REVIEW ARTICLE

OBSESSIVE COMPULSIVE DISORDER - A NEUROPSYCHIATRIC ILLNESS

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ABSTRACT

Until recently, obsessive compulsive disorder (OCD) was thought to be a rare condition. Once viewed predominantly as a manifestation of psychodynamic conflict, OCD is now considered a model neuropsychiatric disorder. While clear differences exist between OCD patients and normal controls, there are more similarities between OCD and Tourette's Syndrome than most other neurotic disorders in neurological signs, electrophysiology and neuropsychology. These include a lack of laterality, bilateral or dominant (left) frontal lobe dysfunction, shortened REM latency in sleep electroencephalogram, shortened latency of N200 and P300 components in visual evoked potentials, abnormal glucose metabolism in the caudate nucleus, and greater ventricle to brain ratios in OCD patients. Neuropharmacological and neuroendocrinological researches have increasingly shown that serotonin plays an important role in the complex aetiology in OCD. Finally, psychopharmacological trials have consistently demonstrated the effectiveness of the selective serotonin reuptake inhibitors in the treatment of OCD.

Keywords: *obsessive compulsive disorder, soft signs, neuropsychology, electrophysiology, neuropharmacology*

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INTRODUCTION

Until recently, obsessive compulsive disorder (OCD) was thought to be a rare condition. However, with the advent of effective anti-obsessional treatments - both behaviourally and pharmacologically - there has been a surge in research on the aetiology, epidemiology, and pathophysiology of this condition. Once viewed predominantly as a manifestation of psychodynamic conflict, OCD is now considered a model neuropsychiatric disorder. This article considers the psychological phenomena of obsessions and compulsions from a biological viewpoint. This is made possible with the rapid growth and development in the research on the neurobiology of brain functions, including molecular genetics, neuroimaging and receptor subtyping, as well as neuroendocrinological studies in OCD patients.

NEUROLOGICAL FINDINGS

Neurological findings in OCD include its onset following head injury[1,2] and Von Economo's encephalitis[3,4]. Birth trauma[5] as well as a higher incidence of childhood onset OCD in males[6] suggest possible neurological dysfunction as a result of early developmental trauma in some OCD patients. Premorbidly, there are reports of a high prevalence of neurological insults in OCD patients, such as meningitis, encephalitis, seizures and Sydenham's chorea[7] - the latter suggests involvement of the basal ganglia[8]. The well-known association between obsessions and compulsions with the neuropsychiatric condition of Tourette's Syndrome (TS), as well as a high rate of OCD in the first-degree relatives of TS patients suggests a genetic linkage[9,10]. Moreover, approximately 20% of OCD patients satisfy the criteria for a comorbid diagnosis of TS or other tic disorder, while more than 50% of TS patients also meet the Diagnostic and Statistical Manual Criteria for OCD[11]. Finally, the simultaneous occurrence of obsessional neurosis in nine diabetes insipidus patients point to a possible hypothalamic disturbance in OCD[12,13].

Laterality

Psycholinguistic techniques, handedness, electroencephalography (EEG) and dichotic listening tasks have been used to investigate laterality. In a small group of nine childhood OCD patients, Rapoport et al[6] reported that dichotic listening findings indicated a lack of laterality in childhood OCD patients compared to normal, suggesting less dominance of the left hemisphere. In addition, 22% of the patients were left-handed compared to 10% in the general population. OCD patients also displayed a lack of left hemispheric dominance on EEG during verbal tasks. However, as the absence of laterality has also been reported in other psychiatric disorders, this may be a nonspecific findings[14].

