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Structural and Functional Abnormalities in the Caudate Nucleus of Schizophrenic Patients with and without Obsessive Symptoms

--Manuscript Draft--

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Abstract:	Background: Obsessive compulsive symptoms (OCS) have been frequently described in schizophrenic populations. There is a controversy on whether this co-occurrence is more than just co-morbidity or represents a distinct subgroup in schizophrenia. Aim of the work: to investigate if there are possible underlying structural and functional differences between the schizophrenic patients with and without OCS. Methodology: participants in this study were divided into 3 groups: 20 patients having schizophrenia with OCS; 20 patients having schizophrenia without OCS (both were diagnosed according to DSM-IV-TR); and 20 matching controls. All subjects underwent a magnetic resonance imaging for volumetric measurement of the caudate nucleus; and a magnetic resonance spectroscopy (MRS) to measure choline (Cho), creatine (Cr) and N-acetyl aspartate (NAA) in the caudate nucleus. Results: Caudate volume was found to be reduced in either schizophrenic patients with or without OCS (P≤ 0.05). MRS findings showed that the schizophrenic patients without OCS have significant increase in Cho concentration (P≤ 0.05) while, they have average NAA concentration. On the other hand, schizophrenic patients with OCS had significant reduction in NAA concentration (P≤ 0.05) with average Cho concentration. Conclusion: Schizophrenic patients with OCS may have an atypical set of neuro-radiological characteristics which would specifically categorize it within the schizophrenia spectrum.
Response to Reviewers:	1- Title: we changed the title

	2- Aim of the study: we changed and completed it 3- In Patients and Methods: * In exclusion criteria: what are the organic brain disorders: examples are listed * Where your 3 groups age and sex-matched? We stated it * Diagnosis according to DSM-IV-TR * In Magnetic Resonance Spectroscopy (MRS): What does the abbreviation ppm mean? parts per million 4- Statistical analysis: standard deviation is corrected 5- Results: * Standard Deviation are added between the brackets * Stars are correctly placed with significance below the tables 6- Discussion:Grammar is revised * Concentration is completed as a word 7- References: We updated the references

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Dear Prof. Asaad,

Please find enclosed a manuscript entitled "Structural and Functional Abnormalities in the Caudate Nucleus of Schizophrenic Patients with and without Obsessive Symptoms" that we wish to submit as an original article for publication in your honorable journal "Middle East Current Psychiatry"

The study reported in this paper has been approved by the medical ethical committee of the Mansoura University and we have received the patients' consent as stated in the Methods section.

Our study aimed to investigate if there are possible underlying structural and functional differences between the schizophrenic patients with or without obsessive compulsive symptoms.
We believe that this will be an original addition to our knowledge in Neuropsychiatry by understanding some neuro-radiological aspects of schizophrenic patients with or without obsessive compulsive symptoms.

We confirm that this manuscript has not been published elsewhere and is not under revision in any other journal.

All authors have approved the manuscript and agree to its submission to Middle East Current Psychiatry Journal.

I take full responsibility for the data, the analyses and interpretation, and the conduct of the research; I have full access to all of the data; and have the right to publish any and all data separate and apart from any sponsor.

Please address all correspondence to my mail: mostashfa_elmogy@yahoo.com
Thank you so much in advance and looking forward to hearing from you.

Yours sincerely,
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Structural and Functional Abnormalities in the Caudate Nucleus of Schizophrenic Patients with and without Obsessive Symptoms

Running title: Caudate Nucleus in Schizophrenic Patients with and without Obsessive Symptoms

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Structural and Functional Abnormalities in the Caudate Nucleus of Schizophrenic Patients with and without Obsessive Symptoms

INTRODUCTION

Obsessive compulsive symptoms (OCS) have been frequently described in schizophrenic populations (1). The prevalence of OCS in schizophrenia vary widely across the studies (10%–64%) (2). Several studies suggested increased rates of OCS and obsessive-compulsive disorder (OCD) among schizophrenic patients; up to proposing the existence of a distinct diagnostic sub-group of schizo-obsessive disorder (3). Whether this co-occurrence is more than just co-morbidity and represents a distinct subgroup still remains controversial (4)**.**

It has been described the presence of a disrupted cortico-striato-thalamo-cortical circuits in schizophrenic patients (5,6), and obsessive-compulsive disorder (OCD) patients (7,8). Magnetic resonance imaging (MRI) and magnetic resonance spectroscopy (MRS) are non-invasive in vivo methods that allow studying these functional circuits.

The MRI allows a volumetric measurement of the basal ganglia structures including the caudate nucleus (9), while, the MRS provides useful information on the brain metabolites (10) such as N-Acetyl aspartate (NAA) (11), choline (12) and creatine (13). Several studies showed disturbance in these metabolites in the caudate of schizophrenic patients (14, 15,16) and OCD patients (17,18).

