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COGNITIVE FLEXIBILITY AND MOTOR INHIBITION IN OBSESSIVE COMPULSIVE DISORDER AND THEIR UNAFFECTED FIRST DEGREE RELATIVES

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Abstract

The purpose of the study was to evaluate cognitive flexibility and motor inhibition as in Obsessive compulsive disorder and to examine their relation with cognitive and motor functions, in their unaffected healthy first degree relatives and control, respectively. Study had a cross sectional design with purposive sampling with three groups having 20 subjects each. Tools-Patients with Obsessive compulsive disorder, their first degree relatives and matched healthy normal controls were assessed using General health questionnaire (GHQ), Yale-Brown Obsessive compulsive scale, Barratt's impulsiveness scale, Trail making test (TMT), Stroop test, Decision style inventory. Results -show higher trait impaired cognitive flexibility and motor inhibition in patients with Obsessive compulsive disorder and first degree relatives in comparison to normal controls.

INTRODUCTION

Obsessive-compulsive disorder (OCD) is a highly heritable neuropsychiatric disorder, with risk to first-degree relatives much greater than for the general population**.** OCD may constitute part of a spectrum of disorders characterized by overlapping co morbidity, familiarity, and difficulties suppressing inappropriate repetitive behaviour.

OCD is characterized by obsessions, which are repetitive intrusive thoughts that are highly anxiety provoking and compulsions which are either mental or behavioural rituals or avoidances intended to alleviate the distress caused by obsessions(4).

Diminished cognitive flexibility has been noted in patients with OCD. Cognitive flexibility refers to mental ability to adjust thinking or attention in response to changing goals and environmental stimuli. More specifically described as capacity to shift or switch one's thinking or attention between different task and operation.

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RATIONALE FOR STUDY

One may expect obsession and compulsions to have a detrimental effect on cognitive performance. However, the literature provides inconsistent evidence of the effects of obsession and compulsions on cognitive and motor function in obsessive compulsive disorder. Given that these patients already suffer from compromised cognition, it is necessary to determine whether the first degree relatives may also have added impairments, remedies core deficits, or whether the effects are inconsequential. An extensive literature search showed that there is only one study in India and few worldwide which investigated the impaired cognitive flexibility and motor inhibition in unaffected first degree relatives of obsessive compulsive disorder patients. In spite of high prevalence of obsessive compulsive disorder patients there is scarcity of systemic studies from India assessing cognitive flexibility and motor inhibition in OCD patients from their first degree relatives and healthy matches controls. So future studies are needed to elucidate the outcome in the first degree relatives of these patients.

AIM:

Aim of this study is to assess cognitive flexibility, motor inhibition and decision making ability of unaffected First degree relatives of OCD patients, patient probands and matched healthy comparison subjects without a family history of OCD.

OBJECTIVES

1. To assess cognitive flexibility, motor inhibition and decision making ability of unaffected First Degree Relatives of OCD patients.
2. To assess cognitive flexibility, motor inhibition and decision making ability of OCD patients probands

MATERIALS AND METHODS

STUDY DESIGN: Cross sectional hospital based study

STUDY VENUE: Institute of Mental Health & Hospital (IMHH), Agra

SAMPLE SIZE: 60 SUBJECTS

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- 20 unaffected First Degree Relatives of OCD patients.
- 20 patients with OCD probands.
- 20 matched healthy comparision subjects without a family history of OCD.

INCLUSION CRITERIA FOR UNAFFECTED FIRST DEGREE RELATIVES AND NORMAL HEALTHY COMPARISION GROUP

1. Age group between 18-50 yrs.
2. Unaffected first degree relatives and normal healthy control giving written, informed consent.
3. Minimum education of 10^{th} grade.