Neurological soft-signs

The presence of neurological soft-signs is often cited as evidence favouring a neurobiological basis for OCD. More abnormalities in fine motor co-ordination, involuntary and mirror movements, and visuospatial functions were found in OCD patients than matched controls[15,16]. In a fairly substantial sample of 54 childhood OCD patients examined by a neurologist using the Physical Neurological Examination for Soft-Signs (PANESS), 44 were found to have abnormal neurological findings, and only 10 had no evidence of neurodevelopmental abnormalities[17]. The former included 18 with choreiform movements, 13 with nonspecific neurodevelopmental signs, 8 with left hemisyndrome and 5 with other miscellaneous findings. It was suggested that choreiform movements may be a marker for caudate/basal ganglia abnormalities and frontal-caudate disinhibition. Adult OCD patients were also found to demonstrate significantly more soft-signs than normal control[18]. In spite of these impressive findings, studies have also documented a link between neurological soft-signs and other psychiatric illnesses such as asocial schizophrenia and emotionally unstable character disorder[19] as well as childhood hyperactivity and minimal brain dysfunction[20,21].

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Report of neuropsychological tests in OCD patients demonstrated bilateral[22] or dominant (left) frontal lobe dysfunction[23]. OCD patients were also found to have marked abnormal tendency to perserverate[24] which is again due to frontal lobe impairment. Yet, Insel et al failed to confirm frontal lobe dysfunction in OCD, and instead, OCD patients showed impaired tactile performance test, indicating possible difficulty in visuospatial orientation[25]. Like most other psychiatric disorder, OCD is probably a clinical syndrome, and thus it is not surprising that not all OCD patients manifest a common cognitive deficit which could be tapped by a standardised neuropsychiatric battery or psychometric testing. There may be subgroups of OCD patients who exhibit visuospatial/visuoperceptual deficits, some with more circumscribed deficits such as frontal lobe dysfunction, and others with a more global organicity[16].

Electrophysiology

Abnormalities in electroencephalography (EEG) have been reported in OCD patients[26,27], with similarities to the EEG of temporal lobe epileptics[28] or shortened REM latency in the sleep EEG of OCD patients as seen in depression[29]. Visual evoked potential (EP) studies demonstrate shortened latencies of late event-related potentials in the regions of N200 and P300 compared to controls, with group differences becoming greater during more difficult discrimination tasks[30,31]. This suggests that OCD patients are hypervigilant and react very strongly to novel stimuli. Furthermore, the more difficult the discrimination task, the more hyperviligant the OCD patient becomes and the shorter the P300 latency[16]. In contrast, normals show longer latencies for more difficult discrimination tasks. Moreover, the briefer latency of N200 and P300 components in OCD patients contrasts those of other psychiatric disorders (schizophrenia and depression) which show either longer latencies or no differences in comparison to normal controls.

Neuroimaging

Studies using positron emission tomography (PET) have reported abnormalities in the metabolism of glucose in the caudate nucleus of OCD patients[32,33]. An association between metabolic dysfunction in the basal ganglia and the frontal cortex has been observed, suggesting a functional alteration of the cortico-limbic circuits, and involving the orbital prefrontal cortex and the striatum in the mediation of OCD behaviours, as well as those of the related Gilles de la Tourette Syndrome eg Sydenham's chorea and the Merge Syndrome. Interestingly, respondents of OCD patients to clomipramine[34,35] or behaviour therapy[35] showed a return of regional brain metabolism to a more normal level in regions of the orbital frontal cortex and caudate nucleus compared to non-responders to either treatment.

An initial computerised tomography (CT) study on 10 OCD patients (aged 18 to 65) by Insel et al in 1983[25] showed no significant difference between OCD subjects and controls on the ventricle to brain ratios (VBRs). Just a year later, Behar et al's[36] study of childhood onset OCD reported greater VBRs in OCD subjects than controls, especially in those with compulsions alone than in those with obsessions. Luxenberg et al[37] found smaller caudate nuclei in OCD subjects than controls, again implicating the basal ganglia in the pathogenesis of OCD.