Despite the early discovery of this co-morbidity, little attention has been paid to it. Consequently, researches regarding the precise underlying potential neurobiological mechanisms of this co-morbid condition have been limited (3)

The aim of our study is to investigate if there are possible underlying structural and functional differences between the schizophrenic patients with or without OCS.

SUBJECTS AND METHODS

Our case control study was enrolled from January 2013 to January 2014 in the outpatient clinic of Mansoura University Hospitals. We included schizophrenic patients with and without OCS; and a control group of healthy persons. The study was approved by the medical ethical committee of Mansoura University and all subjects accepted to participate after giving either an oral or a written consent.

Clinical assessment:

All patients underwent a neuropsychiatric clinical interview including thorough history taking and examination by a psychiatrist and a neurologist. The diagnosis and the further sub-classification for presence or absence of OCS were done according to Diagnostic and Statistical Manual of Mental Disorders, Fourth division, Text Revised (DSM-IV-TR) criteria (19). The re-confirmation of the diagnosis was done by two blinded psychiatrists. We included all schizophrenic patients ranging from 15-50 years old from both sexes who are drug naïve (if on medication, it should be stopped for at least 4 weeks). We excluded patients with co-morbid mental retardation, organic brain disorders (such as ischemic vascular

diseases, brain tumors, trauma and degenerative disorders), substance use disorders and language or hearing difficulties.

The patients were divided into: group (A): 20 schizophrenic patients with OCS, group (B): 20 schizophrenic patients without OCS; besides, a group (C): 20 control subjects of non psychiatric patients who came to Mansoura university hospital outpatient clinic and some workers in the hospitals. The control group is matching in age and sex with the above mentioned groups of patients.

Imaging Studies:

a) Magnetic Resonance Imaging (MRI):

All the groups were subjected to an MRI of 1.5 Tesla unit (Magnetom Symphony, Siemens, Version VA 12A) using a head coil. MRI protocol included: axial T1-WI; sagittal T2-WI and coronal FLAIR images.

The left and right Caudate nuclei volume was measured. The volumes of 10 subjects were calculated five times on the same scan by two raters to determine the test reliability. All volumes were measured by the raters without knowing the diagnosis or MRS measures. The volume of the caudate was calculated according to manual tracing technique (20,21).

B) *Magnetic Resonance Spectroscopy (MRS):*

Single-voxel localization proton MRS was performed using a spin-echo mode sequence. Two voxels (15x15x15) were placed on either right and left caudate .The raw data were transferred to an off-line workstation and post-processed automatically using a spectroscopic analysis package. Three main metabolites were

identified: NAA at 2.0 parts per million (ppm), creatine at 3.0 ppm and choline at 3.2 ppm. The peak ratios were calculated from the integration of the single peak including NAA /Creatine , NAA/Choline and Choline/Creatine.

Statistical analysis:

The results were computed on an IBM compatible personal computer Pentium IV using Statistical Software Package for Social scientists (SPSS) for windows 11 (SPSS Inc., Chicago, IL, USA). Data were summarized using mean, median, standard deviation (SD) for quantitative data. The qualitative data were described as number and percent.

Chi-square, chi-square with Yates' correction and relative risks was used to test for association between different categorical variables (qualitative data). The difference between groups were tested using t-test for two group comparison and one way ANOVA for analysis of co-variance in more than two groups and post Hoc multiple comparisons test (Scheffe test) for within groups paired comparison (quantitative data). The correlation between two continuous groups was assessed using the Pearson's correlation test. P value is considered significant if ≤ 0.05; and highly significant if ≤ 0.001 at confidence interval 95%.

RESULTS

Socio-demographic results

All socio-demographic results are presented in Tables (1) and (2). Schizophrenic patients with OCS are more likely to live alone, with poorer occupational functioning even that they were of higher education level than schizophrenic patients without OCS (Table 1).

Eighty five percent of schizophrenic patients with OCS were right-handed and 70% of schizophrenic patients without OCS were right-handed with no statistically significant difference (*P=0.449*) (Table 1).

Regarding the disease duration, the mean duration of illness is more among schizophrenic patients with OCS (8.65 +/- 6.53 years) compared to schizophrenic patients without OCS (6.0 +/- 2.22 years) with no statistical significant difference *(P= 0.099)* (table1)

Concerning the age of onset, 55% of schizophrenic patients with OCS have the onset of the disorder before 15 years old in comparison to 25% of schizophrenic patients without OCS who developed the disease earlier than 15 years old. Forty percent of schizophrenic patients with OCS have age onset between 15-30 years old in comparison to 50% of schizophrenic patients without OCS. While only 5 % of schizophrenic patients with OCS have age onset from 35 to 45 years old compared to 25% of schizophrenic patients without OCS who have the same age of onset. The difference in overall age of onset is not statistically significant *(P=0.066)* but Chi-square for trend shows significant difference between both groups at age onset before 15 years old *(P=0.043)* (Table 2)

Caudate Nucleus Volume Results:

The size of caudate nucleus was significantly reduced in schizophrenic patients with OCS compared to schizophrenic patients without OCS and controls on both sides (left; *P= 0.010 and right; P= 0.000) (Table 3).*

Magnetic Resonance Spectroscopy Results:

Choline values are statistically significantly higher in schizophrenia with and/or without OCS than controls at both sides (left; *P=0.000 and right; P=0.042).* A similar significant choline values are detected in the dominant hemisphere *(P=0.000)* (Table 4).