INCLUSION CRITERIA OF PATIENTS WITH OBSESSIVE COMPULSIVE DISORDER

1. Diagnosis of Obsessive Compulsive Disorder Fulfilling ICD 10 (DCR) criterion.
2. Patient age group between 18-50yrs
3. Patients giving written, informed consent
4. Minimum education of 10^{th} grade

EXCLUSION CRITERIA CRITERIA FOR FIRST DEGREE RELATIVES AND NORMAL HEALTHY COMPARISION GROUP

1. Any psychiatric illness or mental retardation or received ECT in past one year.
2. Any medical illness..
3. Not willing to give consent.
4. Mental and behavioral disorder due psychoactive substance use (Excluding Tobacco use).

EXCLUSION CRITERIA OF PATIENTS WITH OBSESSIVE COMPULSIVE DISORDER

1. Any co morbid psychiatric illness or mental retardation or received ECT in past one year.
2. Any medical co morbidity.
3. Not willing to give consent.
4. Mental and behavioral disorder due psychoactive substance use(Excluding Tobacco use).
5. Family history of psychiatric illness other than OCD.

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TOOLS

1. Socio-demographic and clinical data sheet

It includes information like age, sex, education, socio economic status etc. The clinical data sheet includes information like duration of illness, age of onset , number of episodes, history of psychotic features , past history, treatment history, etc.

2. **General Health Questionnaire 12 (GHQ 12)**
3. **Yale Brown Obsessive Compulsive Scale(Y-BOCS)**
4. **Barratt Impulsiveness Scale (BIS-11)**
5. **Trail making test (TMT)**
6. **Stroop Test**

STATISTICAL ANALYSIS:

Appropriate statistics were applied to analyze the data. Categorical socio Demographic variables and study variables were analyzed with mean with standard deviation and with appropriate correction when cell count is less than five. Means of socio-demographic variables on continuous scale, scores of BIS-11, TMT, Stroop Test and DSI were analysed using one way analysis of variance (ANOVA)

RESULTS

The present study was a cross sectional study of 60 subjects, out of which 20 were patients with obsessive compulsive disorder as per ICD 10-DCR (Patients=P), 20 were first degree relatives of patients with obsessive compulsive disorder (Relative=FDR) and 20 were normal healthy controls (Control=C). These are the tables showing the results of the study below:

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Table 1: Socio-demographic characteristics of patient with OCD (PATIENT) (N=20), their first degree relatives (RELATIVE) (N=20) and Normal control (CONTROL) (N=20).

Variables		PATIENT N=20	RELATIVE N=20	CONTROL N=20
Sex	Male	15	15	15
	Female	5	5	5
Marital status	Married	14	13	13
	Unmarried	6	7	7
Religion	Hindu	19	19	19
	Non-Hindu	1	1	1
Occupation	Employed	14	17	15
	Unemployed	6	3	5
SES	Lower	5	2	0
	Middle	15	18	20
Domicile	Rural	5	6	2
	Urban	15	14	1

Table 1: shows the comparison of socio-demographic variables among the three groups. All the groups had 5 female subjects each. 70% of subjects in patient group were married whereas 60% in other two groups which were statistically insignificant. Most of the subjects (57of 60 subjects) in all the groups followed Hindu religion and resided in urban area of the state of Uttar Pradesh where the study was conducted. Most of them were employed (n=14, 16 and 15, respectively) and belonged to middle socioeconomic group (patients=15 and Relative=18, control 20).

