Short and Long Echo ^{1}H Spectroscopy in an Egyptian Sample of Patients with Obsessive-Compulsive Disorder

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Abstract:

Several lines of investigation into the cause(s) of OBSESSIVE-COMPULSIVE DISORDER (OCD) have suggested that it is characterized by dysfunction within a basal ganglia-thalamocortical neuronal circuit ***(Modell et al, 1989; Insel 1992)***. Neuroimaging studies have the potential to increase our understanding of the connection between observable symptoms and associated neurobiology, and perhaps lead to improvements in treatment and in matching treatment to patient needs ***(Rauch, 2000)***.We aim to study the concentrations of various metabolites in the caudate nucleus for a hypothesized difference between both patients and control groups and between both sides within the patient group and to identify a relevant biomarker that is sensitive and specific that could enhance our understanding of the pathophysiology of OCD. Ten OCD patients, who were medication free for at least 6 weeks, were recruited from among persons seeking treatment at the institute of Psychiatry, Ain Shams University, Cairo, Egypt. They were assessed using Y-BOCS and compared to 5 matched healthy controls regarding 'H-MRS Spectroscopy data. NAA/Cho mean was lower on the left corpus striatum than right in patient group and results are statistically significant (t= 2.54, P= 0.03). Also, there is a trend towards an increased level of choline bilaterally in the patient group compared to controls and a negative and statistically significant correlation existed between Cho+Cr and symptom severity (r = -0.63, P = 0.04). Although not statistically significant, level of NAA/Cr is higher on both sides in cases rather than controls. Within the patient group, NAA/Cr is higher on the right than the left but there was no statistically significant correlation with symptom severity. There has been a trend to increased NAA relative to creatine in the corpus striatum supporting the theory of defective neuronal pruning. Increased choline in corpus striatum suggests that choline concentrations can be a sensitive and specific biomarker for OCD.

Introduction:

Obsessive compulsive disorder (OCD) is a prevalent, serious neuropsychiatric disorder ***(Koran et al, 1996)*** of unknown etiology. Several lines of investigation into the cause(s) of OCD have suggested that it is characterized by dysfunction within a basal ganglia-thalamocortical neuronal circuit ***(Modell et al, 1989; Insel 1992)***. Neuroimaging studies have the potential to increase our understanding of the connection between observable symptoms and associated neurobiology, and perhaps lead to improvement in treatment and in matching treatment to patient needs ***(Rauch, 2000)***.

Several investigators have attempted to delineate a neuroanatomic abnormality in OCD by measuring the size or assessing the structural integrity of presumably critical CNS structures. In particular, the corpus striatum has been the focus of a series of computerized tomographic (CT) and, more recently, structural magnetic resonance imaging (MRI) studies ***(Kellner et al, 1991; Scarone et al, 1992; Robinson et al, 1995; Aylward et al, 1996; Jenike et al, 1996; Rosenberg et al, 1997).*** The corpus striatum

has shown abnormalities in patients with OCD compared with normal subjects in several imaging studies ***(Hoehn-Saric and Benkelfat, 1994; Baxter et al, 1992; Schwartz et al, 1996)***. Studies have been remarkably inconsistent, with some finding reduced caudate size ***(Robinson et al, 1995; Rosenberg et al, 1997)***, another finding increased caudate size ***(Scarone et al, 1992)***, and some finding no differences ***(Aylward et al, 1996; Jenike et al, 1996)***. Positron emission tomography (PET) and single photon emission computerd tomography (SPECT) studies were carried to compare patients with OCD with healthy volunteers. The most consistent differences have been in the orbital gyrus and the head of caudate ***(Saxena et al, 2001; Whiteside et al, 2004)***. Functional magnetic resonance imaging (FMRI) studies during symptom provocation have revealed activation within the corpus striatum (specifically in the caudate) along with other brain regions (medial orbitofrontal cortex, anterior cingulate, amygdala) ***(Rauch et al, 1994; Breiter et al, 1996)***. Numerous studies have implicated the thalamus. MRI studies have shown increased thalamic gray matter in medication free adult OCD patients compared to controls ***(Kim et al, 2001)***. Magnetic resonance spectroscopy (MRS) imaging studies have found localized functional neurochemical marker alterations in the left and right medial but not lateral thalamus ***(Fitzgerald et al, 2000; Rosenberg et al, 2001)***.

