Increased Brain Choline Level Observed by 1H MRS Measurement After IV Choline Infusion

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Introduction

Choline plays an important role in neuronal function, as it is a constituent of the neurotransmitter acetylcholine, as well as the cell membrane components phosphatidylcholine and sphingomyelin. Very little choline is synthesized in brain, rather, brain choline is obtained almost entirely through the diet [1] and transported across the blood-brain barrier by facilitated diffusion [2]. There is some evidence that in animals [3] and in humans [4], brain choline uptake is reduced with age. However, in the last several years, divergent results have been reported concerning changes in the ^{1}H MRS choline resonance following choline administration to healthy human subjects [4-6].

Many animal studies have observed increases in choline and its metabolites in brain following choline administration. However, the results have not always been as clear in human studies. There are many possibilities for the differing results in humans. A recent study by our group, using an MRS method designed to minimize intra-subject variance, reported a statistically significant increase of 6.2% in brain choline after oral choline administration in young healthy subjects [7]. Another source of variance in oral dosing studies might be intra-subject differences in the breakdown of choline in the gastrointestinal tract. Intravenous dosing avoids this complication.

Methods and Study Subjects

Healthy male subjects; older (age = 71 ± 2.9 yrs, n=4) and younger (age = 26.4 ± 3.1 yrs, n=5) were given a baseline ^{1}H MRS scan using a 1.5 T GE scanner, then intravenously infused with 1 mg/ml choline for 2 hours. A second ^{1}H MRS scan was performed immediately after infusion was terminated. Two younger subjects and 3 older subjects returned for a second study day, identical except for the infusion contained 2mg/ml choline. All MRS scans used a single voxel ^{1}H MRS, PRESS method, with a voxel size of 2x3x2 cm^3 centered on the left putamen. In each MR session, both short TE (42msec, TR=2.3sec) and long TE (272msec, TR=5sec) 1D MRS spectra were acquired. Number of averages was 128.

All MRS spectra were processed using Felix nD based software (Accelrys, San Diego). Peak areas of Cho, Cr and NAA were obtained using 1D Marquardt non-linear curve fitting algorithm. Using the Cr signal as an internal reference, results were expressed as ratios. Statistical significance of the results was evaluated using Statview.

Results

As shown in the table below, both younger and older subjects had increases in brain cytosolic choline levels after IV choline infusion. **Diff Cho/Cr** is the difference between after and baseline Cho/Cr. **% Diff Cho/Cr** is the percent increase in Cho/Cr from baseline Cho/Cr. Results are expressed as Mean ± SE. The **p** values shown are from paired t-tests between baseline and after choline infusion Cho/Cr. Only the 1 mg/ml dose showed some statistically significant increases, as fewer subjects were able to return for the 2mg/ml dose. There is a significant difference between younger and older subjects at the 1 mg/ml dose with the short TE (p=0.04) but not the long TE (p=0.52) measurement. Higher Cho/Cr increases observed using IV choline infusion, in comparison with our previous study (6.2% in younger subjects) [7], may be due to less gastrointestinal breakdown of choline than with oral choline administration.

Younger	n	Diff Cho/Cr	% Diff Cho/Cr	p	**Older**	n	Diff Cho/Cr	% Diff Cho/Cr	p
Short TE, 1mg/ml	5	0.049 ± 0.011	10.6 ± 2.5%	**0.01**	Short TE, 1mg/ml	4	0.018 ± 0.005	7.4 ± 2.4%	**0.04**
Long TE, 1mg/ml	5	0.093 ± 0.042	9.7 ± 3.1%	0.09	Long TE, 1mg/ml	4	0.057 ± 0.029	15.0 ± 7.2%	0.14
Short TE, 2mg/ml	2	0.135 ± 0.047	26.2 ± 10.3%	0.21	Short TE, 2mg/ml	3	0.022 ± 0.008	9.6 ± 3.7%	0.11
Long TE, 2mg/ml	2	0.173 ± 0.119	16.2 ± 11.6%	0.38	Long TE, 2mg/ml	3	0.033 ± 0.013	9.0 ± 4.0%	0.13

Conclusions

Using IV choline infusion, some significant increases in brain choline signals in both younger and older healthy males were observed using in vivo proton MRS. The results of this study show that intravenously infused choline does get into the brain in both older and younger males, possibly to a greater degree than orally ingested choline.

References

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