Regional Neurochemical Profiles in the Non-human Primate Model by ^{1}H MRS at 7T

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Introduction

The non-human primate (NHP) animal model often serves as a critical link between basic research and human clinical applications. By mirroring human diseases, especially in the case of abnormalities in neurological conditions, the non-human primate model narrows the gap between small laboratory animal models and the complexity of the human brain. In vivo ^{1}H MRS has been widely used to investigate neurochemical changes in neurological diseases because it presents great potential to detect early and progressive biochemical changes that reflect underlying pathology. While the potential of obtaining extended neurochemical profiles from multiple brain regions was recently demonstrated in the human brain at ultra-high field (1,2), this capability remains to be investigated in the NHP model. MRS at ultra-high field with NHPs has potential advantages over human studies since the smaller NHP brain volume enables high transmit power efficiency and SNR in the whole brain with a dedicated coil and problems due to subject motion are minimized in the anesthetized animal. Therefore, the goal of the current study was to demonstrate the feasibility of obtaining high quality MR spectra at 7T from multiple clinically relevant brain regions and to quantify regional neurochemical profiles in the NHP model.

Methods

An anesthetized (propofol, 2 mg/kg IV) female Macaca mulatta monkey (13 years / 13.6 kg) was imaged. The monkey was intubated to secure an open airway and was wrapped in a chemical heating pad to maintain body temperature. Body temperature, pulse oxygenation, pulse rate, expired CO_2, and respiration rate were continuously monitored throughout the imaging session. A 7T MR scanner (Siemens) equipped with a head gradient coil (80mT/m G-maximum, 333mT/m/ms) was used with a custom-built monkey coil. A 21-channel coil consisting of 16 stripline transceiver arrays and 5 smaller localized receive only loops was used (3). 3D T_2-weighted (VFL) anatomical images were acquired to localize the regions of interest. The following parameters were used: resolution of 0.3 x 0.3 x 0.3 mm^3; TEeff/TR: 89/2700 ms; IPAT=3 with 2 averages for a total acquisition time of 23 min. Spectra were measured with a short-echo semi-LASER sequence (TE = 26 ms, TR = 5 s, 128 transients) with VAPOR water suppression and outer volume saturation (4). First- and second-order shims were adjusted using FASTMAP with echo-planar imaging readout (5). Spectra were acquired from the posterior cingulate cortex (10 x 10 x 10 mm^3), putamen (12 x 6 x 8 mm^3), and cerebellum (11 x 9 x 11 mm^3). Metabolites were quantified with LCModel (6) using the unsuppressed water signal as reference. Metabolites quantified with Cramér-Rao lower Bounds (CRLB) < 30% were selected to evaluate regional neurochemical profiles.

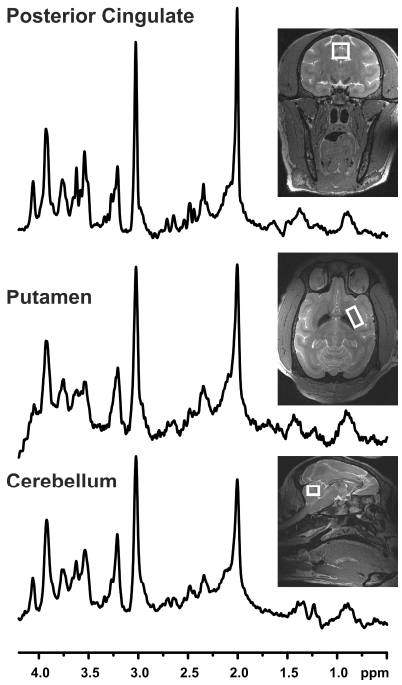

Figure 1. ^{1}H MR spectra obtained in a Macaca mulatta monkey using semi-LASER (TR = 5 s, TE = 26 ms) from three VOIs.

Results and Discussion

Excellent spectral quality was obtained with a small chemical shift displacement error (<5% per ppm in each dimension) in all VOI (Figure 1). The best resolution was obtained in the posterior cingulate with a creatine linewidth of 8 Hz. The spectral quality in this VOI resulted in the quantification of 4 neurochemicals (NAA, total creatine, *myo*-inositol and glutamate) with CRLB ≤ 3%. The SNR and resolution achieved in the 3 brain regions enabled the quantification of a neurochemical profile consisting of at least 11 metabolites (Figure 2). The findings revealed neurochemical similarities between humans and monkeys. For example, the highest Glc+Tau, *myo*-inositol, glutamine and total creatine concentrations were detected in the cerebellum similar to prior MRS studies in humans (1) and in agreement with biochemical literature (7). These findings demonstrate that single voxel ^{1}H MRS at 7T has the potential of becoming an objective tool to monitor neurochemical changes and to test treatment effects in NHP models of neurological disease.

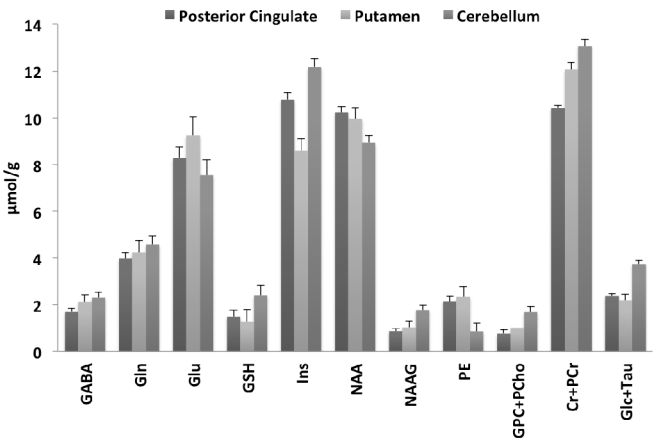

Figure 2. Metabolite concentrations determined by LCModel fitting. The error bars shown are CRLBs.

References:

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