More recently, researchers have begun using MRS to evaluate potential differences in regional brain metabolites between patients and healthy controls. MRS has been used primarily to measure concentrations of metabolites in brain tissue such as N-acetyl-l-aspartate (NAA; a marker of neuronal viability), combined glutamate and glutamine (Glx; a marker for excitatory neurotransmitters), choline (Cho; a marker of cell membrane turnover), myo-inositol (mI; involved in phospholipidmetabolism), and creatine (Cr; a marker of cellular energetics, commonly used as a reference level). ***(Whiteside et al, 2006)***.

Although no studies have found identical results, two have identified unilaterally decreased NAA in the striatum of adults with OCD ***(Ebert et al, 1997; Bartha et al, 1998)***, and two have identified increased absolute concentrations of choline bilaterally in the medial thalami ***(Rosenberg et al, 2001; Smith et al, 2003)***. Recently, it was found that the mean concentration of Cho/Cr was significantly higher in the OCD patients than controls, but only in the parietal white matter and parietal Cho/Cr was positively correlated with the severity of OCD symptoms ***(Kitamura et al, 2006)***. In addition ***Rosenberg et al, (2000)*** found that elevated Glx concentrations relative to water in the left caudate decreased after successful pharmacotherapy. Finally, compared to healthy controls, absolute levels of NAA have been shown to be increased in the right, but not left, dorsolateral prefrontal cortex ***(Russell et al, 2003)***.

It is thus obvious that variability in MRS results in OCD patients occurs on different scopes: there is a variation in the metabolites tested; and a variation in areas in which those metabolites are tested; and in the clinical condition in which those metabolites are tested, let alone variation in ethnicity. In this study, we tried to identify a relevant biomarker that is sensitive and specific and that could enhance our understanding of the pathophysiology of the

disorder and could also help to better define the phenotype in order to reduce heterogeneity in genetic studies as well as facilitate early detection and therapeutic intervention. We thus chose to start at the beginning and to study metabolite levels and concentrations in the corpus striatum of OCD patients who are medication free in an urban Egyptian community.

Material & methods

Ten OCD patients were recruited from among persons seeking treatment at the institute of Psychiatry, Ain Shams University, Cairo, Egypt. They were compared to 5 matched healthy controls with minimal demographic differences regarding age, gender, education and handedness.

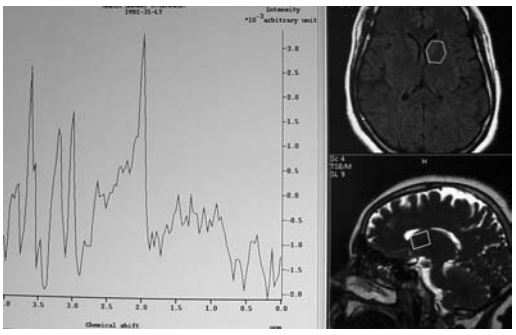
Subjects with OCD were diagnosed according to DSM-VI criteria by an experienced consultant using a semistructured interview [Structured Clinical Interview for DSM-IV-TR Axis I Disorders Clinical Version (SCID-CV)] ***(First et al, 1997)***. Comorbidity, family history, and other illness parameters (e.g. age at onset, duration of illness) were assessed at this time as part of the clinical interview, as was the patient's medical and prior treatment history. The subjects with OCD were required to have been medication free for a minimum of 6 weeks before the day of scanning, to be otherwise in good physical health, and to have no history of significant head injury or seizures. The same experienced interviewer determined the severity of OCD symptoms using Yale-Brown Obsessive-compulsive Scale (Y-BOCS) ***(Goodman et al, 1989)***. All OCD subjects were outpatients, and had no other current comorbid psychiatric disorder including tics. The healthy controls also underwent the SCID-CV clinical interview to ensure that they did not meet the criteria for any Axis I DSM-IV disorder.

The entire brain of each subject was imaged on the same magnetic resonance scanner and on the same day that the 'H-MRS data were acquired to primarily exclude presence of any organic lesion. 'H-MRS Spectroscopy data were acquired on a high-performance superconducting magnet 1.5 Tesla system (Philips Intera, ACS-NT system, Netherlands) MRI machine in a private center in east of Cairo, Egypt.

We used T2-weighted (5100/16, 96/2 [TR/effective TE/NEX]) obtained with a section thickness of 5 mm, gap of 1 mm, turbofactor 5, field of view (FOV) of 230 mm, and in-plane image matrix of 512x 196 imaging to locate the voxels for the ^{1}H-MRS studies. The selection of voxel position in the caudate nucleus was determined visually by examining the MR images in three orthogonal planes (sagittal, coronal, and axial) by the radiologists to ensure proper site of voxel placement. Spectra were then acquired from a 20 x 20 x 20-mm^3 volume of interest on both caudate nucleus. Water unsuppressed spectra were acquired with the use of a stimulated echo acquisition mode sequence (spectral bandwidth 1000 with TE=32 and 144 were acquired respectively).

