Behavioural Neurology (1992), **5**, 3-10

Obsessive–compulsive symptoms in neurologic disease: a review

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Obsessive–compulsive disorder (OCD) is an increasingly recognized disorder with a prevalence of 2–3% (Robins *et al.*, 1984). Once thought to be psychodynamic in origin, OCD is now generally recognized as having a neurobiological cause. Although the exact pathophysiology of OCD in its pure form remains unkown, there are numerous reports of obsessive–compulsive symptoms arising in the setting of known neurological disease. In this paper, we review the reported cases of obsessive–compulsive symptoms associated with neurologic diseases and outline the known facts about the underlying neurobiology of OCD. Finally, we synthesize these findings into a proposed theory of the pathophysiology of OCD, in both its pure form and when it accompanies other neurological illness.

INTRODUCTION

Sigmund Freud in his legendary case, *The Rat Man*, described a patient with obsessive–compulsive symptoms. Freud speculated that these symptoms arose from some underlying neurotic conflict (Freud, 1959). However, OCD has proven to be refractory to individual psychotherapy (Jenike *et al.*, 1986). Within the past decade substantial evidence has emerged that OCD can be effectively treated with behavioral therapy and potent new serotonergic agents. Concurrently there has been a resurgence of interest in the underlying neurobiology of this interesting disorder.

It is likely that patients who suffer from OCD symptoms represent a spectrum of diseases, much as the symptoms of parkinsonism can arise from Parkinson's disease (idiopathic) or other brain pathology. In one form, OCD is idiopathic, has a marked genetic component, and is sometimes associated with tics or Gilles de la Tourette's syndrome. Other patients with OC symptoms suffer from various neurologic and metabolic illnesses (symptomatic OCD). The literature reports of OCD or obsessive–compulsive symptoms in neurologic diseases are examined below. The underlying pathophysiology of OCD is explored in light of these associations and case reports.

DESCRIPTION OF OCD

As described by DSM III-R, obsessive–compulsive disorder occurs in patients with recurrent obsessions or compulsions severe enough to cause marked distress and interference with their normal routine (APA, 1987). Obsessions are persistent ideas, thoughts, impulses, or images that are intrusive and senseless. The person recognizes that the obsessions stem from his own mind and are not imposed from without. Commonly, these obsessions consist of repetitive thoughts of violence, contamination or doubt. Compulsions are repetitive, purposeful and intentional behaviors that are often performed in response to an obsession. The patient normally recognizes that this behavior is excessive or unreasonable. Compulsions commonly involve handwashing, counting, checking, or touching. As a person attempts to resist a compulsion, a sense of mounting inner tension arises.

OBSESSIVE–COMPULSIVE SYMPTOMS ASSOCIATED WITH MASS LESIONS OR INFARCTS

What areas of the brain are important in regulating this abnormal behavior? To begin to answer this question one can study the case reports of OCD patients who had concommitant brain tumors or infarcts—clear evidence of focal CNS damage that might explain the OCD behavior. There are several reported cases of patients who developed obsessive–compulsive symptoms and were later found to have cerebral tumors. Brickner *et al.* (1940) described patients with temporal and frontal lobe tumors and seizures who developed obsessive–compulsive symptoms. Seibyl *et al.* (1989) recently reported an OCD patient with

a right frontal meningioma. A patient with a frontal callosal tumor developed obsessive–compulsive symptoms consisting of excessive writing (Cambier *et al.*, 1988). Thus, tumors of the frontal or temporal lobes can sometimes produce OC symptoms.

The same is true for infarcts and atrophy. Tonkonogy and Barriera (1989) described a patient with progressive right-frontal lobe and bilateral caudate atrophy who had fears of contamination and compulsive hand-washing. Weilburg *et al.* (1989) reported a patient with obsessive–compulsive disorder who, on MRI scan, had a unilateral left-sided abnormality in the head of the caudate nucleus and putamen. This was accompanied by EEG slowing. The presumed etiology of this abnormality was ischemia secondary to perinatal anoxia. McKeon *et al.* (1984) described four cases of obsessive–compulsive disorder following head injury. Hillbom (1960) described a series of closed head injury patients who later developed OCD. Neither of these latter two studies found localizable brain pathology on cranial CT scans.