The choline /creatine ratio significantly increases in schizophrenia with and/or without OCS than controls on the left side (*P=0.000)* while it increases on right but not statistically significant *(P=0.223).* A similar significant choline/creatine values are detected in the dominant hemisphere *(P=0.000)* (Table 4)

The NAA values is significantly lower in schizophrenia with OCS than schizophrenia without OCS and controls on the left side (*P=0.040)* while it decreases on right but not with statistical significance *(P=0.806).* Also, these differences are not significant regarding the dominant hemisphere (*P=0.187)* (Table 4)

A similar results were obtained regarding NAA /creatine ratio which was statistically significant low in schizophrenia with and without OCS than controls on the left *(P=0.000)* and dominant hemisphere *(P=0.000),* while statistically insignificant low on the right side *(P=0.989).* (Table 5)

Choline /NAA ratio was significantly high in schizophrenia without OCS than schizophrenia with OCS and controls on the left *(P=0.001)* and dominant hemisphere *(P=0.000)* with higher values in schizophrenia with OCS , while statistically insignificant low on the right side *(P=0.059)* again with higher values in schizophrenia with OCS. (Table 5)

DISCUSSION

In the present study we performed a volumetric assessment and MRS study on the caudate nucleus to investigate if there are possible underlying structural and functional differences between the schizophrenic patients with and without OCS.

Our results for the handedness showed that 85% of schizophrenic patients with OCS were right handed and 15% were non-right handed (left handed and mixed handed). On the other hand, the schizophrenic patients without OCS showed more tendencies to be left handed (70% right handed and 30% non right handed). It is important to note that right-handedness, left cerebral dominance for language and normal cerebral asymmetry are considered to be secondary to a dominant allele, the 'right-shift factor' (23). In schizophrenia, several studies reported an excess of non-right handedness, decreased language lateralization on the dichotic listening paradigm (24) and decreased anatomical asymmetry (25). It has been postulated that the genetic mechanism underlying normal left hemispheric dominance is altered in schizophrenia. The discovery of the 'right-shift factor' might identify a locus where genetic aberrations predispose for schizophrenia (26). The difference between both groups of schizophrenic patients either with or without OCS as regard the handedness may support the idea of being different disorders with different genetic predisposition.

Concerning the age group, our results showed that the age of about half of all schizophrenic patients with OCS were below 30 years old in comparison to one third of schizophrenic patients without OCS. This can be justified by the earlier onset of symptoms: 55% of schizophrenic patients with OCS has an age of onset

below 15 years old in comparison to 25% of schizophrenic patients without OCS with a statistically significant difference.

The age of onset in 95% of schizophrenic patients with OCS was below 30 years old in comparison to 75% of schizophrenic patients without OCS. This may be explained by the denial of illness from nearby persons to the patients and decreased knowledge about psychiatric illness resulting in late discovery of the disease. On the other hand, the distressing effect of OCS in schizophrenia may be triggering for early seek for help and treatment.

Regarding the volumetric assessment of the caudate nucleus, it was reduced in both schizophrenic groups compared to controls on both sides. This result is constant with (5,21) whereas, Brandt (9) described an increased in caudate volume in chronic schizophrenic patients. Data from longitudinal studies suggest that neuroleptics may change the brain morphology and these changes are dynamic and might be reversible. Nevertheless, several longitudinal studies have described a greater degree of brain tissue volumes decrease in the early stage of the illness but others have failed to confirm these findings (27). Thus, it remains unclear to what extent the observed structural changes reflect the ongoing illness process and to what extent the type and the duration of antipsychotic medication can modify the neuro-imaging measures.

When we studied the caudate volume in OCD patients, we found only one study which described an increased of the gray matter volume in the head of the left caudate (28), and another one failed to show significant differences in caudate volumes between OCD patients and controls (29). On the contrary, many studies showed reduction in caudate volume of OCD patients (30,31). Based on this

confluent data, we can say that our caudate volume results need further studies on larger groups of patients involving schizophrenic and OCD patients under different types of medication for better evaluation of the results.

Nevertheless, many neurodegenerative disorders such as Parkinson's disease (PD) and Huntington's disease (HD) are associated with neuropsychiatric symptoms such as OCS, impulse control, depression (32) and psychotic symptoms (33). Interestingly, a recent study showed that pre manifest HD exhibit small volume of the caudate nucleus (34,35). These recent studies highlight the need of further researches on the functional circuit dysfunction described in many neuropsychiatric disorders for better evaluation and early management.