All spectra were reviewed for quality, and spectra of insufficient quality were not included in the final analyses. Spectra of poor quality were identified by an increased line width of the water resonance (a measure of the field homogeneity in the region of interest). The metabolite concentrations were determined by using manufacturer supplied spectroscopy processing software, and manual determination of area under each of the metabolite peak in arbitrary units (integral

value) was performed focusing on N-acetylaspartate (NAA) and Choline (Cho) metabolites being the center of attention for a hypothesized difference, NAA/Cr, NAA/Cho ratios as well as Cho+Cr were also calculated.



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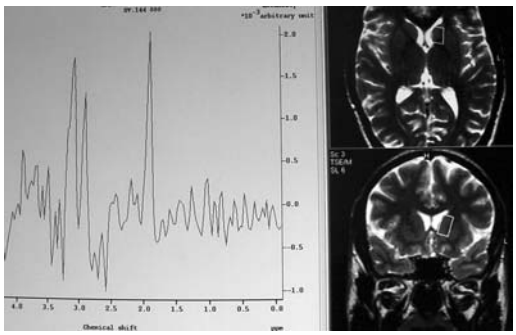

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Fig. 1. (a) Short echo 'H-MRS Spectroscopy (TR=2000 msec, TE=32) acquired from a volume of interest (VOI) on head of left caudate nucleus. (b) long echo 'H-MRS Spectroscopy (TR=2000 msec, TE=144) with outlined white rectangle of VOI over left caudate nucleus.

Qualitative variables were described in number and percentages and mean ± standard deviation (SD) if quantitative. Student t and ANOVA tests were used when comparing quantitative data between 2 or more than 2 groups respectively. Pearson correlation coefficient was used as an indicator of correlation between 2 quantitative variables. P value was always set at 0.05. All data manipulation and statistical analyses were performed using SPSS (Statistical Package for Social Sciences) version 11.

Results:

Ten outpatients with OCD disorder (cases), who were medication free for at least 6 weeks; and 5 healthy controls who were matching regarding age, gender, social class and education were imaged using entire brain MRS spectroscopy after obtaining an informed consent.

OCD patients were psychologically assessed using Y-BOCS in order to determine symptom severity and phenomenology (mean score 28.2 ± 8.9). Among the patients group, 2 (13.3%) were mild; 2 (13.3%) were moderate; 6 (40%) were severe; 4 (26.7%) experienced only obsessions; 1 (6.7%) experienced only compulsions and 5 (33.3%) experienced mixed symptoms.

Testing if case and control groups were matching was done using chi square and independent sample t - test as appropriate. table (1).

Preliminary analysis of results showed that 50% (n=5) of patients had ratio of NAA/Cr to be *lower* on the left than on the right whereas in all subjects of the control group 100% (n=5) the ratio of NAA/Cr is *higher* on the left than on the right. Association between reversal and type of patient was not statistically significant as (X2=3.75, P=0.06). Similarly, within the patient

group, reversal was not associated with type of symptoms (X^2 = 2.2, P=0.3) or severity of the disorder (X^2=0, P=1).

Both cases and controls were compared, using independent sample *t*- test, regarding the NAA/Cr, NAA/Cho, Cho/Cr ratios, and Cr + Cho in the right and left corpus striatum and difference was not statistically significant. It is worth mentioning that NAA is increased relative to Cr used as a reference level in patients, compared to controls on both sides. Cho is also increased in patients, relative to Cr of contols on both sides as well.

In an attempt to detect any statistically significant difference in mean metabolite ratios between the right and left basal ganglia in patients, paired sample *t*- test was performed and results were not statistically significant for all ratios except for the the NAA/Cho, which was lower on the left side and the difference was of statistical significance. Table (3) shows the details.

We then attempted to detect any statistically significant correlation between various metabolite ratios on the left side and symptom severity and type using bivariate analysis and ANOVA where appropriate and found a negative and statistically significant correlation between the sum of creatine + choline, and symptom severity. Table (4) shows the details

Table (1): Both case and control groups are matching:

		Case N (%)	**Control N (%)**	**X^2**	**P**
GENDER	male	5 (50)	4 (80)	1.25	0.26
	female	5 (50)	1 (20)		
SOCIAL CLASS	middle	7 (70)	3 (60)	0.15	0.69
	low	3 (30)	2 (40)		
EDUCATION	Illiterate, primary	2 (20)	1 (20)	2.4	0.5
	preparatory	0 (0)	1 (20)		
	Secondary, technical	4 (40)	2 (40)		
	university	4 (40)	1 (20)		
HANDEDNESS	right	8 (80)	5 (100)	1.15	0.28
	left	2 (20)	0 (0)		
		Case Mean (±SD)	**Control Mean (±SD)**	***t***	**P**
AGE		33.5 (± 14.2)	32 (± 14.6)	0.19	0.8

Table (2) shows means and significance in details.

