

# First evidence that frontal lobe choline-containing compounds further decrease and NAA increases during early abstinence in alcohol dependent patients

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**Background:** In previous MRS studies of recently detoxified alcohol dependent patients and healthy controls we found two interesting changes of the signal from choline-containing compounds (Cho) in frontal brain regions: within the first month of abstinence we found a decreased Cho signal which increased, if patients remained abstinent for 3 months (1). In healthy controls we observed an increase of the Cho signal with increasing alcohol consumption (2). This led us to two possible models: either Cho might only increase during active drinking and dramatically decreases during detoxification or there is a turning point of Cho increase with increasing alcohol consumption (and beginning alcohol abuse) and the Cho signal decreases at a certain level of alcohol abuse.

**Method:** In this pilot study 5 alcohol dependent patients (41-50 yrs, mean 45.6 yrs) early during detoxification and again 2 weeks into abstinence, 5 heavy alcohol drinkers with a diagnosis of alcohol abuse (39-54 yrs, mean 45.4 yrs, more than 50 g alcohol per day) and 10 age-matched light to medium social drinkers (38-49 yrs, mean 43.1 yrs; 0-29 g alcohol per day during the last 2 weeks) were examined with single voxel <sup>1</sup>H MRS of frontal white matter (fWM).

All MR measurements were performed on a 3 T Siemens TRIO with a 12-channel head coil (Siemens Medical Solutions, Erlangen, Germany). A set of sagittal and transverse scout MR images was first obtained to determine patient position. Based on the scout images a 15x40x15 mm<sup>3</sup> single voxel was positioned in the frontal white matter. Reduced water suppression localized spectra were acquired with a PRESS sequence using following parameters: TE = 30 ms, TR = 6000 ms, BW = 2400 Hz, 2048 data points and 40 averages.

In addition six fully relaxed unsuppressed water spectra were acquired with TR = 10 s and different TE (30, 80, 276, 552, 1000 and 1500 ms) to estimate the absolute water signal at TE = 0. This was used to correct data for different coil loadings and possible coil inhomogeneities. The correction factor includes the absolute water signal in vitro divided by the absolute water signal acquired in vivo and was applied to each metabolite value. Different water concentrations in the phantoms (1.0) and in white matter (0.71) were accounted for. For absolute quantification the QUEST module from the jMRUI 3 software was used with a basis set of phantom spectra (NAA, Cr, Cho, GABA, Glu, Gln, ml) which were acquired identical to the in vivo spectra at TE = 30 ms and TR = 6000 ms. The "subtract" approach was used for background handling.

**Results:** In the spectra from light to medium social drinkers we could corroborate our previous findings of a positive correlation between the frontal white matter Cho signal and daily alcohol consumption. The mean Cho value in the still actively drinking alcohol abusing group is not further increased but slightly lower than in medium drinkers. The five alcoholic patients during detoxification show a decreased Cho signal already early during abstinence. After two weeks of abstinence the Cho concentration is further decreased (Figure 1).

The NAA signal is not correlated with alcohol consumption in the light to medium drinking group. The comparison with the mean value of the alcohol abusing groups shows that NAA is slightly decreased in the alcohol abusers, has dropped a lot in the patients undergoing detoxification and seems to recover to some extent during the first 2 weeks of abstinence (Figure 2) – in contrast to the Cho concentration.

**Conclusion:** We see first evidence for our hypothesis that alcohol triggers non-linear dynamic changes of the Cho concentration (2): Cho initially increases with alcohol consumption but starts to decrease when alcohol consumption becomes alcohol abuse and significantly decreases during alcohol detoxification and early abstinence although it has been shown to increase again with longer lasting (3 months and more) abstinence.

Further data will be needed to decide how much of the Cho decline in our early detoxified patients is due to the (relatively short) detoxification and how much decrease already happened during active alcohol consumption (and maybe daily/regular times of withdrawal symptoms before the next alcohol was consumed). In contrast NAA shows a trend towards recovery within the first 2 weeks of abstinence corroborating other studies (e.g. 3).

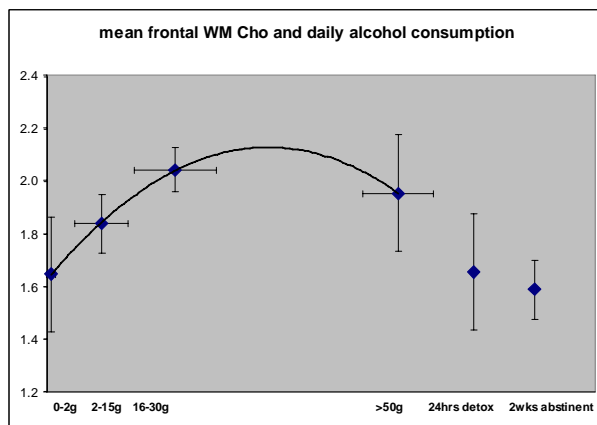


Figure 1: The Cho concentration in fWM varies with alcohol consumption and seems to further decrease during early abstinence.

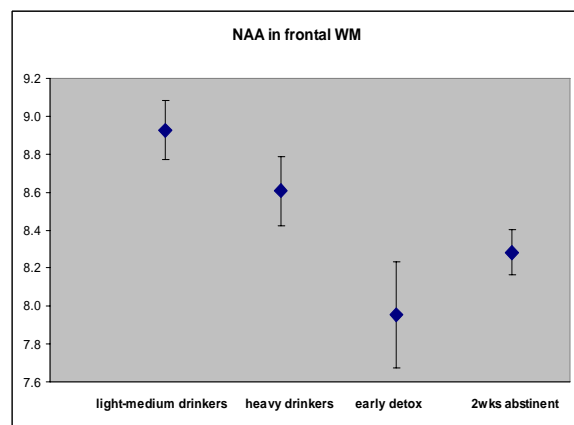


Figure 2: The NAA concentration seems to decrease when alcohol consumption turns into abuse and increases during early abstinence.

## References

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