VARIABLE	PATIENT MEAN±SD	RELATIVE MEAN±SD	CONTROL MEAN±SD	F (df=2,57)	p	post hoc

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TMT-A (in sec)	83.28 ±48.65	65.96 ±32.63	59.57 ±25.12	2.211	0.11	
TMT-B (in sec)	192.34 ±78.61	149.00 ±85.86	113.12 ±58.72	5.554**	<0.01	P,R>C
TMT (B-A) (in sec)	109.06 ±56.97	83.04 ±71.31	53.55 ±42.12	4.581**	0.01	P,R>C
STROOP WORD (in secs)	104.86 ±36.97	75.23 ±34.44	76.48 ±28.51	5.005*	0.01	P>R,C
STROOP COLOUR (in secs)	232.20 ±57.72	219.52 ±95.84	176.09 ±39.02	3.701*	0.03	
STROOP (C-W) (in secs)	127.35 ±63.47	144.29 ±84.57	99.61 ±36.16	2.445	0.01	P,R>C
STROOP W-ERROR	0.85 ±1.42	1.10 ±1.68	0.15 ±0.37	2.913	0.06	
STROOP C- ERROR	10.70 ±5.59	8.15 ±7.15	2.50 ±2.95	11.607**	<0.01	P,R>C

Table 2: Comparison of Cognitive functions among the three study groups

**significant at 0.01 level (2-tailed); *significant at 0.05 level (2-tailed)

Table 2:

Shows the comparison of cognitive tests among the three study groups. One-way Analysis of variance (ANOVA) was done for comparison of means. Bonferroni Post-hoc analysis was used to know the unequal variance among the groups. Two tests were applied to assess cognitive functions viz., Trail making test with two parts (A&B), Stroop test with word and colour tests. Trail Making test (TMT) with time scores of TMT-A, TMT-B and the difference between TMT-B and TMT-A were compared. Comparative analysis showed significantly higher time ($F=5.554, p<0.01$) taken by

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patients (mean=192.34seconds) and First degree relatives(mean149.00seconds) in completing TMT-B in comparison to normal controls (mean=113.12 seconds).Also there was a significant higher time difference between the two parts of the test, with higher difference in patients(mean=109.06 seconds, SD=56.97) and First degree relatives (mean=83.04,SD=71.31)compared to normal control (mean=53.55 seconds, SD=42.12). Post hoc analysis showed significant differences in scores of TMT B and TMT B-A of patients and first degree relatives when compared to healthy matched control group.

Stroop test included Stroop word and colour tests. The time taken to complete the task was compared as well as the number of errors (commission and omission errors) in each task. Patients (word mean=104.86 seconds, colour mean=282.2 seconds) took significantly more time in completing the two tasks (F=5.005 and 3.701 respectively) when compared to normal controls (mean=76.48 seconds and 176.09seconds respectively). On post hoc analysis with Bonferroni Post-hoc Analysis, the patients(mean=104.86 seconds) scored significantly higher on Stroop word than other two comparison groups and relatives had a time score (mean=75.28 seconds) comparable to controls, which was significantly less than that of patients in stroop word but there is no difference in Stroop colour test. Although all the three groups had shown no statistically significant variation in Stroop interference, but errors were more in patients (mean error=10.7) and relatives (mean error= 8.14) compared to healthy matched comparison group (mean error=2.5).

Table 3: Comparison of motor inhibition among three study groups

VARIABLE	PATIENT MEAN±SD	RELATIVE MEAN±SD	CONTROL MEAN±SD	F df=	P	post hoc
BIS Attention facet I	14.6 ± 2.10	7.95 ± 1.76	6.8 ±1.73	102.08**	<0.01	P>R,C
BIS Attention facet II	8.4 ± 1.5	5.45 ± 2.2	5.35 ± 0.98	22.613**	<0.01	P>R,C
BIS Motor	18.4± 3.6	15.05 ± 2.7	12.7 ± 2.46	18.322**	<0.01	P,R>C

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facet I						
BIS Motor facet II	8.5 ± 2.4	7.6± 1.9	7.8 ± 1.4	1.306	0.279	
BIS Planning facet I	18.4 ±3.6	11.6 ±2.8	8.3± 0.97	68.195**	<0.01	P,R>C
BIS Planning facet II	12.1± 2.6	12.05± 2.2	9.12±1.5	12.164**	<0.01	P,R>C

Table 3: shows Comparison of motor inhibition measures among the three study groups. One way ANOVA was done for comparison of means.

