

¹H MRS Suggests Derangement in Glial and Myelin Support to Neurons in Encephalopathy due to Occupational Exposure to Organic Solvents

Kim Vuori¹, Sainio Markku², Jesper Lundbom¹, Tapio Vehmas², Anna-Maija Häkkinen³, Kiti Müller², Nina Lundbom¹
¹Helsinki University Central Hospital, Department of Radiology, Helsinki, Finland; ²Finnish Institute of Occupational Health, Department of Occupational Medicine, Helsinki, Finland; ³Helsinki University Central Hospital, Department of Oncology, Helsinki, Finland;

Introduction

Long term occupational exposure to organic solvents may lead to encephalopathy, as inhalation of solvents are taken up into lipid-rich myelin in the brain (1). This psycho-organic syndrome is characterized by neuropsychological symptoms related to slowing of cognitive functioning. The symptoms include impaired concentration and memory, depression, fatigue, lack of activity, and emotional lability. Neuropsychological findings are impairments in attention, memory, executive functioning, psychomotor speed, and reaction time (2).

¹H MRS studies have not been reported on patients exposed to organic solvents. A possible chemical pathology detected with MRS might give an insight into the pathogenesis of the disease.

Subjects and Methods

Thirteen painters (age 50 - 60 yrs, mean 56) with 20 to 40 years of exposure to mixtures of organic solvents together with their age- and education-matched controls, construction workers (48 - 62 yrs, mean 54) with normal neuropsychology and no history of solvent exposure, were studied with ¹H MRS. The painters had a characteristic encephalopathy and pathological findings in neuropsychological testing, SPECT and MRI. Brain dysfunction had not progressed during 2 to 5 years of follow up after discontinuation of solvent exposure. Extensive differential diagnostic tests failed to reveal other than occupational etiology.

Single voxel ¹H MRS was performed with a 1.5 T MR imager (Magnetom Vision, Siemens) with a standard CP head coil. A STEAM sequence with TR 3000 ms (water TR 5000 ms) and TE 270 ms was used with and without water suppression. Six to eight cm³ voxels were placed in the left Thalamus area and in the left posterior frontal white matter (WM). Postprocessing was performed with Spectrum Wizard program (3) modified for ¹H MRS. The data was corrected for gain, coil loading, and voxel size. A paired Student's t-test was used in between groups comparisons.

Results

Table 1. shows the corrected metabolite intensities and ratios in the thalamus area. There was no difference in NAA. Cho and Cr intensities however, showed suggestive increases in the patients and the sum of Cho and Cr was 15 % higher in the patient group. WM metabolites did not differ between patient and control groups.

Discussion

The central nervous system symptoms of chronic solvent exposure have been well documented. However, clinical diagnosis remains difficult due to the nonspecificity of the symptoms and findings. Also, localization of the brain pathology is difficult. MRI in solvent exposure has shown basal ganglia hypointensity, diffuse white matter hyperintensities, and loss of gray-white differentiation together with cortical atrophy in T2-weighted images (4). The studies have not been able to define which of the brain tissue compartments, neurons, myelin, or myelin producing oligodendroglia, is affected.

We found the sum of Cho and Cr to be increased in the thalamus of the painters with a long time exposure to organic solvents. Cho has been shown to increase in enhanced cell membrane destruction or turnover (5). Cr is a marker of energy metabolism (6). Concomitant increase of Cho and Cr occur e.g. in hippocampal sclerosis reflecting a gliotic process. We postulate that the increase in Cho and Cr observed in the thalamus of painters reflects alterations in myelin membrane metabolism combined with chronic glial cell reaction. The neural marker NAA was not reduced, suggesting that the number and viability of neurons is unaltered.

It is reasonable to assume that solvent exposure preferably damages the lipid-rich component of the brain, the myelin. Derangement of myelin metabolism together with accompanying compensating glial cell reaction may cause the support of the glial cells to neurons to become defective, thus predisposing to neural network malfunction. Similar mechanisms for the pathogenesis of neural dysfunction have been suggested in multiple sclerosis (7) and in

Alzheimer's disease (8). Our results are in agreement with the neuropsychological observation of slowness of cognitive functions in solvent exposure encephalopathy. We suggest that the disease manifestations are due to slowing down of axonal signal transmission, rather than to a loss of neurons in thalamus, an important relay station.

References

1. White, RF. et al., Lancet., 349, 1239, 1997.
2. Reinvang, I. et al., J Neur Neurosurg Psych., 57, 614, 1994.
3. Järvi, S. et al., Comp. Meth. and Progr. in Biom., 52, 213, 1997.
4. Thuomas, KÅ. et al., Acta Radiol., 37, 177, 1996.
5. Miller, BL. et al., Life Sci., 58, 1929, 1996.
6. Urenjak, J. et al. J Neurosci., 13, 981, 1993.
7. De Stefano, N. et al., Ann Neurol., 38, 901, 1995.
8. Kantarci, K. et al., Neurology., 55, 210, 2000.

Table 1. Thalamus

	CONTROLS	PATIENTS	Student's t-test
	(mean ± SD%)		P =
Cho	3.4 ± 16%	3.8 ± 24%	0.10
Cr	2.5 ± 24%	3.0 ± 27%	0.06
NAA	6.7 ± 12%	6.9 ± 13%	0.3
Cho+Cr	5.9 ± 15%	6.8 ± 23%	0.05 *
NAA/Cr	2.9 ± 29%	2.4 ± 20%	0.06
NAA/ Cho+Cr	1.2 ± 25%	1.0 ± 16%	0.09
H ₂ O	1.6 ± 19%	1.7 ± 17%	0.4