The MRS results in our study showed an increase in choline concentration in schizophrenia with or without OCS in comparison to controls. The choline concentration is higher in absence of OCS. This is in agreement with (13) (14) (15) who found significant higher levels of choline than the comparison subjects. Similar results were found in choline /creatine ratio which is in agreement with Gao and his colleagues (36) who found that the NAA /creatine and choline/creatine ratios were lower in the frontal cortex bilaterally among patients with schizophrenia , higher NAA/creatine ratio in the left frontal lobe, and a higher choline/creatine ratio in the right caudate. The latter finding was observed in our study but in left caudate.

The NAA concentration is markedly reduced among schizophrenic patients with OCS than controls and schizophrenic patients without OCS. This is constant with older results (16,17,37). Meanwhile, Grošić V (38) revealed a significant rise in the NAA/Creatine level in the studied group that stayed on the same antipsychotic

treatment and a significant drop in NAA/Creatine in the studied group that switched the antipsychotics. In our study we did not address the effect of medications as all our patients were drug naïve.

Schizophrenic patients without OCS showed relative increase in NAA concentration either in left or dominant caudate nucleus while they showed more or less similar NAA concentration as controls in right hemisphere which is in agreement with (39).

The NAA /creatine ratio is markedly reduced among schizophrenic patients with OCS and to less extent in schizophrenic patients without OCS than controls which is congruent with other authors (16,17,39,40). The increase in choline to NAA ratio in patients with or without OCS in comparison to controls is in agreement with different studies (13,39, 41).

NAA is considered to reflect both, neuronal density and integrity of neuronal mitochondria. Thus, reduction of NAA may represent diminished neuronal integrity (41) or an altered functional (metabolic) state of neurons (42). This functional finding was described in other psychiatric disorders and recent studies reported reversal of decreased NAA concentration with treatment reflecting a functional restoration (42).

Deicken and co-authors (43) stated that the most consistently replicated findings in schizophrenia are reduced NAA measures in the hippocampal regions while, this finding is less consistent in the frontal cortex, basal ganglia, cingulate region, and thalamus in schizophrenia. Furthermore, there are no consistently replicated findings for choline or creatine alterations in any of the brain regions examined in schizophrenia.

Recently, Dengtang and his colleagues (36) found a decreased NAA/Creatine ratio in the prefrontal cortex among schizophrenic patients. However, most studies found no significant changes in the Choline/Creatine ratio. These findings support the hypothesis of the early damage of neurons in the frontal cortex and fronto-striatal connection in the individuals with schizophrenia.

Choline has been proposed as a marker for neuronal astrocytosis associated with neurodegenerative diseases and other brain injury (44). Elevated Creatine suggests abnormal local cell-energy demand and elevated Choline suggests a phospholipid membrane disturbances in patients with early age-of-onset schizophrenia (41).

Schizophrenic patients with OCS may be a disorder with two pathologies (schizophrenia with normal NAA level and OCD with decreased NAA level as postulated by Bartha and others (17, 18,45).The more reduction of NAA in caudate nucleus in schizophrenic patients with OCS than schizophrenic patients without OCS could be explained by the idea that schizophrenic patients without OCS is one disorder with one pathology referring to Bustillo (37) who showed that schizophrenia alone is associated with normal level of NAA.

CONCLUSION

Schizophrenic patients with OCS may have an atypical set of neuro-radiological characteristics which is reflected on the clinical presentation and perhaps it constitutes a subgroup within the schizophrenia spectrum. More researches on a larger group of patients are warranted for optimal categorization of those patients.

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Figure legends:

(Fig.1): MRS of schizophrenic patient without obsessive compulsive symptoms showing marked increase in choline concentration (8.92ppm) while the N-acetyl aspartate concentration is of average range (12.5ppm).

(Fig.2): MRS of schizophrenic patient with obsessive-compulsive symptoms showing marked decrease in N-acetyl aspartate concentration (3.56ppm) while choline concentration is of average range (3.99ppm).

(Fig.3): MRS of control subject showing average concentration of choline (3.65ppm) and N-acetyl aspartate (12.5ppm).

الملخص العربي

المقدمة:

لقد لوحظ تواجد أعراض الوسواس القهرى في مرضى الفصام بشكل متفاوت و بالرغم من ذلك فإن البحوث لم تستطع تحديد هل أعراض الوسواس القهرى مجرد ملازمة لأعراض الفصام ,أم إنها نوع خاص من أنواع الفصام المختلفة .

الهدف من الدراسة:

البحث إذا كان هناك اختلافات هيكلية أو وظيفية بين مرض الفصام المصحوب وغير المصحوب بأعراض الوسواس القهرى.

الوسائل:

تم تقسيم المشاركين في هذا البحث إلى ثلاث مجموعات وهي مجموعة الفصام المصحوب بأعراض الوسواس القهرى وعددهم 20ومجموعة الفصام الغير مصحوب بأعراض الوسواس القهرى وعددهم 20 وقد تم فحص هاتين المجموعتين اكلينيكيا و تشخيصهم باستخدام الدليل الأمريكي الرابع المعدل لتشخيص الأمراض النفسيه و أخيرا العينه الضابطه وعددهم أيضا 20.