Bonferroni Post-hoc analysis was used to know the unequal variance among the roups. One test Barret Impulsivity Scale (BIS) was applied to assess motor inhibition. The scale consist of different set of question in three parts Attention facet(I,II) Motor facet(I,II), Planning facet (I,II).Comparative analysis showed significantly higher value in scoring of Attention facet (I,II) in patients (AFI mean =14.6); (AFII mean=8.4) when ompared to first degree relatives(AFI :mean=7.95); (AFII: mean=6.45) and control group (AFI mean=6.8); (AFII: mean 5.35).

Comparative analysis also showed significantly higher value in scoring of Motor facet I) in patients (MFI: mean=18.4) and first degree relatives (MFI: mean=15.05) when compared to control (MFI: mean=12.7) Comparative analysis showed significantly higher value in scoring of Planning facet (I, II) (CFI: mean=18.1)(CFII: mean=12.1) when compared to first degree relative (CFI: mean=11.6) (CFII: mean=9.12) and control (CFI: mean=8.3) (CFII mean=8.05). Post hoc analysis showed that patient scored higher in attention facet compared to first degree relatives & control group, its non significant only in BIS MFII in comparison between three groups, but in planning facet both the patients and first degree relatives scored higher compared to control group.

DISCUSSION

The present study was conducted in Institute of mental health and hospital, Agra with the aim

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to investigate the cognitive flexibility and motor inhibition in Obsessive compulsive disorder, their unaffected first degree relatives and healthy matched control group.

The current study was aimed at evaluation of cognitive flexibility, motor inhibition and decision making ability as endphenotype in Obsessive compulsive disorder by evaluating the heritability of these factors.

Impaired levels of all the factors were hypothesised to co-segregate in the families of affected probands. A comparison of these constructs within the groups of patients, their first degree relatives and a group of healthy controls, with no familial mental disorders was carried out as an endophenotypic study.

We had studied only one of the first degree relatives of the patients. And had a more vigorous criterion for inclusion of healthy matched control group by excluding those with any blood relation to mentally ill person either in first degree or second degree. Our study also attempted at minimizing the variable of the cultural and environmental factors by taking controls among the guardians accompanying the patients to hospital. The guardians were not necessarily with Obsessive compulsive disorder or the patient under evaluation for the study. They mostly were patient's spouses or member of in laws family or a friend, but from the similar socio-cultural and geographical background as that of the patients or their relatives. Care was taken to ensure that these controls had no family history of any psychiatric illness.

A few studies have been conducted studying Cognitive functions, motor inhibition and decision making ability as endophenotyes. In Obsessive compulsive disorder, current study had assessed cognitive functions using trail making test, colour-word stroop test. Trail making test and Stroop test were applied using standard procedures recommended by the authors after proper training under the guidance of a Clinical Psychologist.

Trail making test collaborates two parts, part A and B. Part A where randomly spread numbers are to be sequentially connected evaluates sustained attention, perceptual tracking and simple sequencing. Part B requires subjects to alternatively connect numbers and alphabets in sequence there by assessing focused attention and cognitive flexibility in addition to the above. A difference in Part B and A thus measure the cognitive flexibility specifically. Cognitive inflexibility

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has been shown to precede impulsivity. Stroop test also consists of two parts, the word reading part and the colour naming part. The reading part requires sustained attention to complete the task. The naming part in addition requires response inhibition, by suppressing habitual response of reading the word in favour of unusual response of naming the colour of the word. Response inhibition is a well known factor of impulsive system.

Cognitive functions would mark the three sub domains of impulsiveness (cognitive, motor and planning), respectively. Barratt's impulsiveness scale used in the current study to assess motor inhibition is a well validated and reliable scale popularly used. It measures only the trait impulsivity with sub domains of cognitive, planning and motor facet.

