1.5T with a trend to correlation with the UPDRS [2]. We suggest that increased preSMA activity may predate decreased NAA but whether this is a compensatory mechanism awaits further investigation.

References