BASELINE COMPARISON OF BRAIN METABOLITES BETWEEN RHESUS MONKEYS AND HUMANS BY MRS

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Introduction: Magnetic Resonance Spectroscopy (MRS) provides a unique possibility to non-invasively detect and quantify brain metabolites in vivo. A variety of research such as neurological and neurotoxicological studies are being performed in monkeys and in humans using MRS [1-4]. However, little is known about the difference of brain metabolites between monkeys and humans using MRS.

Materials and Methods: Here we compare the baseline difference of brain metabolites, especially of the major inhibitory neurotransmitter gamma-aminobutyric acid (GABA), between the two species using exactly the same imaging sequence on the same type of scanner. Brain metabolites of 7 rhesus monkeys (male, mean age = 6.5y, about 20y in human years) and 8 healthy humans (male, mean age = 26.2y) were acquired on a 3T Philips Achieva clinical MRI scanner (8 channel extremity coil for monkeys and 8 channel head coil for humans). GABA data was obtained from a brain volume containing thalamus and adjacent basal ganglia structures (6 ml for monkeys and 22.5 ml for humans) by the MEGA-PRESS sequence [5] (TR/TE=2000/68 ms, 128 averages with the editing pulse centered at 1.9 ppm and 128 averages with the pulse centered at 7.6 ppm in an interleaved fashion for humans, while 16 and 16 averages for monkeys). The result is referred to as GABA+ due to the contribution of homocarnosine and co-edited macromolecules. GABA+ was scaled to total creatine to compare with literature results [6,7]. Other brain metabolites were obtained by short TE MRS (TR/TE=2000/32ms, 256 averages for monkeys; TR/TE=1500/30ms for humans) and the results were scaled to unsuppressed water in volumes of frontal cortex (1 ml for monkeys and 8 ml, 96 averages for humans) and thalamus (1 ml for monkeys and 22.5 ml, 30 averages for humans), including N-Acetyl-aspartate (NAA, a neuronal marker), myo-inositol (mI, a glia cell marker), glutamate (Glu, the major excitatory neurotransmitter), total creatine (tCr) and choline (tCho). MRS data processing and quantification were performed with LCModel [8], fitting each spectrum as a weighted linear combination of basis spectra from individual metabolites.

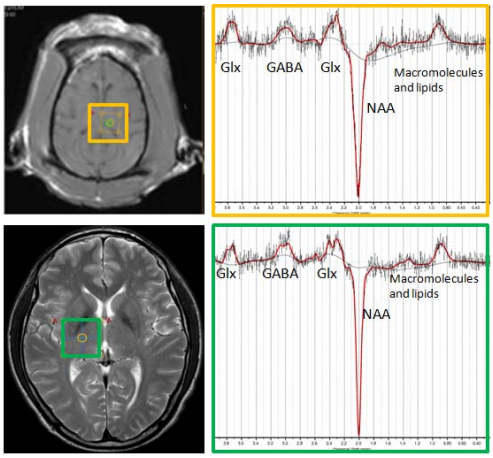

Figure 1: Volume of interest for the thalamus region and representative MEGA-PRESS difference spectra withLCModel fitting for both monkeys (upper) and humans (lower).

Results: Figure 1 depicts the thalamus volume and a representative spectrum for both monkeys and humans. The metabolite levels are shown in Table 1. We found that monkey thalamus showed higher GABA/tCr than human thalamus, with a difference of 27.6% ($p<0.05$). Monkeys had lower NAA in both the frontal cortex ($p<0.01$) and thalamus ($p<0.05$). Levels of Glu and tCho were higher in human frontal cortex ($p<0.05$), while tCr was higher in human thalamus ($p<0.05$).

	Thalamus						Frontal cortex				
	GABA+/tCr	NAA	mI	tCr	Glu	tCho	NAA	mI	tCr	Glu	tCho
Monkeys	0.25±0.05	6.04±0.54	5.12±0.73	5.49±0.45	6.48±0.81	1.62±0.22	5.02±1.04	5.53±1.44	4.99±1.39	7.70±0.71	1.08±0.29
Humans	0.18±0.03	6.64±0.37	4.50±0.43	6.13±0.57	5.80±0.97	1.81±0.10	6.89±0.50	5.69±0.72	5.96±0.45	8.59±0.78	1.69±0.23

Table1: metabolite levels in the thalamus and frontal cortex regions for both monkeys and humans.

Discussion: These results provide first-hand information on the baseline differences of various brain metabolites between rhesus monkeys and humans. Our results suggest that brain metabolites of monkeys are similar, but not identical to those of humans. GABA/tCr was previously shown to be 0.35 in the basal ganglia of a 12y female rhesus monkey using double quantum coherence technique [6], which is relatively comparable with our result.

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