Decision Style Inventory is used in the current study is also a well validated and reliable scale popularly used. It measures Decision style which describes individual's personality, self competence, interpersonal competence, situational awareness and problem solving capability. In our current study sex was matched between patients, first degree relatives and normal healthy controls. In our current study age was matched between first degree relatives and normal healthy controls.

There was no significant difference in most of the socio demographic profile between three groups. Males were predominant in the study groups. The hospital where the study was conducted is a public sector hospital, utilized mostly by the lower and lower middle socio economic groups of society. Female literacy in these populations is less than that in higher socio economic Groups. The cut-off of matriculation or minimum 10 years of education for the purposive sampling of this study.

Also the majority of subjects in all the groups were married, following Hindu religion and were employed. All the groups had comparable economic status, lower and middle, and domicile, urban and rural. Age group and education status were also comparable. Thus known confounding socio-demographic variables of age, education and sex was reduced. Clinical profile of patients with obsessive compulsive disorder showed a wide range of onset from 13-36years. The mean age of onset is in line with in early adulthood with mean of 24years.

CONCLUSION

Cognitive flexibility and motor inhibition are found to be segregating in families of patients with Obsessive compulsive disorder, and May Characterize endophenotype with more basic

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biological mechanisms and genetic representation. As evidences are growing against a neat biological distinction between the psychiatric disorders, a Conceptualization of spectrum of clinical phenotypes with cognitive flexibility and motor inhibition as they may enhance future research and understanding.

REFERENCES

1. Nestadt G, Samuels J, Riddle M, Bienvenu OJ III, Liang KY, La-Buda M, Walkup J, Grados M, Hoehn-Saric R: A family study of obsessive-compulsive disorder. Arch Gen Psychiatry 2000; 57:358–363.
2. Leboyer M, Belivier F, Nosteen-Bertrand M, et al. Psychiatric Genetics: Search for phenotypes. Trends Neurosciences 1998; 21(3):102-5.
3. Gottesman II, Gould TD. The Endophenotypic concept in Psychiatry: Etymology and Stratergic intention. Am J Psychiatry 2003; 160:636-45.
4. Kessler RC, Berglund P, Demler O, et al Lifetime prevalance age of onset distributions of DSM - IV disorders in National Comorbidity Survey Replication. Archives of General Psychiatry (2005), 62(6), 593 – 602.
5. 1Salzman, L. And Thaler, F.H Obsessive compulsive disorder: a review of literature. The American Journal of Psychiatry.(1981), 138,286-96.
6. Robins, L.N., Helzer, J.E.,Weissman, M.M., et al, Lifetime prevalence of specific psychiatric disorders in three sies. Archives of General Psychiatry (1984)., 41,949-58.
7. Karno, M., Golding, J.M., Srenson, S.B., et al, The epidemiology of obsessive compulsive disorder in five US communities. Archives of General Psychiatry. (1988)., 45, 1094-9.
8. Flament, M.F.,Whitaker, A., Rapoport, J.L., et al. Obsessive compulsive Disorder in adolescence: an apidemiological study. Journal of American Academy of Child and Adolescent Psychiatry.(1988),27,764-71
9. Weissman, M.M.,Bland, R.C., Canino, G.J.,et al .The cross national epidemiology of obsessive compulsive disorder. The Journal of Clinical Psychiatry (1994)., 55, (Suppl.3), 5-10.
10. *The Book of Margery Kempe, a modern version by W. Butler-Bowdon* (London: Jonathan Cape, 1936) (originally 1436), pp. 352-3; see also pp. 34-5, 217-9; *also excerpted in* Dale Peterson, ed., *A Mad People's History of Madness* (Univ. of Pittsburgh Press, 1982), pp. 3-18.
11. Sigmund Freud, "The Sense of Symptoms." In James Strachey, *The Standard Edition of the Complete Psychological Works of Sigmund Freud* (London: Hogarth Press), Vol. 16, pp. 264-269.
12. WHO. The ICD-1O classification of mental and behavioural disorders: Diagnostic criteria for research. Geneva: WHO; (1993)
13. Comprehensive Textbook of Psychiatry; Kaplan & Sadock., Benjamin James Sadock, Virginia Alcott Sadock., Pedro Ruiz.,; 9th edition
14. Freud S [The Complete Psychological Works of Sigmund Freud], vols. **1**-London, Hogarth Press, (1983).
15. Bleuler E: Lehrbuch der Psychiatrie, ed **2.** Berlin, Springer-Verlag, (1920)**,** pp 22-38.
16. Janet **P:** Les Obsessions et a1 Psychasthenie, ed **2.** Pans, Bailliere, (1904).
17. Kraeplin E: Lectures on Clinical Psychiatry. New York, William Wood & Co., (1913).
18. Foa EB, Kozak MJ, Goodman WK, et al: DSM-IV field trial: Obsessive compulsive disorder. Am J Psychiatry, (1995)., 15290-96.
19. Rasmussen S, Eisen J: The Epidemiology and clinical features of obsessive compulsive disorder. Psychiatric Clinics of N. America., (1994). 15:743 – 758.
20. Swedo S Rapoport J, Leonard H, et al: Obsessive compulsive disorder i n children and adolescents: Clinical phenomenology of 70 consecuive cases. Arch Gen Psychiatry, (1989). 46:335-341.
21. Rachman S Hoggson RL: Obsessions and Compulsion. Upper Saddle River NJ, Prentice Hall, (1980).