جميع المشاركين بالبحث خضعوا للرنين المغناطيسي لقياس حجم النواة الذيلية و الرنين المغناطيسي الطيفى لقياس معدلات الكولين و الكرياتين و الان اسيتيل اسبرتات فى النواة الذيلية.

النتائج:

أوضحت الدراسة أن حجم النواة الذيلية صغير في مرضي الفصام مَع أو بدون أعراض الوسواس القهري مقارنه بالعينه الضابطه.

كما أوضح الرنينَ المغناطيسيَ الطيفي أن مرضى الفصام بدون أعراض الوسواس القهري لديهم زيادة هامة و دالة إحصائيا في تركيز مادة الكولين ,مع الاحتفاظ بالمعدل الطبيعي لتركيز مادة الإن أسيتيل اسبرتات. و من الناحية الأخرى فأن مرضى الفصام مع أعراض الوسواس القهري لديهم تركيزاً اقل لمادة إن أسيتيل اسبرتات و هوهام و دال إحصائيا مع الاحتفاظ بالمعدل الطبيعي لتركيز مادة الكولين.

الاستنتاج:

ان مجموعة مرضى الفصام المصحوب بأعراض الوسواس القهرى قد يكون لها خصائص عصبية إشعاعية مختلفه من شأنها أن تصنفها كمجموعه فرعيه محدده داخل طيف الفصام.

Table

Tables

Table (1): The socio-demographic data among the studied groups

Variable		Schizophrenia with OCS	Schizophrenia without OCS	X2	P	R.R.
		Number (%)	Number(%)			
Sex	Male	15 (75%)	12 (60%)	1.026	0.311	1.444
	Female	5(25%)	8(40%)			
Handedness	Non right	3 (15%)	6(30%)	0.573	0.449	0.722
	Right	17(85%)	14(70%)			
Marital status	Single	15(75%)	11(55%)	4.868	0.088	0.608
	Married	5(25%)	6(30%)			
	Divorced	0 (0%)	3(15%)			
	Widow	0(0%)	0(0%)			
Occupation	Not working**	12(60%)	10(50%)	7.141	0.068	1.476
	Student**	3(15%)	1(5%)			
	Semi-skilled**	3(15%)	8(40%)			
	Skilled**	2(10%)	1(5%)			
Education	<6 years**	3(15%)	9(45%)	6.134	0.047*	1.333
	6-12 years**	10(50%)	9(45%)			
	>12 years**	7(35%)	2(10%)			
Residence	Rural	16 (80%)	14(70%)	0.533	0.465	0.778
	Urban	4(20%)	6(30%)			
Duration	Mean (SD)	8.65 (±6.53)	6.00(±2.22)	1.718	0.099	

OCS=obsessive compulsive symptoms
** Classification according to UK National Statistics Socio-Economic Classification (22)
* Statistically significant difference

Table (2): Age and age of onset distribution among the studied groups

Age	Schizophrenia with OCS Number (%)	Schizophrenia without OCS Number (%)	X2 for Trend	P	R.R.	X2	P
<15	0(0%)	0(0%)	0	0			
15-30	10(50%)	6(30%)	1.66	0.197	1.49		
					0.642		
30-45	7(35%)	12(60%)	2.51	0.113	0.595		
					1.65	**2.543**	**0.280**
>45	3(15%)	2(10%)	0.229	0.633	1.23		
					0.777		
Age Of onset							
0-15	11(55%)	5(25%)	3.75	0.043*	1.834		
					0.5		
15-30	8(40%)	10(50%)	0.404	0.525	0.814		
					1.22		
30-45	1(5%)	5(25%)	1.765	0.184	0.298	**5.44**	**0.066**
					1.89		
>45	0(0%)	0(0%)					

OCS=obsessive compulsive symptoms
** Correlation is significant at at P ≤ 0.001 level (2-tailed).
* Correlation is significant at≤ 0.05 level (2-tailed).

Table (3): Caudate size among studied groups

Overall comparison (One way ANOVA)						Post Hoc Multiple comparisons test (Scheffe test)					
		Controls	Schizophrenia with OCS	Schizophrenia without OCS	P	Controls/schizophrenia with OCS		Controls/schizophrenia without OCS		Schizophrenia with OCS/schizophrenia without OCS	
Rt caudate	Mean	5.41416	3.91782	4.10193	0.000**	Mean differences	P	Mean differences	P	Mean differences	P
	SD	0.612240	0.398860	0.415288		0.880200	0.000**	0.771900	0.000**	-0.10830	0.732
Lt caudate	Mean	5.56818	4.21209	3.862791	0.003*	Mean differences	P	Mean differences	P	Mean differences	P
	SD	0.617961	0.918221	0.533191		0.797700	0.018*	1.003170**	0.002*	0.205470	0.647

OCS=obsessive compulsive symptoms, Rt= right, Lt=left, SD= standard deviation
** Correlation is highly significant at P ≤ 0.001 level (2-tailed).
* Correlation is significant at P ≤ 0.05 level (2-tailed).