Neuropharmacology and neuroendocrinology

Initial clinical trials demonstrating the effectiveness of clomipramine, the 3-chloro analog of the tricyclic imipramine, in the treatment of resistant depression with concomitant obsessive compulsive symptoms led to a surge into the research of the serotonin-hypothesis of OCD. Two double-blind studies at 21 centres in 520 OCD patients reported a mean reduction of 41% in the Yale-Brown Obsessive Compulsive Scale score in clomipramine-treated patients compared with only 4% for patients on placebo[38]. That serotonin is the important neurotransmitter in the aetiology of OCD was further strengthened by controlled trials of fluvoxamine and clomipramine versus desipramine, a potent noradrenergic reuptake inhibitor with little or no serotonergic effect; these trials demonstrated their anti-obsessional efficacy and superiority over desipramine[39-41]. Furthermore, levels of clomipramine and not its metabolite desmethylclomipramine (a potent inhibitor of noradrenergic reuptake) corresponded with improvement of OCD symptoms[42,43].

Development of new selective serotonin reuptake inhibitors (SSRIs) and their unequivocal efficacy in OCD patients give additional credibility to the serotonin-hypothesis. These included a multicentre double-blind, placebo-controlled trial of fluvoxamine in more than 300 OCD outpatients by Greist et al[44], a multicentre trial of fluoxetine in 355 OCD patients by Tollefson et al[45], and another multicentre trial of sertraline in 87 OCD patients by Chouinard et al[46].

At a neuroendocrine level, the pharmacological probe meta-chlorophenylpiperazine (mCPP), administered orally[47] or intravenously[48], has been shown to induce an acute exacerbation of OCD symptoms. In addition, these studies also demonstrated that administration of metergoline (a potent serotonin antagonist) prior to mCPP administration prevented the exacerbation of OCD symptoms.

CONCLUSION

The shift from a psychoanalytical approach in OCD towards a more neuropsychiatric stance is evidenced by the various studies cited above. OCD as a whole shows more differences than normal controls, and more similarities to Tourette Syndrome than most other neurotic disorders in neurological signs, electrophysiology and neuropsychology. Yet OCD is probably not a homogenous condition, with a subgroup that responds extremely well to purely psychological and behavioural treatment, and another only on drugs, especially the selective serotonin reuptake inhibitors. Studies are still required to identify the presence of distinct subgroups of OCD patients, so that appropriate treatment may be instituted, and hopefully with good response. In this way, the sufferings of both patients and their families may be alleviated.

References

1. Hillbom E. After effects of brain injuries. Acta Psychiatr Neurol Scand 1960; 35 (Supp 142): 1-195.
2. McKeon J, McGuffin P, Robinson P. Obsessive-compulsive neurosis following head injury. A report of four cases. Br J Psychiatry 1984; 144: 190-2.
3. Schilder P. The organic background of obsessions and compulsions. Am J Psychiatry 1938; 94: 1397-416.
4. Jenike MA. Behavioural aspects of neurotic syndromes. Contemp Psychiatry 1982; 1: 109-12.
5. Capstick N, Seldrup U. Obsessional states. A study in the relationship between abnormalities occurring at birth and subsequent development of obsessional symptoms. Acta Psychiatr Scand 1977; 56: 427-39.
6. Rapoport JL, Elkins R, Langer DH, Sceevy W, Buchsbaum MS, Gillin JC, et al. Childhood obsessive-compulsive disorder. Am J Psychiatry 1981; 12: 1545-55.
7. Grimshaw L. Obsessional disorder and neurological illness. J Neurol Neurosurg Psychiatry 1964; 27: 229-31.
8. Rapoport JL. Obsessive compulsive disorders in children and adolescents. Washington DC: American Psychiatric Press, Inc. 1988.