OBSESSIVE–COMPULSIVE SYMPTOMS FOLLOWING INFECTIONS

Infections directly or indirectly involving the basal ganglia have been reported in association with obsessive compulsive behavior. The most notable examples are the Von Economo's encephalitis cases of the 1920s and 1930s (Jellife, 1929). Schilder (1938) described several patients recovering from this encephalitis of unknown etiology. During recovery, patients developed obsessions and compulsions accompanied by various movement disorders. They had facial rigidity and mask-like faces with accompanying flexor rigidity in the arms. This led Schilder (1938) to speculate that "it is obvious that the organic disease of the central nervous system is an indispensable factor in the genesis of the psychic symptoms which have been mentioned". In looking at the spectrum of obsessive compulsive disorder, Schilder speculated that approximately one-third of OCD patients had a structural brain etiology. In another third there was a strong hint of an organic background and in the final third there was an unknown cause of the OCD symptoms. Wohlfart *et al.* (1961) reported a case of compulsive shouting (klazomania) that was associated with oculogyric spasms in a patient who had suffered epidemic encephalitis. The shouting attacks lasted an hour and were accompanied by a normal EEG.

Recently, Swedo *et al.* (1989a) interviewed rheumatic fever patients with or without Sydenham's chorea. Sydenham's chorea is a movement disorder which follows rheumatic fever (10–30%) presumably when anticaudate antibodies are formed (Husby *et al.*, 1976). When compared with patients who only had rheumatic fever, the Sydenham's chorea patients scored significantly higher on criteria for obsessive–compulsive disorder. The authors argue that this lends evidence to a basal ganglia dysfunction theory of the etiology of OCD. A case report by Laplane *et al.*, (1981) follows this same thinking of infection causing damage to the basal ganglia with resultant OC behavior. Their patient developed obsessive–compulsive symptoms following a wasp sting which produced secondary necrosis of the basal ganglia.

OBSESSIVE–COMPULSIVE SYMPTOMS ARISING IN THE SETTING OF METABOLIC DISORDERS

In addition to OC symptoms associated with known infections or CNS lesions, there are many examples of obsessive–compulsive symptoms arising in the setting of other systemic neurologic disorders. George *et al.* (1989) reported a patient with multiple sclerosis and obsessive–compulsive disorder. The patient's cranial CT scan showed diffuse periventricular white matter lesions. Schwab *et al.* (1951) noted that many of their Parkinsonism patients, some of whom had post-encephalitic Parkinsonism, also had obsessive–compulsive disorder. Their obsessions were often sudden and paroxysmal and subsided after 15–30 min. Lees *et al.* (1989) recently reviewed the neurobehavioral abnormalities found in Parkinson's disease and concluded that there was a strong relationship between Parkinson's disease and some of the psychomotor retardation seen in obsessive–compulsive disorder.

ANTECEDENT ILLNESS AND OCD

Some authors have examined whether there is an increased rate of perinatal abnormalities in patients who develop obsessive–compulsive disorder. For example, Capstick and Seldrup (1977) compared 33 OCD patients to 33 psychiatric controls. Eleven OCD patients self-reported a history of abnormal birth, whereas only two from the other group gave a similar story. These findings are interesting, but hard to assess due to the problems of being retrospective self-report studies, with mixed psychiatric patients as controls.

OC SYMPTOMS ASSOCIATED WITH EPILEPSY

Some authors have remarked that many of the interictal personality changes seen in patients with temporal lobe epilepsy (TLE) resemble behaviors seen in obsessive compulsive disorder (Bear and Fidio, 1977; Blumer, 1975; Bruens, 1969; Waxman and Geschwind, 1975; Ciesielski *et al.*, 1981; Epstein and Bailine, 1971). They proposed that obsessionalism might be a specific consequence of a repeatedly-firing temporal epileptic focus. Kettle and

TABLE I. Obsessive–compulsive symptoms in neurologic disease

			References
Lesions	Tumors	Temporal lobe	Brickner *et al.* (1940)
		Right Frontal	Seibyl *et al.* (1989)
		Frontal	Cambier *et al.* (1988)
		Caudate	Tonkonogy and Barreira (1989)
	Infarction	Striatum	Weilburg *et al.* (1989)
Closed head injury			McKeon *et al.* (1984)
			Hillbom (1960)
Post-infectious	Post-encephalitic Parkinson's		Schilder (1938)
	Wasp sting		Laplane *et al.* (1981)
	Von Economo's encephalitis		Wohlfart *et al.* (1961)
	Sydenham's chorea		Swedo (1989*a*, *b*)
Others	Multiple sclerosis		George *et al.* (1989)
	Parkinson's disease		Schwab *et al.* (1951)
	Hypoglycemia		Rippere (1984)
	Tourette's syndrome		Gilles de la Tourette (1885)
			Lees *et al.* (1989)
	Perinatal complications		Capstick and Seldrup (1977)
	Temporal lobe epilepsy		Bear and Fedio (1977)
	Diabetes insipidus		Barton (1965)
	Manganese poisoning		Mena *et al.* (1967)
	Amphetamine psychosis		Ellinwood (1967)