Table (4): Brain metabolites among the studied groups

MRS parameter	Overall comparison (One way ANOVA)					Post Hoc Multiple comparisons test (Scheffe test)					
		Controls	Schizophrenia with OCS	Schizophrenia without OCS	P	Controls /schizophrenia with OCS		Controls /schizophrenia without OCS		Schizophrenia with OCS/schizophrenia without OCS	
Lt Cho	Mean	3.21200	4.06000	5.36150	0.000**	Mean differences	P	Mean differences	P	Mean differences	P
	SD	0.91146	0.84360	1.89500		-0.84800	0.292	-2.149	.001**	-1.3015	0.017*
Rt Cho	Mean	3.67800	4.64450	5.12550	0.042*	-0.96650	0.231	-1.447	.042*	-.48100	0.574
	SD	0.76405	1.71119	1.37384							
Dominant Cho	Mean	3.24800	4.10250	6.00550	0.000**	-0.85450	0.233	-2.75	0.000**	-1.903	0.000**
	SD	0.73635	0.84126	1.74433							
Lt Cho/ Cr	Mean	0.50270	0.53073	0.76535	0.000**	-0.28820	0.910	-0.26260	0.001**	-0.2346	0.000**
	SD	0.18126	0.14036	0.18193							
Rt Cho/ Cr	Mean	0.58000	0.72020	0.87966	0.223	-0.14020	0.730	-0.29966	0.246	-0.15946	0.545
	SD	0.13539	0.44703	0.55075							
Dominant Cho/ Cr	Mean	0.54470	0.55279	0.88850	0.000**	-0.81803	0.991	-0.3438	0.000**	-0.3357	0.000**
	SD	0.13893	0.14539	0.16895							
Lt NAA	Mean	11.75600	9.53650	11.19250	0.040*	2.21950	0.082	0.56350	0.844	-1.65600	0.121
	SD	2.18776	3.40508	1.23117							
Rt NAA	Mean	10.91100	10.73950	11.41550	0.806	0.17150	0.991	-0.50450	0.926	-.67600	0.814
	SD	3.10340	3.66938	3.06416							
Dominant NAA	Mean	10.46600	9.53650	11.12550	0.187	0.92950	0.677	-0.65950	0.821	-1.58900	0.189
	SD	3.18195	3.40508	1.30007							

OCS=obsessive compulsive symptoms, Rt= right, Lt=lef, SD= standard deviation t, Cho=choline, Cr= creatine, NAA+N-acetyl aspartate

** Correlation is highly significant at P ≤0.001 level (2-tailed).

* Correlation is significant at P ≤0.05 level (2-tailed).

Table (5): **N-acetyl aspartate /Creatine and choline / N-Acetyl aspartate among studied groups.**

NAA /Cr		Overall comparison (One way ANOVA)				Post Hoc Multiple comparisons test (Scheffe test)					
		Controls	Schizophrenia with OCS	Schizophrenia without OCS	P	Controls /schizophrenia with OCS		Controls /schizophrenia without OCS		Schizophrenia with OCS/schizophrenia without OCS	
Lt	Mean	1.73350	1.04750	1.57950	0.000**	Mean differences	P	Mean differences	P	Mean differences	P
	SD	0.25239	0.10992	0.426702		0.59805	0.000**	0.24895	0.217	-0.3491	0.014*
Rt	Mean	1.87450	1.67850	1.68900	0.989**	-0.39802	0.994	-0.28803	1	-0.42802	0.990
	SD	0.36182	0.83247	1.21372							
Dominant	Mean	2.03450	1.04750	1.62900	0.000**	1.06015	0.000**	0.67020	0.001**	-0.3899*	0.026*
	SD	0.57927	0.10992	0.62702							
Cho / NAA											
Lt	Mean	0.28580	0.51410	0.49950	0.001**	-0.2283	0.001**	-0.213	0.002*	1.46802	0.953
	SD	8.7092E-02	0.17817	0.14036							
Rt	Mean	0.32543	0.39340	0.42875	0.059	-0.67802	0.282	-0.10332	0.059	-0.353802	0.594
	SD	7.9853E-02	0.11447	0.11488							
Dominant	Mean	0.28403	0.52080	0.55275	0.000**	-0.2367	0.000**	-0.2687	0.000**	-0.32802	0.746
	SD	6.3816E-02	0.17408	0.10298							

OCS=obsessive compulsive symptoms, Rt= right, Lt=lef, SD= standard deviation t, Cho=choline, Cr= creatine, NAA=N-acetyl aspartate

** Correlation is highly significant at P ≤ 0.001 level (2-tailed).

* Correlation is significant at P ≤ 0.05 level (2-tailed).