9. Montgomery MA, Clayton PJ, Friedhoff AJ. Psychiatric illness in Tourette Syndrome patients and first degree relatives. In: Friendhoff AJ & Chase TN. cd. Gilles de la Tourettc Syndrome. New York: Raven Press, 1982: 335-9.
10. Pauls DL, Towbin KE, Leckman JF, Zahner GEP, Cohen DJ. Gilles de la Tourette Syndrome and obsessive compulsive disorder. Arch Gen Psychiatry 1986; 43: 1180-2.
11. Baer L. Overlapping symptoms in OCD and Tourette Disorders. American Psychiatrc Association Annual Meeting 1994, Philadephia, Pennsylvania.
12. Barton R. Diabetes insipidus, obsessional neurosis and hypothalamic dysfunction. Proc R Soc Med 1954; 47: 276-7.
13. Barton R. Diabetes insipidus and obsessional neurosis: A syndrome. Lancet 1965; 1: 133-5.
14. Wexler BE. Cerebral laterality and psychiatry: A review of thc literature. Am J Psychiatry 1980; 137: 279-91.
15. Hollander E, Schiffman E, Cohen B, Rivera-Stein MA, Rosen W, Gorman JM, et al. Signs of central nervous system dysfunction in obsessive-compulsive disorder. Arch Gen Psychiatry 1990; 47: 27-32.
16. Hollander E, Liebowitz MR, Rosen WG. Neuropsychiatric and neuropsychological studies in obsessive-compulsive disorder. In: Zohar J, Insel T, Rasmussen S, eds. The psychobiology of obsessive-compulsive disorder. New York: Springer Publishing, 1991: 126-45.
17. Denckla MB. Neurological examination. In: Rapoport JL. ed. Obsessive compulsive disorder in children and adolescents. Washington DC: American Psychiatric Press, Inc. 1988: 107-15.
18. Hollander E, Schiffman E, Liebowitz MR. Neurological soft signs in obsessive compulsivc disorders. New Research Abstract 182. American Psychiatric Association Annual Meeting Chicago, Illinois, 1987.
19. Quitkin FM, Rifkin A, Klein DF. Neurologic soft signs in schizophrenia and character disorders: organity in schizophrenia with premorbid asociality and emotionally unstable character disorders. Arch Gen Psychiatry 1976; 33: 845-53.
20. Denckla MB. Minimal brain dysfunction. In: Chall J, Mirksy AF, Relage KJ. eds. Education and the brain. Chicago: University of Chicago Press, 1978.
21. Nichols PL. Minimal brain dysfunction and soft signs. In: Tupper D, Orlando FL. eds. The collaborative perinatal project. In soft neurological signs. Grune & Stratton, 1987: 179-99.
22. Flor-Henry P, Lind J. Further neuropsychological studies of obsessive compulsive syndrome (abstract 211). Society of Biological Psychiatry Scientific Program, Montreal, Canada 1988.
23. Flor-Henry P, ed. The obsessive-compulsive syndrome. In: Cerebral basis of psychopathology. Bonston: John Coright, 1983.
24. Harvey NS. Impaired cognitive set-shifting in obsessive compulsive neurosis. IRCS Medical Science 1986; 14: 936-7.
25. Insel T, Donnelly EF, Lalakea ML, Alterman IS, Murphy DL. Neurological and neuropsychological studies of patients with obsessive compulsive disorder. Biol Psychiatry 1983; 18: 741-51.
26. Flor-Henry P, Yendall LT, Koles ZJ, Howarth BG. Neuropsychological and power spectral EEG investigations of the obsessive compulsive syndrome. Biol Psychiatry 1979; 14: 119-30.
27. Jenike MA, Brotman AW. The EEG in obsessive compulsive disorder. J Clin Psychiatry 1984; 45: 122-4.
28. Epstein AW, Bailine SH. Sleep and dream studies in obsessional neurosis with particular reference to epileptic states. Biol Psychiatry 1971; 3: 149-58.
29. Insel TR, Gillin JC, Moore A, Mendelson WB, Loewenstein RJ, Murphy DL. Sleep in obsessive-compulsive disorder. Arch Gen Psychiatry 1982; 39: 1372-7.
30. Beech HR, Ciesielski KT, Gordon KT. Further observations of evoked potentials in obsessional patients. Br J Psychiatry 1983; 142: 605-9.
31. Ciesielski HR, Beech HR, Gordon PK. Some electrophysiological observations in obsessional states. Br J Psychiatry 1981; 138: 479-84.