Marks (1986) reported two cases of OCD developing in teenage patients soon after the onset of epilepsy. One woman with OCD had worsening obsessive–compulsive symptoms corresponding with increasing spike and wave discharges on her EEG (Gibson and Kennedy, 1960). Yaryura-Tobias and Neziroglu (1983) have described further cases of epilepsy with ictal or interictal OC symptoms.

To complete the survey, Barton (1965) noted that a patient with diabetes insipidus had obsessive–compulsive disorder. Rippere (1984) described two patients with hypoglycemia who had obsessive–compulsive symptoms. Obsessive–compulsive symptoms have also been reported in manganese poisoning (Mena *et al.*, 1967) and amphetamine psychosis (Ellinwood, 1967; Koizumi, 1985).

GILLES DE LA TOURETTE DISEASE

By far the most imporant neurologic illness associated with obsessive–compulsive disorder is Gilles de la Tourette's syndrome (GTS) (Cummings and Frankel, 1985; Pitman *et al.*, 1987; Robertson *et al.*, 1988). The fundamental connection between obsessive–compulsive disorder and de al Tourette's was first recorded by Gilles de la Tourette (1885) who, in his original paper, noted that the Marquisa de D had obsessive–compulsive symptoms. The relation between obsessive–compulsive disorder and Tourette's has been neglected and rediscovered throughout recent neurologic history. Lees *et al.* (1984) recently reviewed this fundamental link. Reports of the comorbidity between OCD and GTS vary between 90% (Nee *et al.*, 1984), 67% (Montgomery *et al.*, 1982) and 51% (Frankel *et al.*, 1986). Recent genetic studies have shown that OCD and GTS may be different phenotypic expressions of the same gene (Pauls, 1986). Patients with OCD are known to have higher rates of tic and movement disorders. The occurrence of OCD and GTS within the same families, the clinical similarities between OCD and GTS, and the fact that both syndromes can stem from basal ganglia pathology argue that GTS and OCD might have similar neurobiological mechanisms.

SUMMARY

Obsessive–compulsive symptoms arise in conjunction with numerous neurologic illnesses (Grimshaw, 1964; Jenike, 1984; Ketti and Marks, 1986; Rapoport, 1988, 1989; Wexberg, 1938). Mass lesions or infarcts, particularly in the striatum or frontal or temporal lobes can cause OC symptomatology. There is an increased rate of obsessive–compulsive disorder in patients who have had closed head injury. Some infections (Sydenham's chorea, Von Economo's encephalitis, a wasp sting) cause secondary brain damage, particularly in the basal ganglia, which later results in obsessive–compulsive disorder. Obsessive–compulsive disorder patients self-report higher rates of previous neurologic illness. OCD also occurs with Parkinson's disease, multiple sclerosis, and most importantly, Gilles de la Tourette's syndrome. Additionally a fundamental link exists between Gilles de la Tourette's syndrome, tics, and obsessive compulsive disorder. Clearly, OCD can arise from focal neurologic disease (sympto-

TABLE II. Neuroanatomic and neurophysiologic studies in OCD

Study	Finding	Reference
Imaging		
CT	↕Caudate volume	Luxenburg *et al.* (1988)
MRI	Prolonged T_1, in right frontal white matter	Garber *et al.* (1990)
PET	↕Orbital–frontal metabolic rates	Baxter *et al.* (1988)
		Swedo *et al.* (1988*a*)
Electrophysiological		
EEG	Left frontal dysfunction with power-spectral analysis	Flor-Henry *et al.* (1979)
	3/12 OCD with temporal sharp waves	Jenike and Brotman (1984)
	2/18 OCD with abnormal EEG	Insel *et al.* (1983)
Electrical simulation studies		
	↕Stereotyped behavior with cingulate stimulation	Grey-Walter (1979)
		Talairach *et al.* (1973)

matic OCD). But, what is happening in the brains of patients with idiopathic OCD, or OCD in the absence of detectable brain pathology?