Table (2): Difference in mean metabolite levels in basal ganglia of both groups

	Case Mean (±SD)	Control Mean (±SD)	*t*	P
Rt. NAA	1.964 (± 2.356)	0.642 (± 0.393)	1.22	0.24
Lt. NAA	2.184 (± 2.934)	0.607 (± 0.430)	1.17	0.26
Rt. Choline	1.072 (± 1.251)	0.45 (± 0.252)	0.96	0.35
Lt. Choline	1.5232 (± 2.123)	0.485 (± 0.246)	0.95	0.36
Rt. NAA/Cr.	1.959 (± 0.895)	1.64 (± 0.192)	0.69	0.5
Lt. NAA/Cr	1.868 (± 0.778)	1.435 (± 0.12)	1.08	0.3
Rt. NAA/Cho	1.66 (± 0.3)	2.09 (±0.95)	-1.33	0.2
Lt. NAA/Cho	1.37 (± 0.25)	1.56 (± 0.16)	-1.38	0.2
Rt. Cho/Cr	1.17 (±0.43)	0.99 (±0.33)	1.13	0.3
Lt. Cho/Cr	1.42 (±0.93)	0.93 (±0.2)	1.44	0.2
Rt. Cr + Cho	2.07 (±2.669)	0.945 (± 0.372)	0.82	0.4
Lt. Cr + Cho	2.686 (± 3.814)	1.01 (± 0.454)	0.85	0.4

Table (3): difference between the right and left BG

		Right BG Mean (±SD)	Left BG Mean (±SD)	*t*	P
Cases	**NAA/Cr.**	1.959 (±0.895)	1.868 (± 0.778)	0.34	0.73
	NAA/Cho	1.66 (± 0.3)	1.37 (± 0.25)	2.54	0.03*
	Cho/Cr	1.17 (0.43)	1.37 (± 0.25)	1015	0.3
	Cr + Cho	2.07 (±2.669)	2.686 (± 3.814)	-1.59	0.14
Controls	**NAA/Cr.**	1.64 (± 0.192)	1.435 (± 0.12)	1.38	0.26
	NAA/Cho	2.09 (±0.95)	1.56 (± 0.16)	1.06	0.36
	Cho/Cr	0.99 (±0.33)	0.93 (±0.2)	0.15	0.9
	Cr + Cho	0.945 (±0.372)	1.01 (± 0.454)	-0.47	0.67

***indicates statistically significant result P≤0.05, P>0.05=non significant**

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Table (4): Correlation between symptom severity, phenomenology and Metabolite levels on the left BG of patient group.

Y-BOCS (Total)	NAA/Cr	NAA/Cho	Cr + Cho	Cho/Cr
r	0.34	-0.11	-0.63	0.368
P value	0.33	0.76	0.04*	0.3
Symptom severity	**Mean (±SD)**	**Mean (±SD)**	**Mean (±SD)**	**Mean (±SD)**
Mild	1.6 (±6.8)	1.5 (±0.15)	8.1 (±6.5)	1.11 (±0.2)
Moderate	1.6 (±2.7)	1.4 (±0.3)	1.5 (±2.1)	1.2 (±0.3)
Severe	2.0 9±1.0)	1.3 (±0.3)	1.3 (±1.5)	1.6 (±0.8)
f (P)	0.26 (0.77)	0.17 (0.84)	4.27 (0.06)	3.64 (0.08)
Phenomenology	**Mean (±SD)**	**Mean (±SD)**	**Mean (±SD)**	**Mean (±SD)**
Obsessions	1.5 (±0.2)	1.5 (±0.1)	4.8 (±5.5)	1.0 (±0.15)
Compulsions	1.2 (0)	1.5 (0)	0.9 (0)	0.8 (0)
Combined	2.3 (±0.96)	1.2 (±0.3)	1.5 (±1.5)	1.9 (±0.7)
f (P)	1.53 (0.28)	1.58 (0.27)	1.09 (0.38)	0.47 (0.64)

***indicates statistically significant result P≤0.05, P>0.05=non significant**

Discussion

Short echo proton magnetic resonance spectroscopy (1H-MRS) can be used to obtain information about several metabolites that are highly relevant to our understanding of the mechanisms of dysfunction within neuronal circuits in OCD and other neuropsychiatric disorders ***(Dager et al, 1992; Stanley et al, 1995)***.

