Cross-sectional grey matter metabolic correlation in adolescent with obsessive-compulsive disorder and a subgroup of anorexia nervosa by 1H-MR spectroscopy

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Introduction Neuroanatomical models, neuropsychological studies, and functional studies evaluating cerebral metabolism and perfusion by PET and SPECT have pointed out the hypothesis of abnormal functioning involving the frontal region in obsessive-compulsive disorder (OCD) and patients with anorexia nervosa (AN) (1,2,3,4,5). It has been also reported a metabolic alterations in the frontal grey matter of adolescents with anorexia nervosa by proton magnetic resonance spectroscopy (6). We have previously presented a pilot study (ISMRMB, Berlin 2007), which the hypothesis that similar altered metabolites levels in the frontal area might to be present in a group of child and adolescent anorexic patients and patients with OCD, probably related to a common neuropsychological alteration, was not confirmed. Since relative tissue content can affect both metabolite levels and water intensity used for quantification (7), we have considered that has to be included in the analysis a corrected absolute metabolite values to remove any effect produced by tissue content or CSF contamination in the VOI.

Purpose Our aim was prospectively to investigate the possible differences for metabolic alterations in the prefrontal cortex in young adolescent among both groups of pathologies by localized proton magnetic resonance spectroscopy (^{1}H-MRS), and evaluate the impact to use a corrected metabolite concentration values after calculation of the volume of interest (VOI) composition.

Study Design Twenty-six young adolescent patients with a short duration of illness with AN, and twenty-two with OCD were investigated at the admission. Twenty-two healthy controls were recruited and were handedness right as the patients.

Methods The protocol was approved by the Research Ethics Committee of the Institution. All subjects participating and their parents were oral and written informed of the study and procedure and signed written informed consent agreements. The Structural Clinical Interview for DSM-IV criteria for OCD and AN to both sexes was used to establish the DSM-IV diagnosis of OCD and AN, and to exclude psychopathology in control subjects. A clinical evaluation was carried out in all subjects with a semistructural interview and rating scales (including LOI-CV -Leyton Obsessive Inventory, child version in all groups) and neuropsychological evaluation. Scans were performed using a 1.5 T whole body scanner (Signa LX, GE Medical Systems, Milwaukee, WI). ^{1}H-MRS was acquired using a 12 cm3 (2x3x2 cm) single voxel short-echo PRESS (TE=35ms, TR=1500ms, data points 2048, number of phase encoding steps 24x24 and FOV of 250x250 with automatic shimming and water suppression) in the midline bilateral frontal grey matter on axial 3D FSPGR images. Fitting of all ^{1}H-MRS data was performed using LCModel software (version 6.1-4A), applying an eddy current correction and using internal water signal reference to calculate absolute metabolite concentrations. We considered a set of glycerophosphocholine-phosphocholine (GPC+PCh or total Cho), total N-acetyl-aspartilglutamate (NAA+NAAG or total NA), myo-inositol (Ins) and Glutamate+Glutamine (Glx) located at 0.09 ppm, and the metabolites ratios with creatine (Cr). We only considered the absolute metabolite values when the coefficient of variation for the LCModel concentrations was below 20%, indicating that these metabolites could be reliable estimated (Provencher, 2001). To correct the absolute metabolite values we calculated the VOI composition in percentages of grey matter (GM), white matter (WM) and CSF for each subject, applying a specific mask including the VOI on each whole brain segmented tissue maps applied (using SPM2 software, running in Matlab 6.5, Math Works, Natick, MA), and after we applied the mass of water in the different compartments, assuming that the relative densities of MR-visible water in GM, WM and CSF are 0.78, 0.65 and 0.97 respectively. The correction factor used was: "(GM%x0.78) + (WM%x0.65) + (CSFx0.97) / (GM%+WM %) plus use of tissue density of 1.05 Kg/L" (7).

Results The Mann-Whitney U test and Kruskall-Wallis for independent samples was applied in the statistical analysis using the SPSS version 15.0 for Windows. Level of significance was set at $p<0.05$. There were no significant differences among the groups when absolute metabolite quantification of the entire VOI was analysed. However, in the calculated metabolite component of the GM there were substantial decrease in NAA and NAA/Cr in AN compared with controls and OCD patients, a significant decrease Ins/Cr and Glx/Cr levels in AN compared with controls, but there were not significant differences in Ins/Cr and Glx/Cr levels among AN and OCD. The Ins/Cr and Glx/Cr levels in OCD was lower than controls, and although all metabolites levels broadly overlap among them, this suggests a similarity in Ins/Cr and Glx/Cr ratios between AN and OCD patients. The rest of metabolites among AN/OCS/controls not showed significant differences.

Table. ^{1}H-MRS neurometabolites in prefrontal area in AN-OCS patients, OCD patients and control subjects.

	Absolute metabolite				Corrected absolute metabolite in GM			
	AN/OCD	AN/C	OCD/C	AN/OCD/C	AN/OCD	AN/C	OCD/C	AN/OCD/C
Cr	ns	ns	ns	ns	ns	ns	ns	ns
Ins	ns	ns	ns	ns	ns	ns	ns	ns
Ins/Cr	ns	ns	ns	ns	ns	0,002	ns	0,009
Cho	ns	ns	ns	ns	ns	ns	ns	ns
Cho/Cr	ns	ns	ns	ns	ns	ns	ns	ns
NAA	ns	ns	ns	ns	0,032	0,008	ns	0,014
NAA/Cr	ns	ns	ns	ns	0,01	0,002	ns	0,002
Glx	ns	ns	ns	ns	ns	ns	ns	ns
Glx/Cr	ns	ns	ns	ns	ns	0,006	ns	0,006

C= control, ns=no significant. Exact sign (2-tailed) $p<0,05$

Conclusion In this study only AN group showed significant lower levels that controls and OCD group in NAA and NAA/Cr metabolites, however we observed a similarity in the metabolite ratio Ins/Cr and Glx/Cr in anorexic and OCD patients in the grey matter of the frontal area, which showed decreased levels compared to healthy group. The analysis of corrected absolute metabolite concentration in GM after calculation of the VOI composition, improved the detection of differences among groups. Limitations of this study are the size of the groups and that it is not include other cerebral areas. Further assessment including more patients and other cerebral areas is in progress.

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