

A Proton MRS study of brain in patients with OCD and their first degree relatives

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OBJECTIVES

To identify alterations in neurochemical measures that are specific to obsessive compulsive disorder (OCD) using *in vivo* proton MR spectroscopy (MRS) of caudate nucleus, anterior cingulate cortex and medial thalamus in these patients and to identify their role as vulnerability markers by comparing them with the healthy first degree relatives of these patients and healthy controls.

INTRODUCTION

OCD is the fourth most common psychiatric disorder characterised by recurrent intrusive thoughts and repetitive, ritualistic behaviours that are distressing and debilitating to the patient. Despite its high prevalence and the attendant morbidity, the pathophysiology of OCD remains unclear. MRS provides a non-invasive method to characterize bio-chemistry related to OCD. Basal ganglia structures including caudate nucleus and striatum; thalamus and anterior cingulate cortex (ACC) have been documented to be an integral component of CSTC (Cortico-Striato-Thalamo-Cortical) circuit involved in pathogenesis of OCD (Saxena et al, 2000). This study aims to compare the neurochemistry detailed by ¹H-MRS in OCD patients, healthy family members (vulnerable population) and healthy controls in an attempt to identify specific neurochemical changes in OCD patients that might prove to be vulnerability markers of the disease.

MATERIAL AND METHODS

The study groups included subjects diagnosed with OCD (n=26) with duration of illness less than 5 years (Group 1); healthy first degree relatives of patients (n=15) formed the vulnerability group (Group 2) and normal controls (n=16) (Group 3). The general inclusion criterion were right handed individuals, aged 18-60 years. The other selection criteria for the OCD subject group in addition to the general criterion included: duration of illness less than 5 years and no other comorbid psychiatric illness. The exclusion criterion for the three study groups included clinical history of other psychiatric disorders; impaired thyroid function, neurological illness, history of significant head injury and any implants. A cross-sectional case-control study design was employed in line with previous research in this area. Clinical assessment was carried out using a socio-demographic profile, a semi-structured clinical performa, Edinburgh's handedness inventory, Mini-international neuropsychiatric interview (to diagnose DSM-IV-TR psychiatric disorders), Yale Brown obsessive compulsive scale (YBOCS) and YBOCS symptom checklist. Volume-localized ¹H MR Spectroscopy was carried at 1.5 Tesla (MAGNETOM SONATA, Siemens Health Care, Germany) using a phased array head coil. Following the scout images, multislice T2-weighted images of the whole brain were acquired, prior to MR spectroscopy. Using the reference MR images, single voxel proton MR spectra were acquired using the point-resolved spin-echo sequence (PRESS) pulse sequence. The voxel size of 10x10x10 mm³ was positioned in the three regions of interest. The absolute concentration of metabolites was determined using user-independent frequency domain fitting program version 6.1-4A (LC Model), with a basis set of model metabolites. The concentration of metabolites was expressed as milli moles per liter (mMol/L).

RESULTS

The socio-demographic variables of the three study groups were compared using ANOVA or chi-square test as appropriate. The three study groups did not differ in terms of socio-demographic variables. There were significant group differences (p<0.05) in caudate nucleus and anterior cingulate cortex between the OCD, family control and the normal control groups in terms of Glutamate (Glu), Choline (Cho), Inositol (Ino), N-Acetyl aspartate (NAA), Glycerophosphocholine + Phosphocholine (GPC+PC) and Glutamate+Glutamine (Glu+Gln). Post hoc pair wise comparisons (after bonferroni's correction) showed that NAA and NAA+NAAG levels in OCD patient group < family control group < normal controls (p<0.001). Other measures were significantly higher in OCD group > family controls > normal control group (p<0.001) (See Table 1). However, there were no significant group differences between the three groups in terms of the above bio-chemicals in medial thalamus. Absolute neurochemical measures were correlated with disease severity (YBOCS score). In caudate nucleus, they correlated significantly with disease severity (p<0.05). However, the above neurochemical measures did not correlate significantly with disease severity in anterior cingulate cortex or medial thalamus.

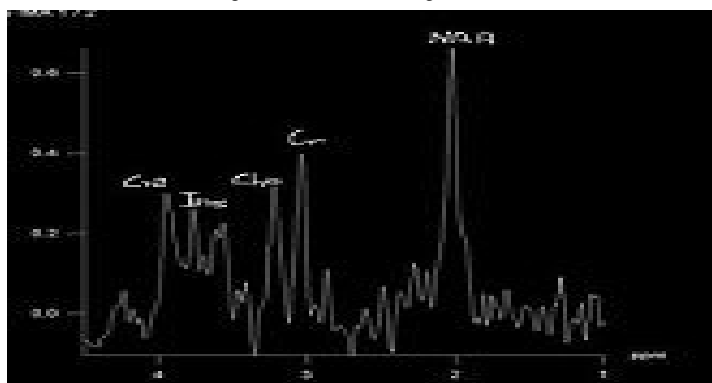


Figure 1: Representative *in vivo* ¹H MR spectrum from caudate nucleus in a patient with OCD

DISCUSSION

This study provides further evidence on the role of caudate nucleus and anterior cingulate cortex in the pathophysiology of OCD. Results from previous studies involving the above regions are similar to our findings (Ebert et al, 1997; Bartha et al, 1998). This is line with the proposed neurodegenerative hypothesis of OCD considering decrease in NAA, a marker of neuronal integrity and increase in Ino, Cho, constituents of the myelin sheath. These findings also suggest abnormalities in membrane synthesis, turn over and signal transduction pathways that are postulated to be central to pathophysiology of OCD. However, normal findings from medial thalamus may suggest intact neuronal viability in this region. Further similar findings in a possible vulnerability group (family controls) suggest the possible role of these neurochemicals as putative disease markers that may aid in early identification. Replication of similar studies and future studies recruiting psychotropic-naïve patients and use of other disorder controls (like depressive disorder) is required for a better understanding.

REFERENCES

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Abso-lute Conc	Group 1 (n=26)	Group 2 (n=15)	Group 3 (n=16)	F (df) with Bonferroni correction	Post hoc Comparison
	(mMol/L)	(mMol/L)	(mMol/L)		
	Mean (SD)	Mean(SD)	Mean (SD)		
Glu	8.91 (0.22)	7.23 (0.62)	5.15 (1.9)	47.37 (2,40,42)	1>2>3***
GPC	0.28 (0.07)	0.15 (0.03)	0.13 (0.02)	20.613 (2,22,24)	1>2>3***
Ino	5.03 (0.28)	3.86 (0.44)	2.72 (0.5)	106.489 (2,32,34)	1>2>3***
NAA	4.49 (0.71)	5.8 (0.50)	6.87 (0.42)	47.183 (2,30,32)	1<2<3***
Glu+ Glx	9.95 (0.65)	8.77 (0.63)	7.68 (0.49)	46.731 (2,33,35)	1>2>3***

Table 1: Comparison of concentration of absolute metabolites in caudate nucleus of OCD patients as compared to family members and controls