Previous research has identified the corpus striatum as a potential area of the brain involved in OCD (***Schwartz et al, 1996; Bartha et al, 1998)***. More recently, researchers have begun using MRS to evaluate potential differences in regional brain metabolites between patients and healthy controls. MRS has been used primarily to measure concentrations of metabolites in brain tissue such as N-acetyl-l-aspartate, combined glutamate and glutamine, choline, myo-inositol, and creatine ***(Whiteside et al, 2006).***

It was found that N-Acetylaspartate levels from the left corpus striatum were significantly lower in the patients with OCD than in the comparison subjects (without differences in either left or right caudate volume between the two groups) which suggests reduced neuronal density in this region (***Bartha et al 1998)***. Also, two studies identified increased absolute concentrations of choline bilaterally in the medial thalami ***(Rosenberg et al, 2001; Smith et al, 2003).*** A third study found the

mean concentration of Cho/Cr was significantly higher in the OCD patients than controls, but only in the parietal white matter and parietal Cho/Cr was positively correlated with the severity of OCD symptoms ***(Kitamura et al, 2006)***.

The present study is the first study in Egypt to use MRS to image the corpus striatum in adults with OCD who are medication free for at least 6 weeks. We hypothesized that reduction of NAA concentrations within the corpus striatum as well as increased choline concentrations will be replicated.

NAA/Cr:

In our study, when we compared NAA/Cr ratios bilaterally in cases and controls, contrary to our hypothesis and to previously mentioned research in which NAA was reduced in corpus striatum (***Bartha et al 1998),*** or there has been no difference in left basal ganglia ***(Sumitani et al, 2007)*** or the lenticular nuclei ***(Ohara et al, 1999)***, there has been increased mean NAA/Cr ratio in patients. . However results were not statistically significant, probably due to small sample size. Our results were similar to a number of previous studies which found elevated NAA/Cr; in the right orbitofrontal white matter ***(Whiteside et al, 2006);*** right, but not left, dorsolateral prefrontal cortex ***(Russell et al, 2003).*** Increased relative levels of NAA found in the present study may be consistent with biologically based theories of OCD. Specifically, NAA is thought to be a marker of neuronal viability, and thus our finding may reflect an abundance of neurons. As such increased NAA/Cr in the corpus striatum could be consistent with neurobiological models of OCD postulating increased activity in the cortex ***(Saxena et al, 2001)*** and/or neurodevelopmental theories of OCD involving inefficient neuronal pruning ***(Rosenberg and Keshavan, 1998).*** Variability of results has been always the case in previous research which may be explained by the heterogenous etiologies of OCD.

Within the patient group, NAA/Cr levels were higher on the right similar to the previously mentioned studies ***(Whiteside et al, 2006; Russell et al, 2003).*** Again, results were not statistically significant.

In our study, there has been no statistically significant correlation between NAA/Cr and symptom severity or type, similar to previous research ***(Bartha et al, 1998)***. This was not the case in previous research where a significant negative correlation existed ***(Whiteside et al, 2006)***. Failure to detect significance in our research may be attributed to the small sample size.

Cho/ Cr & Cr+Cho:

Previous research found statistically significant increase of choline in left and right medial thalami ***(Fitzgerald et al, 2000; Rosenberg et al, 2001)***. Another study failed to detect any difference in Cho concentration in lenticular nuclei between 12 OCD patients and 12 healthy controls ***(Ohara et al, 1999).***

In our study, however, when we compared Cho/ Cr ratios, there has been a trend towards an increased level of choline bilaterally in patients compared to controls, a finding that is similar to most other research. Failure to detect statistical significance may be due to a small sample size.

The Cho spectra, as measured by proton magnetic resonance spectroscopy, primarily arise from glycerphosphocholine and phosphocholine metabolites of phosphocholine ***(Barker et al, 1994; Miller***

et al, 1996). Phosphotidyl choline is known to play a critical role in intracellular signal transduction ***(Ziesel, 1993)*** suggesting that altered Cho concentrations in patients with OCD may alter signal transduction and contribute to the pathogenesis of the disorder ***(Smith et al, 2003).***

When Cho concentrations were observed in OCD patients compared with both healthy control subjects and patients with major depression (MDD), significantly increased left and right medial thalamic Cho concentrations were observed in OCD patients compared with both healthy control subjects and patients with MDD whereas medial thalamic Cho concentrations did not differ significantly between patients with MDD and control subjects ***(Smith et al, 2003).*** This may represent a specific neurobiologic marker of OCD.