Figure
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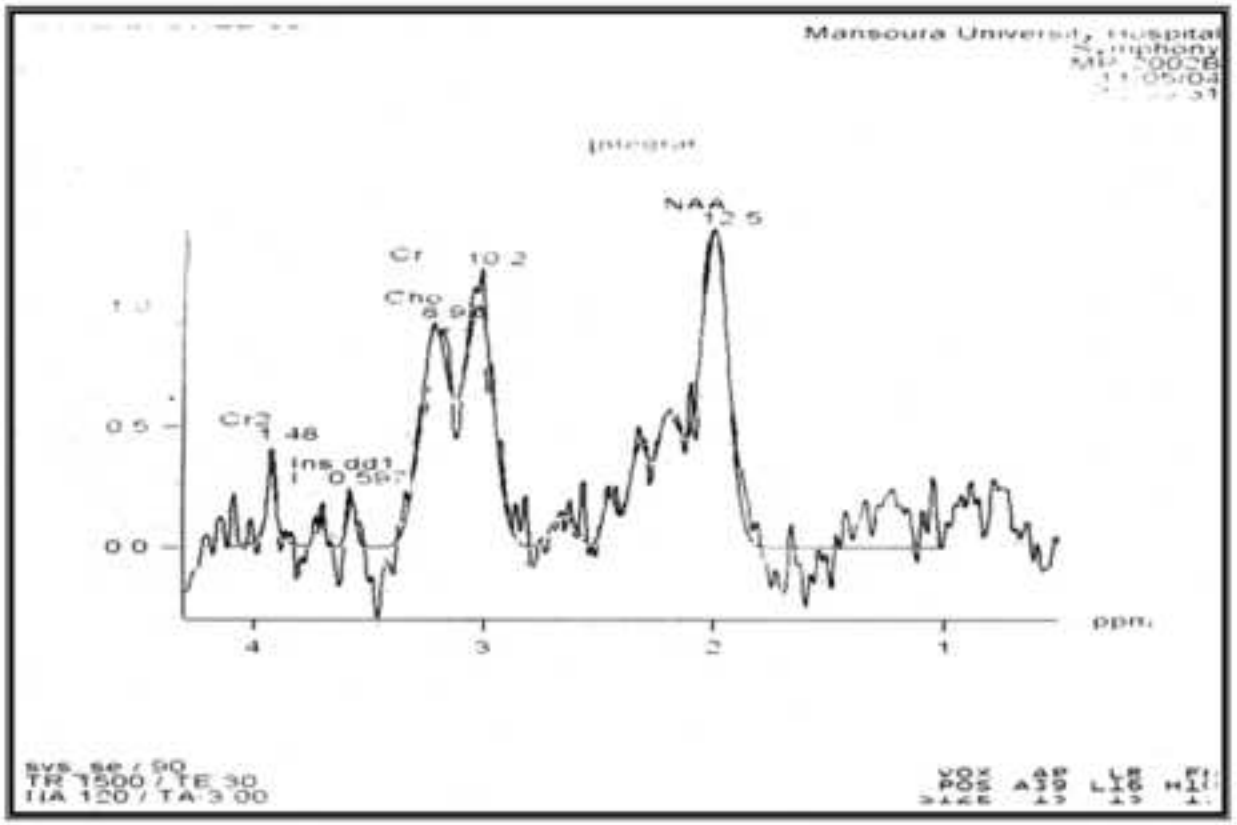

Figure (1)

