Choline abnormalities in panic disorder: A link between anxiety and depression?

S.D. Friedman, M.E. Layton, T.R. Richards, W. Strauss, S. Posse, & S.R. Dager
Departments of Psychiatry & Behavioral Sciences, Bioengineering, and Radiology, University of Washington
and the Center for MR Research, Institüt für Medizin, Jülich,Germany

Introduction: Choline (Cho), an essential nutrient with a critical role in brain development and a precursor to multiple brain constituents, appears to be altered in pathological mood states. Magnetic resonance spectroscopy (MRS) studies have demonstrated brain Cho abnormalities in depression (1), bipolar illness (2,3) and social phobia (4). In previous work, we have used MRS to characterize brain lactate abnormalities during the provocation of panic attacks in subjects with panic disorder (5,6). Because regional loci of Cho abnormalities have been suggested in mood disorders, we evaluated an existing spectroscopic imaging data set (6), to specifically address whether regional brain Cho abnormalities were present in panic disorder.

Methods: Panic subjects (n=17) were diagnosed by structured psychiatric interview using DSM-IV criteria and were free of other Axis I psychiatric diagnoses. Comparison subjects (n=21) had no history of psychiatric disorders. All subjects gave written, informed consent for participation in the study and were fasting overnight prior to scanning. A clinical 1.5 Tesla GE SIGNA whole-body scanner equipped with version 5.4 Genesis operating software and enhanced SNR head coil were used for proton echo-planar spectroscopic imaging (PEPSI) studies (7). High resolution axial T_1-weighted MR images were used for anatomical localization. A 20 mm thick section in the axial plane at the superior aspect of the lateral ventricles was examined with PEPSI (TE=272ms, TR=2000ms, 32x32 spatial matrix; 22cm FOV; nominal voxel size=1cm^3)(7). Metabolic maps for Cho, Cr, and NAA were created by spectral integration. For regional analyses, high resolution images were co-registered with spectroscopic images and regions of interest defined using standard guidelines (8). SPSS Version 6.1.1 was used for statistical analyses.

Results: Cho/Cr and Cho/NAA ratios from all brain regions combined were significantly higher in panic subjects compared with controls (F=9.10, p=.003; F=15.81, p=.0001, respectively) reflecting an overall 6-8% increase in brain Cho ratios.

Cho/Cr ratios for specific brain regions are shown in Table 1. Cho/Cr ratios were significantly elevated in the right basal ganglia among panic subjects compared to controls (F=5.71, p<.05). Representative spectra from the right basal ganglia for a panic and control subject are shown in Figure 1. A trend toward higher Cho/Cr ratios was also observed in left frontal lobe among panic subjects (F=3.63, p<.10). Data from brain regional analysis of Cho/NAA ratios are shown in Table 2. Left frontal and occipital lobe Cho/NAA ratios were significantly higher in subjects with panic disorder (F=4.48, p<.05; 4.26, p<.05, respectively). A trend toward elevated Cho/NAA ratios was also shown in the splenium of panic subjects (F=3.51, p<.10).

Table 1: Cho/Cr ratios

Region	Control		Panic	
	Left	Right	Left	Right
All Regions	1.34±.26		1.42±.31**	
Frontal lobe	1.29±.50	1.37±.47	1.44±.57+	1.38±.45
Caudate	1.68±.69	1.51±.61	1.85±.75	1.58±.61
Basal ganglia	1.37±.51	1.30±.47	1.47±.32	1.46±.32*
Insula	1.24±.23	1.20±.21	1.27±.24	1.25±.27
Thalamus	1.53±.36	1.42±.26	1.53±.25	1.52± .25
Splenium	1.60±.34		1.81±.78	
Parietal lobe	1.28±.24	1.20±.21	1.33±.30	1.31±.26
Occipital lobe	1.32±.28	1.34±.28	1.32±.29	1.33±.36

**=p<.01,*=p<.05, +=p<.10

Figure 1: Spectra from the right basal ganglia ROI of a control (a) and panic subject (b).

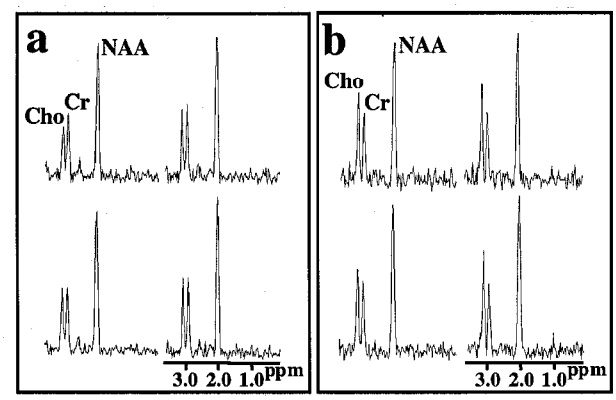

Table 2: Cho/NAA ratios

Region	Control		Panic	
	Left	Right	Left	Right
All Regions	.50±.10		.54±.12**	
Frontal lobe	.47±.18	.48±.16	.56±.22*	.48±.15
Caudate	.63±.25	.66±.26	.69±.28	.64±.25
Basal ganglia	.60±.22	.58±.21	.62±.14	.63±.14
Insula	.50±.08	.51±.08	.52±.10	.52±.08
Thalamus	.56±.09	.55±.07	.59±.11	.58±.08
Splenium	.48±.10		.53±.12+	
Parietal lobe	.45±.06	.45±.06	.46±.10	.48±.08
Occipital lobe	.42±.06	.44±.06	.46±.09*	.44±.09

**=p<.01,*=p<.05, +=p<.10

Discussion: In the literature pertaining to affective disorders, MRS-detectable Cho abnormalities have been found for specific brain regions in association with pathological mood states. In the current investigation, symptomatic panic subjects demonstrated widespread brain Cho elevations having similar regional patterns. These results provide additional evidence for brain metabolic abnormalities underlying panic disorder.

In affective disorders, Cho abnormalities appear to be state-specific with effective treatment normalizing brain levels (1,3). In our work studying panic disorder, behavioral symptoms abate with effective treatment; however, brain lactate abnormalities persist (5). Whether Cho levels normalize with effective treatment of panic subjects remains to be determined.

In summary, regional brain Cho alterations occur in panic disorder that provide evidence of a biological link with the affective disorders.

References

1. Renshaw PF et al. *Biol.Psychiatry,* 41, 837, 1997.
2. Stoll AL et al. *Biol. Psychiatry,* 29, 1171, 1991.
3. Stoll AL et al. *Biol. Psychiatry,* 40, 382, 1996.
4. Tupler LA et al. *Biol. Psychiatry,* 42, 419-424, 1997.
5. Dager SR et al. *Psych Research/Neuroimaging* 76,89,1997.
6. Dager SR et al. *Arch. Gen. Psychiatry*, in press 1999.
7. Posse S et al. *Magn. Reson. Med.,* 37, 858, 1997.
8. Damasio D, Damasio AR , *Lesion Analysis in Neuropsychology*, 1989.