ALTERATION OF T2 RELAXATION AND NAA CONCENTRATION IN SCHIZOPHRENIA EVALUATED IN FRONTAL WHITE MATTER AT 3 T

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Introduction

For over 20 years MR spectroscopic studies of patients with schizophrenia have been reported. The results are in some extent inconsistent. Most of the studies that found reduced NAA in schizophrenic patients acquired spectra with long echo time (TE) for example in the cingulate cortex (Steen et al., 2005) while other studies with short TE and usually higher field strengths of 3 T or more (Bartha et al., 1999; Kegeles et al., 2000) could not consistently replicate these difference. This could be an indication that rather the NAA relaxation might be different due to pathological changes of the microstructure in schizophrenic patients than the NAA concentration itself. Additionally the schizophrenic groups might differ significantly since schizophrenia is an inhomogeneous illness with probably illness progression and eventually medication related metabolite changes. Some studies showed enhanced T2 water relaxation time in white matter in schizophrenic patients (Pfefferbaum et al., 1999), basal ganglia (Buckley et al., 1995) and in the corpus callosum (Aydin et al., 2007 and 2008). Only one abstract has reported reduced NAA relaxation time in schizophrenic patients in the anterior cingulate cortex (Ke et al., 2002). The major problem of individual relaxation time estimation for metabolites is the long measurement time. Nevertheless, only with the knowledge of individual relaxation time it is possible to evaluate and compare absolute concentrations without relaxation bias. In this study we wanted to estimate absolute metabolite concentrations of the frontal white matter in schizophrenic patients while evaluating individual T2 relaxation times and to compare with healthy controls. DTI and fMRI studies gave evidence that there are deficits in frontal-parietal connections, key components of WM circuitry (Schloesser et al. 2007; Karlsgodt et al. 2008). Thus we aimed to determine metabolite alterations in frontal white matter in schizophrenia.

Methods

In vivo single voxel proton spectroscopy has been performed on 24 patients with schizophrenia (SZ), (mean age: 31.5 ± 9 years; 7 females) and 33 healthy controls (HC) (mean age: 32.0 ± 9 years; 7 females). Patients were either unmedicated or treated with an atypical antipsychiatric monotherapy constantly at least 2 weeks before measurement. MR measurements were performed on a 3 T Siemens TRIO with a 12-channel head coil (Siemens Medical Solutions, Erlangen, Germany). A set of sagital, transverse and coronal MR images were first obtained to determine patient position. Based on the images a 10x40x10 mm³ single voxel was positioned in the frontal white matter. Five reduced water suppression localized spectra were acquired with a PRESS sequence using the following parameters: TE = 30, 80, 200, 300 and 420 ms for T2 quantification; with TR = 6000 ms, BW = 2400 Hz, 2048 data points and 40 averages for each spectrum. In addition fully relaxed unsuppressed water spectra were acquired with TR = 10 s and six different TEs for eddy current correction in LCModel and to estimate the absolute water signal at TE = 0. This was used for absolute quantification and to correct data for different coil loadings and possible coil inhomogeneities. Spectral fitting was done with LCModel and GAMMA-simulated basis-sets. LCModel metabolite values for NAA+NAAG (tNAA), PCr+Cr (tCr) and PCh+GPC (tCho) at the different TEs were fitted monoexponentially in Origin 7.0. Glu was analyzed without individual T2 correction because of to high spectral fitting errors at longer TEs. Glu concentrations were estimated with literature T2 values for white matter (Choi et al., 2006). All results were scaled with the interpolated water signal at TE = 0. We also accounted for the different amount of grey matter (GM), white matter (WM) and CSF in the measured voxel and their different water concentration (GM: 45.0 mM, WM: 39.4 mM, CSF: 54.4 mM) by image segmentation of a T1-weighted MPRAGE. Metabolite data were corrected for CSF content. Chemical shift displacement results in a different measured voxel position for the different metabolites. This was accounted for in the in house developed segmentation tool which is based on the SPM2 algorithm. CSF content was less than 1 % in the measured voxel. No correction for T1 was required due to nearly fully relaxed metabolite spectra.

Results

Tab. 1 Mean and SD of T2 relaxation times and metabolite concentrations in HC (N=33) and SZ (N=24)

	HC								SZ							
	tNAA T2 [ms]	tCr T2 [ms]	tCho T2 [ms]	H2O T2 [ms]	tNAA con [mM]	tCr con [mM]	tCho con [mM]	Glu con [mM]	tNAA T2 [ms]	tCr T2 [ms]	tCho T2 [ms]	H2O T2 [ms]	tNAA con [mM]	tCr con [mM]	tCho con [mM]	Glu con [mM]
Mean	340.03	174.90	223.66	64.94	14.01	9.75	2.82	8.99	321.00	167.60	224.78	67.92	12.82	9.62	2.66	8.41
SD	24.96	14.95	21.98	2.78	1.05	0.94	0.38	1.13	37.61	18.15	33.80	3.24	1.38	1.23	0.63	1.77

Schizophrenic patients showed significant reduced tNAA concentrations compared to healthy subject ($p = 0.001$; Fig. 1a). We also found significant reduced tNAA T2 values ($p = 0.037$; Fig. 1b). Additionally, we found a significant enhanced T2 of the H2O signal in SZ white matter ($p=0.001$; Fig. 1c). Neither tNAA concentration, H2O T2 nor tNAA T2 correlated with age, duration of illness or CPZ. No significant difference was found for Glu or the other metabolites and their relaxation times.

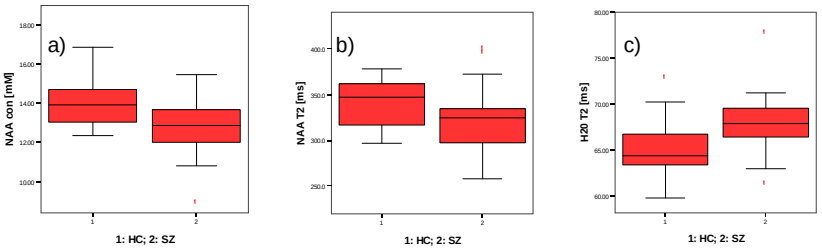

Figure 1: HC: N=33; SZ: N=24 a) tNAA concentration b) tNAA T2 and c) H2O T2 of frontal white matter

Discussion

We found a significant decrease of tNAA concentration in frontal white matter in schizophrenic patients compared to healthy subjects even in individually T2 relaxation corrected data. Additionally, we determined differences in tNAA T2 and water T2 relaxation which we interpreted as a hint for a change in microstructure in schizophrenic patients.

References Ke et al., Proc. ISMRM 10 2002; Steen et al., Neuropsychoph 2005; Bartha et al., Biol Psych 1999; Kegeles et al., Psych Res 2000; Weber-Fahr, W. et al., Neuroimage 2002, Pfefferbaum et al., Psy Res 2005; Buckley et al., Psy Res 1995; Aydin et al., Biol Psych 2008; Aydin et al., Am J Neurorad 2007; Schloesser et al., Schiz Res 2007; Karlsgodt et al., Biol Psych 2008, Choi et al., MRM 2006