NEUROBIOLOGICAL STUDIES OF IDIOPATHIC OCD

Autopsy data

As yet, there have been no exhaustive studies of autopsy findings in OCD patients. This is partly due to the resurgence of interest in OCD and the lack, until recently, of good clinical criteria for the definition of the disease. A well-controlled autopsy study of properly diagnosed OCD patients would add immensely to our understanding.

Imaging data

Cranial CT scans on patients with idiopathic OCD are essentially normal with no pathognomonic lesion (Insel *et al.*, 1983). However, a study by Luxenburg *et al.* (1988) showed decreased caudate nuclei volume in 10 OCD patients compared with controls. Garber *et al.* (1989) found that the spin lattice relaxation time (T_1) for the right frontal white matter was prolonged on MRI scans of OCD patients compared with controls. Additionally, they found that right minus left T_1 differences in the orbital frontal cortex were strongly related to OCD severity. Kellner *et al.* (1991) failed to find any differences on MRI scans between OCD patients and a group of normal controls.

To date there have been at least three positron emission tomography (PET) studies of obsessive–compulsive disorder which have shown similar but not identical results (Baxter *et al.*, 1988; Nordhal *et al.*, 1989; Swedo *et al.*, 1989*b*). Baxter *et al.* (1988) reported 10 OC subjects who showed increased absolute metabolic rate in the heads of the caudate nuclei and orbital gyri when compared to controls, using *f*-2-deoxy-2-fluro-D-glucose. In a second, more carefully designed study, Baxter *et al.* (1990) replicated this initial finding in 10 additional OCD subjects in a medication-free, age and sex matched controlled study. Only the orbital gyri metabolic rate was increased when compared to the ipsilateral hemisphere metabolic rate. Nordhal *et al.* (1989) reported that eight OCD subjects in an age- and sex-matched control study had increased glucose metabolic rates in their orbital gyri relative to the whole brain metabolic rate. Swedo *et al.* (1989*b*) described 18 childhood-onset OCD subjects in an age- and sex-matched controlled study. They found prefrontal and basal ganglia abnormalities in the OCD subjects, with elevated absolute glucose metabolism in the left orbital frontal, right sensory motor and bilateral prefrontal and anterior cingulate regions. The right prefrontal and left anterior cingulate regions showed relatively increased glucose metabolism. In addition, Swedo *et al.* reported a significant positive correlation between the right orbital glucose metabolic rate and the severity of the OCD.

In summary, most imaging modalities (some CT, MRI, and PET scans) indicate that in idiopathic OCD there are abnormalities in metabolism and underlying brain pathology in the caudate and orbital frontal gyri.

EEG data

Much of the EEG literature on OCD is dated and was performed when the diagnostic criteria for OCD were not clearly defined. Thus there are numerous reports of "abnormal" EEGs in OCD patients. However, it is difficult to decide how much weight to place on these studies. Flor-Henry *et al.* (1979) reported left frontal dysfunction in OCD under power spectral EEG analysis. These EEG data correlated with neuropsychological testing showing left frontal impairment in OCD patients. This data gives further weight to the theory that perturbations of the cingulate–orbital–frontal loop might modulate obsessive compulsive symptomatology. Insel *et al.* (1983) reported 2 of 18 OCD patients with abnormal EEGs. One patient had

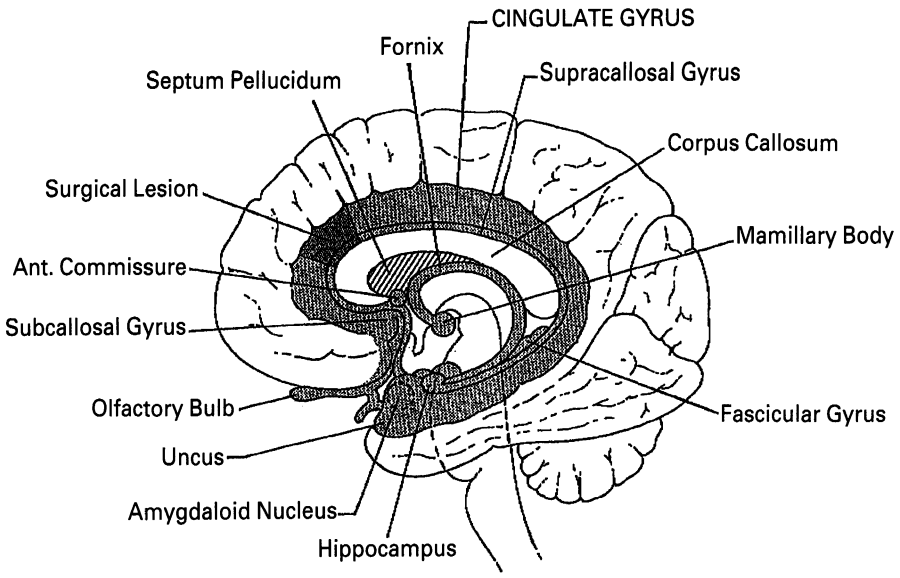

FIG. 1. Line drawing of the cingulum (cingulate gyrus), with the anterior portion highlighted.