32. Baxter LR, Phelps ME, Mazziotta JC, Guze BH, Schwartz JM, Selin CE. Local cerebral glucose metabolic rates in obsessive-compulsive disorder - A comparison with rates in unipolar depression and in normal controls. Arch Gen Psychiatry 1987; 44: 211-8.
33. Benkelfat C, Nordahl TE, Semple WE, King AC, Murphy DL, Cohen RM. Local cerebral glucose metabolic rates in obsessive-compulsive disorder. Patients treated with clomipramine. Arch Gen Psychiatry 1990; 49: 840-8.
34. Baxter LR, Schwartz JM, Guze BH, Bergman K, Szuba MP. PET imaging in obsessive compulsive disorder with and without depression. J Clin Psychiatry 1990; 51 Suppl; 61-9.
35. Baxter LR, Schwartz JM, Bergman KS, Szuba MP, Guze BH, Mazziotta JC, et al. Candate glucose metabolic rate changes with both drug and behaviour therapy for obsessive-compulsive disorder. Arch Gen Psychiatry 1992; 49: 681-9.
36. Behar D, Rapoport JL, Berg CJ, Deckla MB, Mann L, Cox C, et al. Computerized tomography and neuropsychological test measures in adolescents with obsessive-compulsive disorders. Am J Psychiatry 1984; 141: 363-9.
37. Luxenberg JS, Swedo SE, Flament MF, Friedland RP, Rapoport J, Rapoport SI. Neuroanatomical abnormalities in obsessive-compulsive disorder determined with quantitative X-ray computed tomography. Am J Psychiatry 1988; 145: 1089-93.
38. Clomipramine collaborative study group. Clomipramine in the treatment of patients with obsessive-compulsive disorder. Arch Gen Psychiatry 1980; 37: 1281-5.
39. Goodman WK, Price LH, Delgado PL, Palumbo J, Krystal JH, Nagy LM, et al. Specificity of serotonin reuptake inhibitors in the treatment of obsessive-compulsive disorder: comparison of fluvoxamine and desipramine. Arch Gen Psychiatry 1990; 47: 577-85.
40. Leonard H, Swedo SE, Rapoport JL, Koby EV, Lenane MC, Cheslow DL, et al. Treatment of obsessive compulsive disorder with clomipramine and desipramine in children and adolescents. Arch Gen Psychiatry 1989; 46: 1088-92.
41. Zohar J, Insel TR. Obsessive-compulsive disorder: psychological approaches to diagnosis, treatment and pathophysiology. Biol Psychiatry 1987; 22: 667-87.
42. Stern RS, Marks IM, Wright J. Clomipramine: plasma levels, side effects and outcome in obsessive compulsive neurosis. Postgrad Med J 1980; 56 (supp 1): 134-9.
43. Mavissakalian MR, Jones B, Olson S, Perel JM. Clomipramine in obsessive-compulsive disorder: clinical response and plasma level. J Clin Psychopharmacol 1990; 10: 261-8.
44. Greist JH. Fluvoxamine treatment of obsessive compulsive disorder. Presented at the 5th World Congress of Biological Psychiatry, June 9, 1991, Florence, Italy.
45. Tollefson GD, Rampey AH Jr, Potvin JH, Jenike MA, Rush AJ, Dominguez RA, et al. A multicenter investigation of fixed-dose fluoxetine in the treatment of obsessive-compulsive disorder. Arch Gen Psychiatry 1994; 51: 559-67.
46. Chouinard G, Goodman W, Greist J, Jenike M, Rasmussen S, White K, et al. Results of a double-blind placebo controlled trial of a new serotonin reuptake inhibitor, sertraline, in the treatment of obsessive-compulsive disorder. Psychopharmacol Bull 1990; 26: 279-84.
47. Pigott TA, Zohar, J, Hill JL, Bernstein SE, Grover GN, Murphy DL. Metergoline blocks the behavioural and neuroendocrine effects of orally administered m-chlorophenylpiperazine in patients with obsessive-compulsive disorders. Biol Psychiatry 1991; 29: 418-26.
48. Pigott TA, Hill JL, Grady TA, L'Heureux F, Bernstein S, Rubenstein CS, et al. A comparison of the behavioural effects of oral versus intravenous mCPP administration in OCD patients and the effects of metergoline prior to I.V. MCPP. Biol Psychiatry 1993; 33: 3-14.