

Higher GABA Concentrations in the Brainstem in Parkinson's Disease by ^1H MRS at 7T

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Introduction

Parkinson's disease (PD) is characterized by loss of dopaminergic neurons of the pars compacta of the substantia nigra (SN) which project their axons to the putamen (1). *In vivo* ^1H MRS has been used to investigate neurochemical changes of the SN and putamen in PD; however findings have been variable due to challenges associated with the locations of these mid-brain structures, their small size and high iron content (2-4). Meanwhile, recent pathological findings indicate earlier involvement of more caudal brainstem regions in PD before the nigrostriatal system is affected (5). Specifically, there is evidence of loss of aminergic neurons of the pons as well as changes in the medulla and spinal cord (5). These findings motivated recent functional and structural investigations of the brainstem in PD (6-8). Because MRS enables detection of early biochemical alterations associated with neurodegeneration, we hypothesized that suspected abnormalities in the pons in PD would be detectable by high-field MRS. Therefore, the aim of this study was to determine the feasibility of 7T ^1H MRS to detect neurochemical alterations in the pons, as well as the SN and putamen, in PD.

Methods

Eleven individuals with early-moderate PD (54 ± 10 years old, mean \pm SD, Hoehn and Yahr stage 2) and 8 age-matched healthy volunteers (55 ± 7 years old) were studied. Participants were not demented and the early-moderate disease severity of patients was established with the Unified Parkinson Disease Rating Scale and the Hoehn & Yahr Staging. PD enrollees were off their usual antiparkinsonian medications 12 hours prior to imaging. MR experiments were performed using a 7T, 90-cm horizontal bore magnet (Magnex) equipped with a Siemens console. A 16-channel transmit/receive transmission line array head coil was used. Destructive B_1^+ interferences in the volume of interest (VOI) were reduced by localized B_1^+ shimming (9). Spectra were measured by a short-echo STEAM sequence (TE = 8 ms, TR = 5 s) with VAPOR water suppression and outer volume saturation (10). Spectra were acquired from the SN ($6 \times 13 \times 13 \text{ mm}^3$, nt = 384, 5 patients and 4 controls), putamen (PUT) ($12 \times 8 \times 18 \text{ mm}^3$, nt = 128, 11 patients and 8 controls), and pons (30 x 10 x 15 mm³, nt = 128, 11 patients and 8 controls). Metabolites were quantified with LCModel (11) using the unsuppressed water signal as reference.

Results and Discussion

^1H MR spectra with good SNR and spectral resolution were consistently obtained from both patients (Fig. 1) and controls. The high SNR of spectra enabled the quantification of a neurochemical profile consisting of 11 metabolites in pons and putamen (Fig. 2) and 7 metabolites in SN. The neurochemical profiles from the 1 mL SN voxel did not show significant differences between groups (data not shown). On the other hand, higher GABA concentrations were detected in pons ($p < 0.001$) and putamen ($p = 0.06$) in patients relative to controls. This GABA alteration may reflect symptomatic manifestation of the disease as PD subjects were off their usual medications, or could be related to changes in neurotransmitter signaling from the loss of neurons in these regions. In conclusion, further study of ultra-high field MRS may aid in assessing pathogenetic theories of PD.

References

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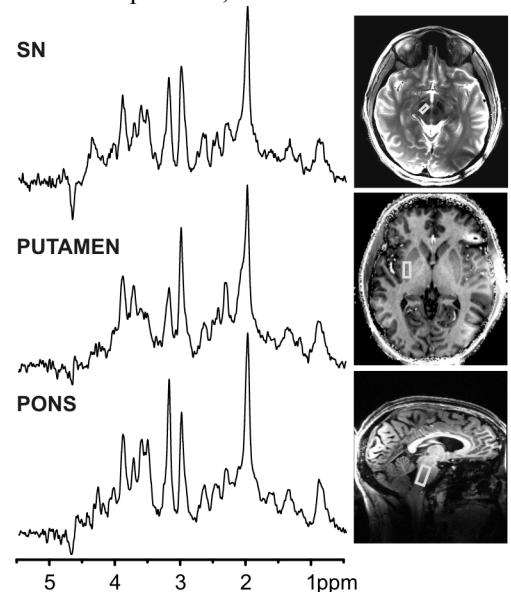


Figure 1. ^1H MR spectra obtained in one PD patient with STEAM (TR = 5 s, TE = 8 ms, TM = 32 ms) from three VOIs.

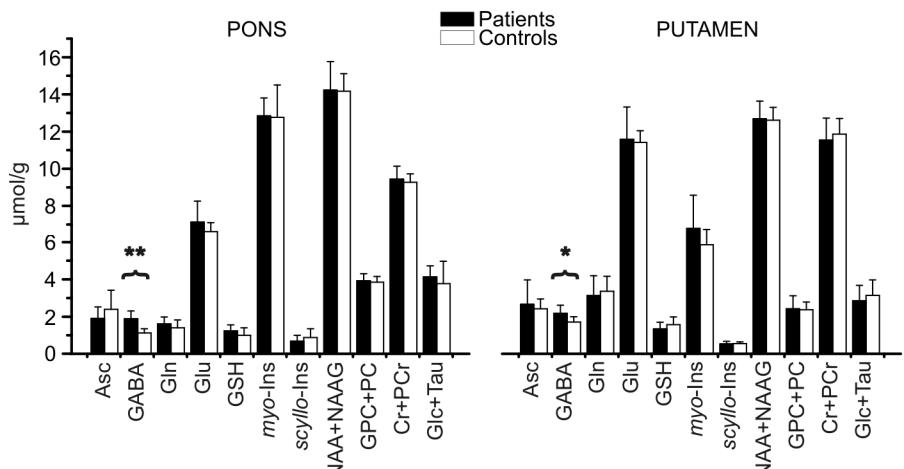


Figure 2. Metabolite concentrations determined by LCModel fitting. Metabolites that were significantly different or showed a trend for a difference between groups are marked with: * $p = 0.06$, ** $p < 0.001$. Error bars: inter-subject SD.