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22. Foa EB, Kozak MJ, Goodman WK, et al: DSM-IV field trial: Obsessive compulsive disorder. Am J Psychiatry, (1995). 15290-96.
23. Thase M. Mood Disorders: Neurobiology. In: Sadock BJ, Sadock VA, Ruiz P. Kaplan & Sadock's Comprehensive Textbook of Psychiatry. 9th Edn Lippincott Williams & Wilkins (2009); 1665-74.
24. Maia., T.V., Cooney R.E., & Peterson., B.S. The neural basis of obsessive compulsive disorder in children and adult development and psychopathology (2008).1251 – 1283.
25. Whiteside., S.P., Port., J.D. Abramowitz., J.S., Ameta analysis of functional neuroimaging of obsessive compulsive disorder. Psychiatric research.(2004),. 132. 69 -79.
26. Alexandar., G.E., DeLong., M.R. and Strick PL., Parallel organisation of functionally segregated circuits linking basal ganglia and cortex. Annual review of neuroscience.,(1986). 9,357 – 381.
27. Saxena S & Rauch S.L., Functional neuroimaging and neuroanatomy of OCD. Psychiatric clinics of N. America ., .,(2000). 23.,563 – 586.
28. Sasson Y. Johar.J., Chopra. M., Lustig. M., Lancu. I.& Handler T., Epidemiology of obsessive compulsive disorder. Seminars in clinical neuropsychiatry 6..,(1997),82– 101.
29. MacLean PD: Brain evolution relating to family, play, and the separation call. Arch Gen Psychiatry 42405417, (1985).
30. Cavedini, P., Riboldi, G., D Annucci, A., Belotti, P., Cisima, M., Bellodi, L. Decision- making heterogeneity in obsessive-compulsive disorder: Ventromedial prefrontal cortex function pre-dicts different treatment outcome. Neuropsychologia, 40, (2002a). 205–211.
31. Zohar, J. And Insel, T Obsessive compulsive disorder: psychobiological approaches to diagnosis, treatment, and pathophysiology. Biological Psychiatry, 22, ,(1987). 667-87.
32. Theoren,P., Asberg,M., Gronholm,B., et al Clomipramine treatment of obsessive compulsive disorder.II. Biochemical aspects. Archives of General Psychiatry,27, .(1980). 1289 – 94.
33. Insel, T.R., Mueller, E.A., Alterman,l., et al., Obsessive compulsive disorder & serotonin: is there a connection?. Biological Psychiatry. .(1985).
34. Weizman, A., Carmi, M., Hermesh, H., et al., High affinity imipramine binding and serotonin uptake in platelets of eight adolescent and ten adult obsessive compulsive patients., The American Journal of Psychiatry,143, (1986).335 – 9.
35. Marazziti. D., Hollander, E., Lensi, P., et al. Peripheral markers of serotonin and dopamine function in obsessive compulsive disorder. Psychiatry Research.,(1992).,42: 41-51.
36. Vtiello, B., Shimon, H., Behar, D., et al., Platelet imipramine binding and serotonin uptake in obsessive compulsive patients. Acta Psychiatrica Scandinavica, (1991). 84; 29-32.