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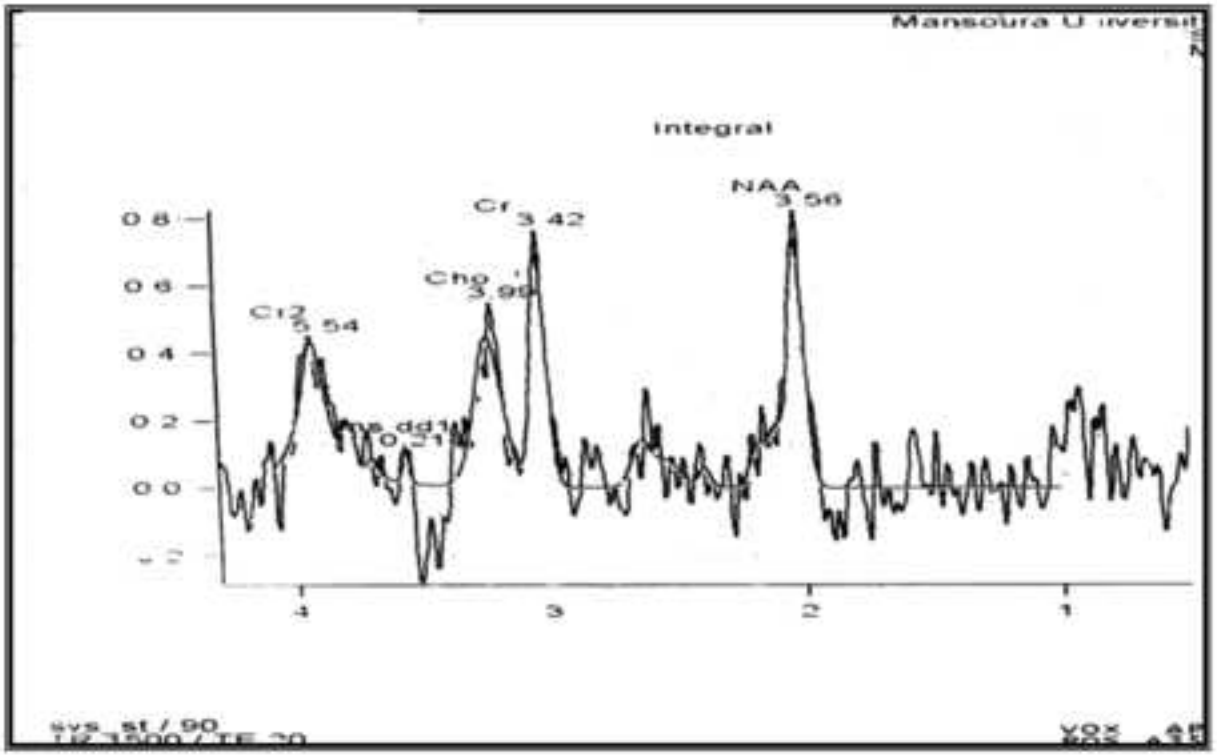

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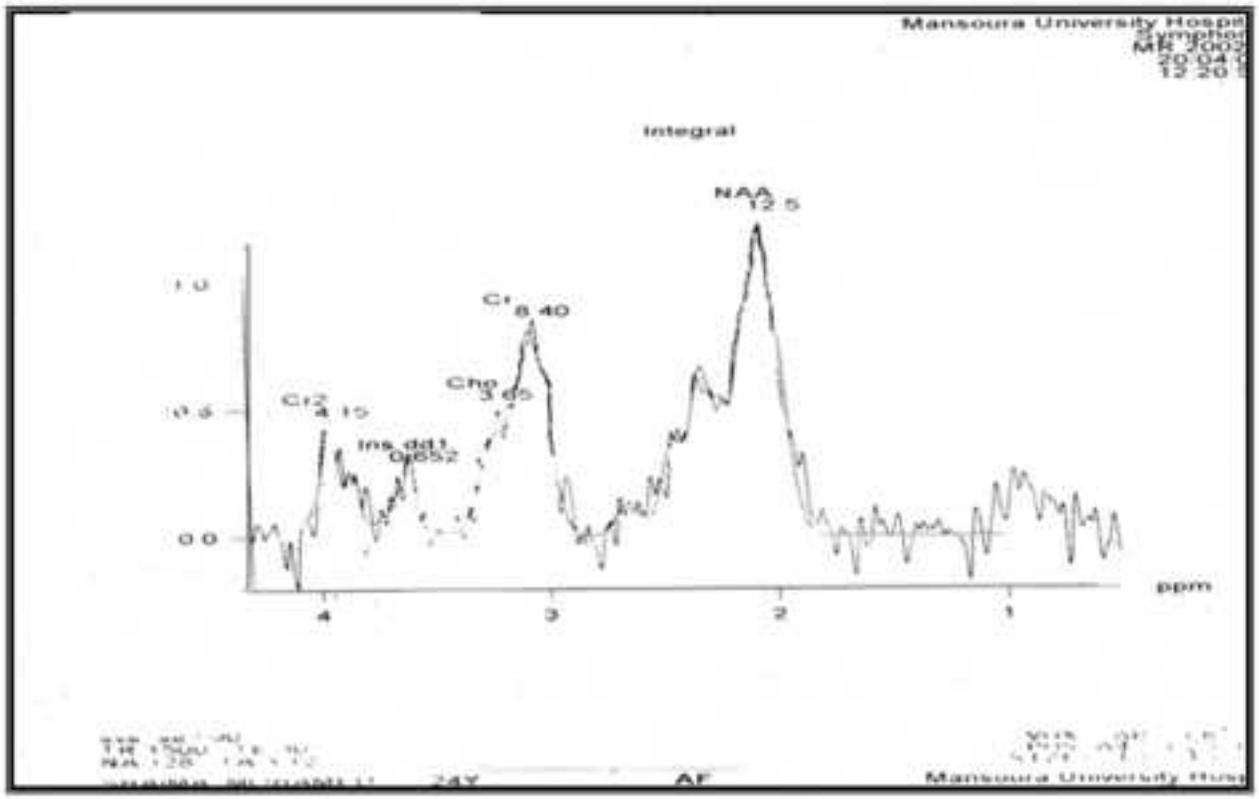

Figure (3)

All authors have approved the manuscript and agree to its submission to Middle East Current Psychiatry Journal.