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CNS findings related to toxin concentration during Methanol poisoning

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Objective: Methanol poisoning is known to cause visual disturbances and cerebral damage, predominantly affecting the basal gangliae. Whereas the mithocondrial toxicity from formate, the ultimate metabolite of methanol in humans, is believed to be the mechanism behind this toxicity, it is unclear whether the higher toxicity is due to an uneven distribution of methanol and/or formate in the different regions rather than a higher susceptibility for hypoxic damage. Our aim was therefore to measure methanol and formate in various areas of the central nervous system of persons who died from methanol poisoning.

Methods: Blood and tissue material was collected according to a prospective protocol from autopsy on patients dying from methanol poisoning in Estonia, and blood from hospital was also collected. Samples were dissected and homogenized, and the post-mitochondrial supernatant was analysed for methanol and formate with a newly developed GC-MS method.

Results: Data and materials were collected from eight fatalities, of whom three died before admission. Methanol concentration varied greatly (from 10.4mM up to 95.76mM), as did the formate concentration (from 0.2 up to 19.8mM). There was no correlation between methanol and formate concentration in the individual cases, illustrating that patients were in different stages of methanol poisoning. In the three patient where the necessary data existed, there were no concentration gradient between the cortex and the basal ganglia (Table 1). Further, in the cerebro-spinal fluid (CSF), the methanol concentration was two to three times higher, whereas the formate concentration was less than two times higher compared to the brain tissue. However, the methanol- and formate concentrations in the CSF were quite the similar with the blood-, urine- and vitreus fluid concentrations.

Conclusion: According to our results, different brain-to-blood ratios of methanol and formate suggest that the patients died in different toxicokinetic stages. Both methanol and formate passes the blood-brain-barrier quite well. Methanol and formate concentration in cerebro-spinal fluid (CSF) was higher

than in the brain tissue. No differences between methanol and formate concentration in cortex area and basal ganglion area was found. Based on the data from this pilot study, the cerebral damages does not seem to be connected to different uptake of methanol and formate in the various regions, but rather an increased sensitivity in some regions based on a higher oxygen consumption in these areas making them more vulnerable for the ensuing mitochondrial inhibition. This supports the dominating theories of basal gangliae predominantely being affected due to their higher oxygen consumption.

Limitations: Due to difficulties in collection and storing, as well as quality of materials, we were not able to collect the full range of data in all eight cases.

Table 1

	Methanol concentration (mM)		Formate concentration (mM)	
Patient	**Cortex**	**Basal ganglia**	**Cortex**	**Basal ganglia**
A	36.8	39.4	8.2	8.9
B	31.7	39.0	2.4	2.8
C	20.4	21.4	3.8	3.6