Increased Brain Choline Level Observed After Choline Bitartrate Ingestion

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Introduction

Choline plays a central role in neuronal metabolism and the brain obtains essentially all of this nutrient from the diet[1]. Over the last several years, widely divergent results have been reported concerning changes in the intensity of ^{1}H MRS choline resonance following the administration of 50mg/kg choline bitartrate to healthy volunteers[2-4].

In animals, brain cytosolic choline levels increase markedly following choline administration[5,6]. One possibility for the divergent results in human studies arises from the small number of subjects enrolled in these studies, as well as the limited number of spectra acquired from each subject. We now report results from a study in which 292 proton spectra were collected from each of 11 healthy volunteers for three hours immediately following choline administration.

Methods

Our subjects consist of 11 healthy young volunteers (9 males and 2 females) aged 20 -29 years. Prior to scanning, each subject ingested capsules of choline bitartrate(50 mg/kg) with water. Immediately after choline ingestion, subjects were put inside the MR scanner(GE SIGNA 5.4) and scanned continuously for three hours. After spending approximately 30 min. to acquire MR images for volumetric measurements, an MRS scan was started using a GE PROBE-P sequence to acquire 1168 FIDs with TR/TE = 8sec./272msec, phase cycling=4 and number of reference FIDs (no water suppression)=16. The voxel of size 2x3x2 cm^3 was centered on the right putamen.

292 proton spectra (4 FIDs/spectrum) from each subject were processed with a fully automated, GE SAGE-based program on a Sun workstation. Excluding 4 brain water spectra, 288 water suppressed spectra were then regrouped into 15 spectra after exact alignment in the frequency domain. The resulting irregularly spaced time series data were smoothed separately for each subject by a variable span smoother[7] and then re-expressed as percent above (or below) subject-specific baseline set at 1.0.

Results

The aggregated-average smooth curves for Cho/Cre and Cho/NAA are shown in Figure 1, demonstrating average increases over time for these ratios. Smooth subject-specific curves were summarized in the following three measures: area under curve (AUC); maximum curve height above (or below) baseline (Cmax); and time at which Cmax is reached (Tmax). Ninety-five percent confidence intervals for these median values are listed in Table 1. Since the 95% confidence interval for AUC does not include zero, we conclude that the observed rise above baseline is statistically significant at the 0.05 level.

Figure 1

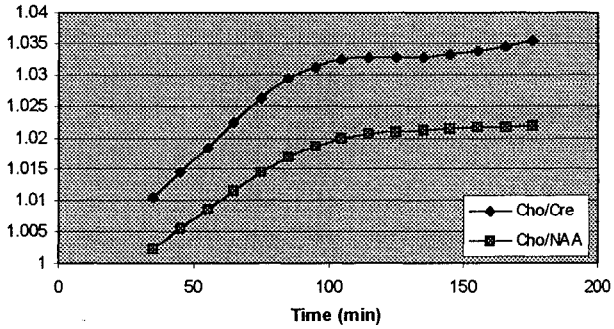

Table 1

	AUC	Cmax	Tmax
Cho/Cre	(0.08, 8.76)	(4.77, 9.23)	(82.9, 146.7)
Cho/NAA	(0.6, 3.61)	(2.73, 3.67)	(104.4, 173.4)

Conclusions

The present results suggest that the 1H MRS choline resonance increases in intensity by 5-9% following oral choline administration. This estimate is lower than our previously reported results[2] as well as data observed in animal studies[5,6]. However, these data also highlight the limitations of drawing conclusions as to whether metabolite intensities change when data are acquired from small numbers of subjects or by averaging over times[3,4].

Reference

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