

LONGITUDINAL CHANGES OF N-ACETYL-ASPARTATE IN EARLY ONSET PSYCHOSIS.

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INTRODUCTION

- Early-onset psychosis (EOP), is a severe condition associated with a number of developmental disturbances and alterations of the brain [1].
- Low concentrations of N-Acetyl-Aspartate (NAA) are interpreted as a biological marker for neural integrity. Reduction of frontal NAA levels has been described as a good predictor for poor outcome in psychosis [2].
- Studies using Proton Magnetic Resonance Spectroscopy (H-MRS) have shown reduced NAA levels in the Dorsolateral Prefrontal Cortex (DLPC) in both chronic and first-episode psychosis [3-4].
- However little is known about the course of these abnormalities as none of them where longitudinal studies or examine the changes over time of NAA levels in first episode early onset psychoses.

HYPOTHESIS

- NAA levels in the Dorsolateral Prefrontal Cortex will differ between patients with EOP and healthy controls at baseline and at two years follow-up.

OBJECTIVES

- To study the of n-acetyl-aspartate (NAA) levels in the Dorsolateral Prefrontal Cortex (DLPC) in child and adolescent psychosis and healthy controls.
- To examine its stability over time.

METHODS

- A sample of 56 (34 males; 22 females) first-episode psychotic patients (<6 months history of positive psychotic symptoms) between 11 and 18 years old and 53 (35 males; 18 females) healthy controls matched for age, gender and years of education completed baseline and longitudinal H-MRS from the original CAFEPS sample (110 patients/98 healthy controls) [5].
- The single voxel proton spectra were obtained in a 1.5 T Philips Gyroscan ACS from the DLPC area with and without water suppression at baseline and 2 years follow up (mean 25 months) (figure 1). The water spectrum was acquired to establish a reference signal for normalization of metabolite concentration (PRESS sequence [TE=136ms, TR=1500ms, NEX=128] Volume 6,75cc).
- Spectra quantification was made with in-house developed software with commercial applications; the QuTIS® software tool using an AMARES non-linear algorithm (figure 2).
- The longitudinal change in NAA was measured as the difference between follow-up and initial NAA/W levels. Paired t-test was performed to examine longitudinal differences in NAA levels between baseline and follow-up within each group. ANCOVA was used in order to examine differences between groups at baseline and at follow-up (within subject) in longitudinal change values using scanner site as covariate.

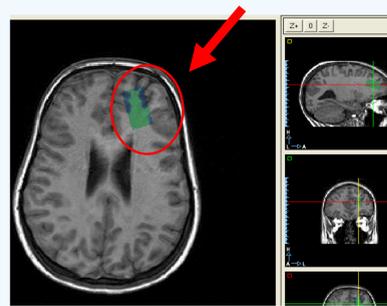


FIGURE 1: Single voxel proton spectra anatomical localization of the left sample volume

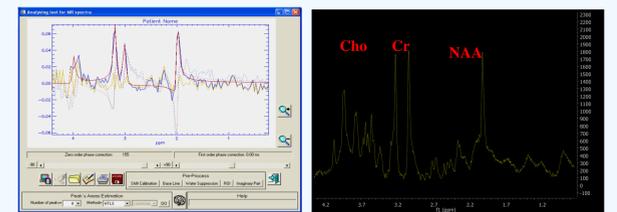


FIGURE 2: Spectra quantification QuTIS® software tool

PRESS sequence (TE=136ms, TR=1500ms, NEX=128)
Volume 6,75cc

RESULTS

	PATIENTS	CONTROLS	CHANGE
Baseline	8,8 ± 2,6	8,2 ± 2,6	F = 5.1 p= 0.0267 df:103,1
2yrs follow-up	9,5 ± 4,1	10,4 ± 3,2	
LONGITUDINAL ANALYSIS	t=1,2 P=0,2215	t=4,0 P=0,0002	

Table 1. Longitudinal Change in patients vs. controls

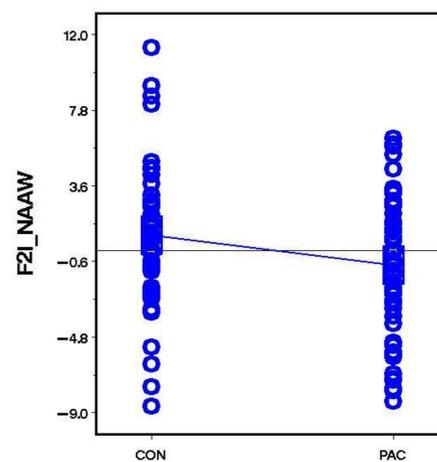


Figure 3. Longitudinal Change in patients vs. controls

- No differences in NAA levels were observed between patients and controls at baseline (table 1).
- Patients showed no significant change in NAA levels (t=1.2 p= 0.2215), whereas controls showed a significant increase (t=4.0 p= 0.0002) at two years follow-up.
- Group differences were only seen at two year follow up (F = 5.1; p= 0.0267; df:103,1) [table 1, figure 3].

- Duration of Antipsychotic treatment was 2,8 ± 2,1 (-2 -7 weeks) at the time of the H-MRS.
- There were no differences between antipsychotic treatment at baseline: 283,23 ± 145,45 (3-640) and at 2-yrs follow-up: 261,24 ± 199,03 (80-800).
- Levels of NAA at follow-up were not related to clorphormazine equivalents.

CONCLUSIONS

- Patients showed deficits of NAA at follow-up. There were no significant differences in these levels at baseline.
- Differences in the NAA/W concentrations in early-onset first episode psychotic patients can be more related to developmental maturation of the brain than to different concentrations at baseline or a medication effect. This reduction of NAA/w with regards to healthy controls may indicate lower neuronal density or viability and, therefore, dysfunction in the left DLPC region which is present at the early course of the illness.

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