There is a negative and statistically significant correlation between the sum of creatine + choline, and symptom severity by YBOCS (r= -0.63, P=0.04). This finding is difficult to interpret and needs replication in further studies, especially in the presence of the positive non significant correlation between Cho/Cr ratio and symptom severity using the same scale (r=0.37, P=0.3).

NAA/ Cho:

Regarding NAA/ Cho which was not studied in previous research involving OCD and was a new variable to be tested, it was found that this ratio has been lower in patients compared to controls bilaterally. However, results were not statistically significant. Regarding laterality difference within the patient group, results were statistically significant (t=2.54, P= 0.03) with lower ratio in the left corpus striatum.

In a previous study, Single-voxel 1H MRS was performed in the left frontal lobe, the anterior cingulate gyrus and the left superior temporal lobe of non schizophrenic subjects at risk. Subjects were followed longitudinally to detect conversion to schizophrenia. A significant reduction of the metabolic ratios NAA/Cr and NAA/Cho in the left frontal lobe and of NAA/Cr in the anterior cingulate gyrus in both at-risk groups and in the schizophrenic patients compared with healthy controls was observed. Those at-risk subjects, who converted to schizophrenia within the observation period, had a higher Cho/Cr and a lower NAA/Cho ratio in the anterior cingulate gyrus compared with non-converters. NAA/Cr did not differ between converters and non-converters. Six at-risk subjects were taking antidepressants, two were taking antipsychotics. There was no difference in any metabolic ratio in any region between at-risk subjects with and without medication. It was concluded that the reduction of the neuronal marker NAA in the left prefrontal lobe and the anterior cingulate gyrus may represent a vulnerability indicator for schizophrenia in at-risk subjects, while elevated Cho in the anterior cingulate gyrus may be a predictor for conversion from the prodromal state to the full disease ***(Jessen et al, 2006).*** Patients with lower NAA/Cho ratio in this study may be a subgroup of OCD patients with poor insight (an item which was not analyzed) or who are a group susceptible to experience syndromal shift to schizophrenia if followed up.

Conclusion:

In this study, increased Cho in corpus striatum was found, replicating previous studies which suggests that Cho concentrations can be a sensitive and specific biomarker for OCD. Also, there has been a trend to increased NAA relative to

Cr in the corpus striatum, supporting the theory of defective neuronal pruning, a hypothesis that needs further study.

The small sample size, which is the main limitation of the study, may have restricted the power to detect differences. However, this is a common problem in the field of neuroimaging, given the expenses, equipment, and time required to complete studies, a potential solution is multi-site collaboration.

Recommendations:

More research in the field is mandatory with replication of the study using a larger sample size and testing the specificity and sensitivity of Choline as a marker of OCD by studying its changes in various psychiatric disorders.

References:

Aylward EH, Harris GJ, Hoehn-Saric R, et al, (1996): Normal caudate nucleus in obsessive-compulsive disorder assessed by quantitative neuroimaging. *Arch Gen Psychiatry* 53:577-584.

Barker P, Breiter S, Soher B, et al (1994): Quantitative Proton spectroscopy of canine brain: In vivo and in vitro correlations. *Magn Reson Med* 32:157-163.

Bartha R, Stein MB, Williamson PC, , et al (1998): A short echo 'H spectroscopy and volumetric MRI study of the corpus striatum in patients with obsessive-compulsive disorder and comparison subjects. *Am J Psychiatry* 155:1584-1591.

Baxter LR Jr, Schwartz JM, Bergman KS, et al, (1992): Caudate glucose metabolic rate changes with both drug and behavior therapy for obsessive-compulsive disorder. *Arch Gen Psychiatry* 49:681–689.

Breiter HC, Rauch SL, Kwong KK, et al, (1996): Functional magnetic resonance imaging of symptom provocation in obsessive-compulsive disorder. *Arch Gen Psychiatry* 53:595–606.

Dager SR & Steen RG (1992): Applications of magnetic resonance spectroscopy to the investigation of neuropsychiatric disorders. *Neuropsychopharmacology* 6:249–266.

Ebert D, Speck O, Konig A, et al, (1997): I-H Magnetic resonance spectroscopy in obsessive-compulsive disorder: Evidence for neuronal loss in the cingulate gyrus and the right striatum. *Psychiatry Res* 74:173-176.

First MB, Spitzer RL, Gibbon M, Williams JBW (eds) (1997): Structured Clinical Interview for DSM-IV Axis I Disorders–Clinical Version (SCID–CV). APA Press: Washington.