left temporal sharp wave activity and the other had a predominance of beta activity over the left hemisphere. These patients' CT scans as a group were indistinguishable from matched non-psychiatric control subjects. Jenike (1984) reported on 3 of 12 patients with OCD who had temporal sharp wave activity. These three patients were tried on anti-seizure medications and only one improved. Thus far, EEG data in studies of OCD are inconclusive with several studies reporting mild temporal sharp wave activity in OCD patients.

Psychosurgery

Imaging data and case reports indicate that the cingulum, an area of the brain just dorsal to the corpus callosum, is intricately involved in obsessive–compulsive disorder (Fodstad *et al.*, 1982; Tan *et al.*, 1971) (see Fig. 1). Grey-Walter (1979) reported the case of a university professor who was compelled to confess to local crimes and was cured when surgical lesions were placed in the cingulum. Grey-Walter theorized that overactivity of the cingulum therefore led to obsessive compulsive behavior. Talairach *et al.* (1973) reported 52 drug-resistant epileptics who had electrodes implanted while being examined for possible lobectomy for seizure management. These patients had stereotypic repetitive motions similar to compulsive rituals when the cingular region was electrically stimulated. Mitchell-Heggs *et al.* (1977) demonstrated that surgery with two small lesions in the cingulum and three small lesions in the lower medial frontal lobe resulted in clinical improvement in 24 of 27 obsessional patients. Recently, Tippin and Henn (1982) described five obsessional patients who improved with modified leukotomy and lesioning of the medial 2–3 cm of white matter coming through the anterior cingulate gyrus.

UNIFYING THEORY OF THE NEUROBIOLOGY OF OCD

OCD is a syndrome that may be caused by numerous central nervous system insults. Brain tumors and trauma to frontal and temporal regions, as well as basal ganglia infarcts, infections, or trauma can all cause symptomatic OCD. Imaging studies of OC patients without obvious neurologic causes (idiopathic OCD) have shown decreased caudate nuclei volume and hyperactivity of caudal-frontal regions. OCD, whether symptomatic or idiopathic, almost always involves dysfunction in the basal ganglia and frontal cortical projections.

There is an interesting correlation between OCD and diseases of the basal ganglia, particularly Gilles de la Tourette's syndrome (Devenport *et al.*, 1981; Schneider, 1984). It remains to be seen what a putative OCD–Gilles de la Tourette's syndrome gene might do that would produce the symptoms seen in these disorders. Treatment with serotonergic agents such as fluoxetine (Fontaine and Chouinard, 1989; Jenike *et al.*, 1989), fluvoxamine, and clomipramine (Insel *et al.*, 1985; Pato *et al.*, 1988) tend to decrease OC symptoms. Similarly, psychosurgery with lesions in the cingulum can markedly improve patients with refractory OCD.

A truly unified theory of the neurobiology of OCD remains to be found. An adequate theory must take into account the neuroanatomic data presented above where symptomatic OCD is cased by lesions in the caudate and

orbital frontal gyri. It must additionally account for the known response of OCD patients to both antiserotonergic agents and psychosurgery involving lesions in the cingulum. Several authors have attempted putative theories (Baxter, 1990; McDougle *et al.*, 1989; Modell *et al.*, 1989). Baxter argues that the orbital cortex has been associated with the mediation of anxiety, with impulse control, and with meticulousness in hygiene. Using animal data, he also argues that behavioral inhibition and extinction as well as perseverative behaviors can be caused by stimulation or lesions of the orbital cortex. Because of the complex enervation of the striatum, pathology scattered throughout the striatum could produce different symptoms (tics, simple obsessive disorder, Gilles de la Tourette's syndrome) depending upon where the lesions are placed. This is an interesting theory which can theoretically be proved or disproved with available imaging techniques.

The neurosciences are at an exciting part of history. Imaging techniques such as MRI, PET, and SPECT will allow us to test putative hypotheses of the neurobiology of OCD and come to a better understanding of this interesting, complex and devastating human illness.

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