37. Marazziti, D., Pfanner, C., Palego, L., et al. Changes in platelet markers of obsessive compulsive patients during a double blind trial of Fluvoxamine versus clomipramine.
38. Lesch, K.P., Hoh, A., Disswlkamp- Tietze, J., et al 5-Hydroxytryptamine 1A receptor responsivity in obsessive compulsive disorder. Comparision of patients and controls., Archives of General Psychiatry(1991),48., 540-7.
39. Denys, D., Zohar, J., and Westenberg, H.G. his role of dopamine in obsessive compulsive disorder: preclinical and clinical evidence. The Journal of Clinical Psychiatry., (2004).65(Suppl.14), 11-17.
40. Femke de Geus, Damiaan A. J. P. Deny, Margriet M. Sitskoorn, Westenberg Attention and cognition in patients with obsessive–compulsive disorder., *Psychiatry and Clinical Neurosciences* (2007), **61**, 45–53.
41. Karen H. Adams, Elsebeth S. Hansen, Lars H. Pinborg, Steen G. Hasselbalch, Claus Svarer, Søren Holm, Tom G. Bolwig, Gitte M. Knudsen. Patients with obsessive–compulsive disorder have increased 5-HT_{2A} receptor binding in the caudate (2005) 391-401.
42. Femke de Geus, Damiaan A. J. P. Deny, Margriet M. Sitskoorn, & Herman. M. Westenberg, Attention and cognition in patients with obsessive–compulsive disorder., Psychiatry and Clinical Neurosciences (2007), **61**, 45–53.
43. Richard Delorme, Catalina Betancur, Jacques Callebert., Nadia Chabane, Jean-Louis Laplanche Marie-Christine Mouren-Simeoni,, Jean-Marie Launay, Marion Leboyer, Platelet Serotonergic Markers as Endophenotypes for Obsessive-Compulsive Disorder. Neuropsychopharmacology 08/2005; 30(8): 1539-47.
44. Stein DJ, Andersen EW, Overo KF., Response to symptom dimensions in obsessive compulsive disorder to treatment with conventional antipsychotics. Rev Bras Psiquiatr .2002;.,29: 303-307., Pubmed.

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45. Chakrabarty K, Bhattacharyya S, Christopher R, et al. Glutamatergic in OCD. Neuropsychopharmacology. 2005; 30:1735–40. [PubMed].
46. Saxena, S, Brody, A. L, Schwartz, J. M, & Baxter, L. frontal-subcortical circuitry in obsessive compulsive disorder 26-37.Pubmed.
47. Bush G, Luu P, Posner MI Cognitive and emotional influences in anterior cingulated cortex. *Trends Cogn Sci* **4**(2000): 215–222.
48. Krawezyk, D. C. (2000). Contributions of the prefrontal cortex to the neural basis of human decision making, Neurosci. Biobehav. Rev (2000).., 26, 631-664.
49. Miller, L. Cognitive risk-taking after frontal or temporal lobectomy. The syn-thesis of fragmented visual information, Neuropsychologia., (1985). 23, 359-369.