Fitzgerald KD, Moore GJ, Paulson LA, et al, (2000): Proton spectroscopic imaging of the thalamus in treatment-naïve pediatric obsessive-compulsive disorder (comment). *Biological Psychiatry* 47:147-182.

Goodman WK, Price LH, Rasmussen SA, et al, (1989): The Yale-Brown obsessive-compulsive scale: Development, use and reliability. *Arch Gen Psychiatry* 46(11):1006-1011.

Hoehn-Saric R & Benkelfat C (1994): Structural and functional brain imaging in obsessive-compulsive disorder, in Current Insights in Obsessive-Compulsive Disorder. Hollander E, Zohar J, Marazziti D, Olivier

B (eds). New York, John Wiley & Sonspp 183–211.

Insel TR (1992): Toward a neuroanatomy of obsessive-compulsive disorder. *Arch Gen Psychiatry* 49:739–744.

Jenike MA, Breiter JC, Baer L, et al, (1996): Cerebral structural abnormalities in obsessive-compulsive disorder: a quantitative morphometric magnetic resonance imaging study. *Arch Gen Psychiatry* 53:625–632.

Jessen F, Scherk H, Träber F, et al, (2006): Proton magnetic resonance spectroscopy in subjects at risk for schizophrenia. *Schizophrenia Research* 87:81-87.

Kellner CH, Jolley RR, Holgate RC, et al, (1991): Brain MRI in obsessive-compulsive disorder. *Psychiatry Res* 36:45–49.

Kim JJ, Lee MC, Kim J, et al (2001): Gray matter abnormalities in obsessive-compulsive disorder: Statistical parametric mapping of segmented magnetic resonance images. *Br J Psychiatry* 179:330-334.

Kitamura H, Shioiri T, Kimura T, et al,(2006): Parietal white matter abnormalities in obsessive-compulsive disorder: a magnetic resonance spectroscopy study at 3-Tesla. *Acta Psychiatr Scand* 114(2):101-8.

Koran LM, Thienemann ML, Davenport R (1996): Quality of life for patients with obsessive-compulsive disorder. *Am J Psychiatry* 153:783–788**.**

Miller BL, Chang L, Booth R, et al (1996): In vivo I-H MRS choline: Correlation with in vitro chemistry/histology. *Life Sci* 58:1929-1935.

Modell JG, Mountz JM, Curtis GC, Greden JF (1989): Neurophysiologicdysfunction in basal ganglia/limbic striatal and thalamocorticalcircuits as a pathogenetic mechanism of obsessive-compulsive disorder. *J Neuropsychiatry Clin Neurosci* 1:27–36.

Ohara K, Isoda H, Suzuki Y,et al (1999): Proton magnetic resonance spectroscopy of lenticular nuclei in obsessive–compulsive disorder. *Psychiatry Research: Neuroimaging* 92:83-91.

Rauch SL (2000): Neuroimaging research and the neurobiology of obsessive-compulsive disorder: where do we go from here? (comment). *Biological Psychiatry* 47:168-170.

Rauch SL, Jenike MA, Alpert NM, et al (1994): Regional cerebral blood flow measured during symptom provocation in obsessive-compulsive disorder using oxygen 15-labeled carbon dioxide and positron emission tomography. *Arch Gen Psychiatry* 51:62–70.

Robinson D, Wu H, Munne RA, et al(1995): Reduced caudate nucleus volume in obsessive-compulsive disorder. *Arch Gen Psychiatry* 52:393–398.

Rosenberg DR, Amponash A, Sullivan A, et al (2001): Increased medial thalamic choline in pediatric obsessive-compulsive disorder as detected by quantitative in vivo spectroscopic imaging. *Journal of Child Neurology* 16:636-641.

Rosenberg DR, Keshavan MS, (1998): AE Bennett Research Award. Towards a neurodevelopmental model of obsessive-compulsive disorder. *Biological Psychiatry* 43:623-640.

Rosenberg DR, Keshavan MS, O'Hearn KM, et al (1997): Frontostriatal morphology in treatment-naïve children

with obsessive-compulsive disorder. *Arch Gen Psychiatry* 54:824–830.

Rosenberg DR, Macmaster FP, Keshavan MS, et al (2000): Decrease in caudate glutamatergic concentrations in pediatric obsessive-compulsive disorder patients taking paroxetine. *Journal of the American Academy of Child and Adolescent Psychiatry* 39:1096-1103.

