Effects of Smoking on Brain Metabolite Concentrations

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Introduction:

Several MRS studies of substance abusers have indicated that use of drugs, such as cocaine, methamphetamine, or alcohol, is associated with changes in brain metabolism, generally reductions in N-acetylaspartate (NAA) or NAA/creatine (Cr) ratios.[1-3] Altered levels of Cr and choline (Cho) have also been reported.[1-3] Nicotine is another widely used addictive drug. However, despite both positive and negative reports about the effect of nicotine on brain function, there are no MRS studies examining the independent effects of smoking on brain metabolites. The similarities between nicotine and other drugs of abuse suggest that altered metabolite levels, particularly reductions in NAA, would occur with prolonged exposure. In a study of recovering alcoholics and light-drinking controls, Durazzo, et al.[3] found that recovering alcoholics who smoked had lower NAA concentrations in frontal white matter and midbrain and lower midbrain Cho than recovering alcoholics who were non-smokers. They also found that chronic cigarette smoking in recovering alcoholics and light drinkers was associated with lower midbrain NAA and Cho and with lower vermian Cho.

To determine the effects of smoking on brain metabolites, we used proton MRS to measure brain metabolite levels in normal smoking and non-smoking subjects. We hypothesized that, as with other substances of abuse, smokers would have reduced NAA levels in frontal white matter, but no change in the metabolites in other brain regions.

Methods:

Twelve smokers (7 males, 5 females, mean age 43 ±12) and thirteen non-smokers (6 males, 7 females, mean age 32 ±12) were recruited for this study, which was approved by the local institutional review board. Participants were screened for substance abuse and psychiatric disorders (with the exception of nicotine dependence for cigarette smokers). Eligible smokers had to report smoking 20 or more cigarettes per day, have a Fagerstrom Test for Nicotine Dependence (FTND) score of at least 5, and meet DSM criteria for nicotine dependence. Control subjects self-reported that they did not smoke cigarettes. Smoking subjects did not smoke for at least one hour prior to the exam. Smoking status was biochemically verified via carbon monoxide (CO) breath test.

T1-weighted sagittal, axial, and oblique images were acquired for voxel localization. Single voxel spin echo proton spectra (TR 2000/TE 144 ms) were acquired on a GE LX 1.5T scanner using the PROBE software. Voxels of approximately 15 mm on a side were acquired in the thalamus, parietal cortex, and frontal cortex. Oblique voxels of approximately 10 x 15 x 30 mm^3 were acquired in the hippocampus. Spectra were processed using SA/GE (GE, Milwaukee, WI). For three of the smokers, only two voxels of data were acquired due to time constraints. Metabolite concentrations were calculated from peak areas corrected for relaxation times and using water as an internal reference. The data were not used if the corresponding spectra contained obvious artifacts. Metabolite levels between smokers and non-smokers were compared using an analysis of covariance with smoking being the factor and age the covariate. The analysis was conducted with the MIXED procedure in SAS version 9.1 (SAS Institute, Cary, NC, USA) and at the 0.05 significance level.

Results:

The mean metabolite concentrations are shown in the table. Although NAA was lower in the frontal cortex of smokers than in non-smokers, this finding did not reach significance. NAA in smokers tended to be increased in thalamus, while Cr in smokers tended to be increased in both parietal and frontal cortex. Cho in smokers was significantly reduced in frontal cortex.

Conclusion:

While a larger data set is necessary to draw conclusions about the effects of smoking on brain metabolites, these data are in general agreement with the findings of Durazzo et al.[3] and indicate regional changes in brain metabolism in chronic smokers independently of age or other addictive behaviors. The decreased Cho suggests reduced cell membrane functionality or turnover. These data suggest that the effects of smoking on brain metabolism are similar to the effects of using other drugs. Furthermore, smoking status should be included as a variable in MRS studies.

References:

1. Li SJ, et al. Biol Psych 1999;45:1481-7. **2.** Nordahl TE, et al. Psychiatry Res 2002;116:43-52. **3.** Durazzo TC, et al. Alcohol Clin Exp Res 2004;28:1849-60.

Mean Metabolite Concentrations

	NAA		Cr		Cho	
	Smokers	Non-smokers	Smokers	Non-smokers	Smokers	Non-smokers
Thalamus	13.0 ± 1.2 (10)$^{+}$	11.9 ± 1.6 (13)	9.2 ± 1.7 (9)	9.2 ± 1.3 (13)	2.8 ± 0.3 (9)	2.9 ± 0.4 (13)
Parietal Cortex	10.8 ± 1.3 (10)	10.4 ± 1.5 (13)	8.2 ± 1.3 (9)	7.1 ± 1.3 (11)§	2.2 ± 0.3 (10)	2.4 ± 0.6 (12)
Frontal Cortex	9.8 ± 1.8 (9)	10.7 ± 1.1 (13)	10.1 ± 1.5 (9)	8.4 ± 1.6 (12)**	2.9 ± 0.6 (9)	3.7 ± 0.7 (12)*
Hippocampus	7.7 ± 1.4 (7)	7.4 ± 1.3 (13)	7.4 ± 1.5 (6)	6.9 ± 1.1 (12)	2.9 ± 0.4 (6)	3.0 ± 0.5 (12)

Values are shown as mM concentration ± std. deviation (number of subjects). *p=0.0135. **p=0.0474. $^{+}$p=0.0682. §p=0.0936.