Proton MRS of Bilateral Substantia Nigra in the Human Brain at 4 Tesla with Hadamard Encoding

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Introduction

Parkinson's disease (PD) is characterized by loss of dopaminergic neurons in the substantia nigra (SN), but its etiology remains poorly understood (1). *In vivo* ^{1}H MRS may provide a non-invasive alternative to cell culture and animal model, as well as post-mortem studies, that are more commonly utilized to understand the pathogenesis of PD. However, due to its small size, the MRS investigation of the SN in the human brain is difficult (2). We have previously reported the feasibility of obtaining a neurochemical profile from a 2.2 ml volume encompassing the unilateral SN by ^{1}H MRS with LCModel analysis (3). Since PD characteristically is an asymmetric condition, acquiring data from VOI encompassing the SN contralateral and ipsilateral to the clinically first and more severely affected side of patients is desirable. The aim of the current study was to determine the feasibility of acquiring STEAM spectra from right and left SN simultaneously using Hadamard encoding (4).

Methods and Subjects

All studies were performed on a 4 Tesla / 90 cm magnet (Oxford/Varian). A TEM volume coil (5) was used as the transceiver. STEAM combined with OVS and VAPOR water suppression (6) (TE=5ms, TM=44ms, TR=4.5s, NEX=416) was used to simultaneously obtain spectra from two voxels (2.2 ml) around the right and left SN in 10 healthy volunteers (5 M/5 F, average age±SD: 65±10 years). For this, the 90° slice selective RF pulse in x-direction in the STEAM sequence was Hadamard encoded. Power adjustment of this pulse and the other 2 STEAM pulses were performed separately in each volunteer. First- and second-order shims were adjusted in a volume encompassing both voxels using FASTMAP with echo-planar readout (7). Metabolites were quantified with LCModel (8) using reference water signals collected similarly from both voxels using Hadamard encoding.

Results and Discussion

Despite the broad linewidths of ^{1}H MR spectra (Fig.1) due to the high iron content in the SN and the necessity to shim over both voxels, nine metabolites including GABA, glutamate, glutathione and *myo*-inositol were quantified using LCModel with average Cramér-Rao lower bounds (CRLB) $\leq$ 35% (Fig. 2). The neurochemical profile, as well as the CRLB, were very similar to our previous results obtained from unilateral SN spectra using single-voxel STEAM (3). No differences were observed between the right and left neurochemical profiles, therefore we fitted the sum of the right and left SN spectra of each volunteer with LCModel to increase the S/N by ~40%. The metabolite concentrations obtained this way were identical to fitting the right and left spectra separately, indicating the reliability of quantifying the right and left spectra individually. CRLB decreased as expected (Fig. 2).

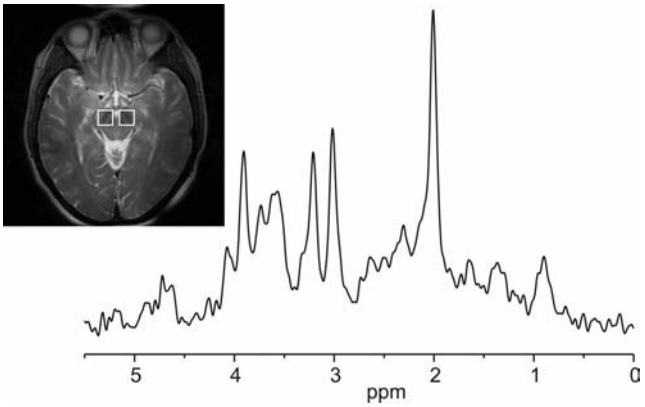

Fig. 1. Spectral quality obtained in one volunteer using STEAM (TE = 5ms, TR = 4.5s, VOI = 2.2ml x 2, NEX=416) with Hadamard encoding. The sum of spectra obtained from the right and left SN are shown. Voxel positioning is indicated on T_2-weighted image.

GABA concentrations were substantially higher and glutamate lower than the values reported in cortex, in very good agreement with autopsy results (9), as well as our previous findings in single voxel spectra (3), and consistent with lower number of glutamatergic and higher number of GABAergic neurons in SN.

In conclusion, MRS at 4 T can be used to evaluate neurotransmitters GABA and glutamate, and the antioxidant GSH simultaneously in right and left SN. Hadamard encoding enables acquisition of this information in half the time than would be required to obtain single voxel spectra from both sides. Furthermore, spectra from the two sides can be summed to increase S/N while eliminating partial volume effects due to the CSF space at the midline.

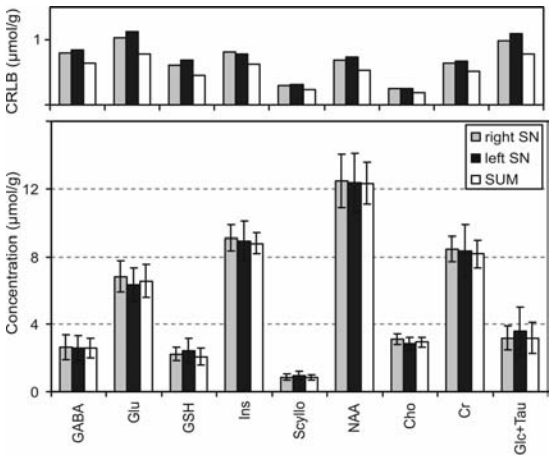

Fig. 2. Average (± SD) metabolite concentrations and Cramer-Rao lower bounds obtained from right and left SN and the sum of two sides. Metabolites listed are: GABA, glutamate, glutathione, *myo*-inositol, *scyllo*-inositol, N-acetylaspartate + N-acetylaspartyl-glutamate, choline-containing compounds, creatine + phospho-creatine, glucose + taurine.

References

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