Russell A, Cortese B, Lorch E, et al (2003): Localized functional neurochemical marker abnormalities in dorsolateral prefrontal cortex in pediatric obsessive-compulsive disorder. *Journal of Child and Adolescent Psychopharmacology* 13(1):S31-S38.

Saxena S, Bota RG, Brody AL (2001): Brain-behavior relationships in obsessive-compulsive disorder. *Seminars in Clinical Neuropsychiatry* 6:82-101.

Scarone S, Colombo C, Livian S, et al (1992): Increased right caudate size in obsessive-compulsive disorder: detection with magnetic resonance imaging. *Psychiatry Research: Neuroimaging* 45:115–121.

Schwartz JM, Stoessel PW, Baxter LR Jr, et al (1996): Systematic changes in cerebral glucose metabolic rate after successful behavior modification treatment of obsessive compulsive disorder. *Arch Gen Psychiatry* 53:109–113.

Smith EA, Russell A, Lorch E, et al (2003): Increased medial thalamic choline found in pediatric patients with obsessive-compulsive disorder versus major depression or healthy control subjects: a magnetic resonance spectroscopy study. *Biological Psychiatry* 54:1399-1405.

Stanley JA, Drost DJ, Williamson PC, Carr TJ (1995): In vivo proton MRS study of glutamate and schizophrenia, in NMR Spectroscopy in Psychiatric Brain Disorders. Edited by Nasrallah HA, Pettegrew JH. Washington, DC, American Psychiatric Press pp 21–44.

Sumitani S, Harada M, Kubo H and Ohmori T (2007): Proton magnetic resonance spectroscopy reveals an abnormality in the anterior cingulate of a subgroup of obsessive–compulsive disorder patients. *Psychiatry Research: Neuroimaging* 154:85-92.

Whiteside SP, Port JD, Abramowitz JS (2004): A meta-analysis of functional neuroimaging in obsessive-compulsive disorder. *Psychiatry Research: Neuroimaging* 132:69-79.

Whiteside SP, Port JD, Deacon BJ, Abramowitz JS (2006): A magnetic resonance spectroscopy investigation of obsessive-compulsive disorder and anxiety. *Psychiatry Research: Neuroimaging* 146:137-147.

Ziesel SH (1993): Choline phospholipids: Signal transduction and carcinogenesis. *FASEB J* 7:551-557.

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الصjq القصير والطويل للرنين المڇناطيسى الطيڤى فى عينة مصرية مڏ مرضى الوسواس القهرjn

الخطوط المتعددة للتحقق من أسباب إضطراب الوسواس القهرى إقترحت وجود خلل وظيفى فى الدائرة العصبية بين العقد القاعدية والمهاد والقشرة المخية. وبما أن الدراسات التصويرية العصبية تزيد من فهم الصلة بين الأعراض الملاحظة والتڇيرات البيولوجية العصبية المصاحبة، فربما يؤدى ذلك إلى تحسين العلاج وملائمته لإحتياجات المريض. الهدف من هذا البحث هو دراسة تركيزات الإشتقاقات الأيضية المختلفة فى العقد القاعدية وإيجاد مؤشر حيوى محدد وحساس يزيد من فهمنا لڷاعتلال الوظيفى فى مرضى الوسواس القهرى. وقد تم إختيارعشر مرضى مصابين بالوسواس القهرى من مركز الطب النفسى بجامعة عين شمس لم يخضعوا للعلاج بالعقاقير النفسية خلال الست أسابيع السابقة للبحث (على الأقل) وتم مقارنة نتائج الصدى القصير والطويل للرنين المڇناطيسى الطيفى لهؤلاء المرضى بنتائج مجموعة سيطرة مكونة من خمس نظراء أصحاء. وقد وجد أن مستوى الإن- أسيتيل أسبارتات/كولين أقل فڏ الجانب الأيسر فى الحالات عن مجموعة السيطرة و كانت النتائج ذات دلالة. كذلك كان هناك أتجاه لزيادة الكولين علڏ الجانبين فڏ الحالات عنه فڏ مجموعة السيطرة . وأيضا كانت هناك علاقة سلبية ذات دلالة إحصائية بين مستوى الكرياتين والكولين معاً على الجانب الأيسر وبين شدة الأعراض.

وقد أستنتج من البحث أن الإتجاه نحو زيادة مستوى الإن- أسيتيل أسبارتات/كرياتين فى العقد القاعدية يؤيد نظرية القصور فى تقليم الأعصاب التى قد تفسر حدوث مرض الوسواس القهرى وأيضا زيادة الكولين فى العقد القاعدية يطرح الإحتمال ان يكون الكولين مؤشر حيوى محدد وحساس لمرضى الوسواس القهرى.