ABSTRACT:

The presence of obsessive-compulsive symptoms (OCS) or obsessive-compulsive disorder (OCD) is common in patients with schizophrenia. The impact of OCS and OCD on the severity of psychotic symptoms has been assessed in several studies. There is growing evidence that patients with comorbid obsessive–compulsive disorder (OCD) and schizophrenia may represent a special category of the schizophrenia population. Contemporary investigators contend that there may be a specific pattern of neurobiologic dysfunction in this subgroup of patients that accounts for symptom co-expression. Accurate diagnosis is important, given that current treatments for OCD and schizophrenia differ and the choice of diagnosis made has prognostic implications.

Key Words: obsessive-compulsive disorder, schizophrenia, comorbidity

INTRODUCTION

Schizophrenic patients may have obsessive-compulsive (OC) symptoms and patients that have obsessive-compulsive disorder (OCD) may have psychotic symptoms. The lifetime comorbidity rate of schizophrenia and OCD was reported to be higher than the individual lifetime prevalence rate of each disorder and, therefore, researchers suggest that there might be a psychopathological relationship between schizophrenia and OCD. Both disorders have early age onsets. Both disorders have a chronic course and affect males and females similarly. Both disorders are characterized by disturbing thoughts and bizarre behaviour. A growing literature suggests that obsessive-compulsive symptoms (OCS) and obsessive-compulsive disorder (OCD) occur in a higher proportion of patients with schizophrenia than was originally suspected. There is a common assumption that both disorders affect the same anatomical pathways, and that afferent impulses are not filtered adequately by the thalamus. Although the neurobiological basis of schizophrenia and OCD have been explained with comparative studies and despite all supportive epidemiological and biological findings, the relationship between OCD and schizophrenia is not well understood (Gülcan et al., 2008, Kumbhani et al. 2010).

REZUMAT:

Prezența simptomelor obsesiv-compulsive este comună la pacienții cu schizofrenie. Impactul OCS și OCD asupra severității simptomelor psihotice a fost prezentat în diferite studii. Există tot mai multe dovadă care susțin că pacienții cu schizofrenie și tulburare obsesiv compulsivă ar putea reprezenta o categorie specială. Studiile arată că ar putea exista un model specific de disfuncție neurobiologică la acest subgrup de pacienți, care să determine co-expresia simptomelor. Un diagnostic corect este important, deoarece tratamentele pentru OCD și pentru schizofrenie sunt diferite, iar diagnosticul ales are și implicații asupra prognosticului.

Cuvinte cheie: tulburare obsesiv compulsivă, schizofrenie, comorbiditate.

COMORBIDITY BETWEEN SCHIZOPHRENIA AND OBSESSIVE-COMPULSIVE DISORDER

Co-occurrence of obsessive–compulsive symptoms (OCS) and psychotic illness was first recognized over a century ago (Bottas et al. 2005). Early descriptions of obsessive-compulsive symptoms in schizophrenia can be found in Bleuler’s monography on “dementia praecox”. “compulsive thinking (obsession) is the most common of all the automatic phenomena”, Bleuler stated, and further described OCS in schizophrenia as “automatisms,” which are comparable to auditory or visual hallucinations in that they are “hallucinations of thinking, striving, and wanting”. Confirming these observations, case reports and larger systematic studies have since suggested that more than a third of the persons with schizophrenia experience clini-
cally significant OCS, while roughly 10% to 25% meet full
diagnostic criteria for obsessive compulsive disorder
(OCD) (Lysaker et al. 2009). Many patients with schizophre
nia can distinguish the egodystonic OC symptoms,
perceived as coming from within, from the egosyntonc
delusions perceived as intruding from the outside. Follow-
up studies demonstrate diagnostic stability over time and it
seems that the presence of OCD in schizophrenia predicts
a poor prognosis. The presence of OCD or significant OCS
in patients with schizophrenia has been associated with
more severe psychosis and depression, poorer social func-
tioning, lesser likelihood of being employed, and poorer
prognosis. Due to the different (poorer) prognosis of
patients with schizo-obsessive symptoms, as well as pre-
liminary data regarding their response to specific therapeu-
tic intervention (i.e., the combination of antipsychotic and
antiobsessive medications), and taking into account the
high prevalence of this presentation, several researchers
have suggested that a “schizo-obsessive” category may be
considered. Schizophrenia patients with concurrent OCS
constitute an intriguing subgroup of individuals. Three
main types of interrelation between OCS and psychotic
disorder are described: 1) those whose OCS are independ-
ent from psychosis; 2) those whose OCS are partially relat-
ed to their psychosis; and 3) those whose OCS represent a
continuum of their psychosis. Clinically and anamnestically,
we are able to distinguish three main subgroups of
patients: 1) those who met the DSM-IV criteria for OCD
before the development of schizophrenic process; 2) those
who began to exhibit OC symptoms around the onset (i.e.
in prodromal phase) or at any time during the course of
schizophrenia; and 3) schizophrenic patients having tran-
sient OC symptoms on different stages of their disease,
or under specific circumstances (infections, i.e streptococcal;
iatrogenic, i.e. under some atypical neuroleptics, etc).
Existence of these three groups may explain (at least, in
part) the diversity in epidemiological data, clinical mani-
festations and course, neuropsychological correlates, out-
comes of various prognoses and treatments. (Reznik et
al., 2004; Bottas et al., 2005, Lee et al., 2009, Kumbhani et
al. 2010)

DIAGNOSTIC CHALLENGES

The differential diagnosis of a patient who presents
with both psychotic and obsessive-compulsive symptoms
can include comorbid schizophrenia and obsessive-
compulsive disorder, OCD with poor insight, or schizo-
phrenia with antipsychotic-induced obsessive-compulsive
symptoms. If the psychotic symptoms are subthreshold or
attenuated in form, the individual may have OCD and
putative prodromal schizophrenia. No biological markers
exist to differentiate between these possibilities, and there
is debate as to the relationship of schizophrenia and OCD,
especially early in the course of evolving symptoms.
However, accurate diagnosis is important given that cur-
rent treatments for OCD and schizophrenia differ, and
first-line medications for one may exacerbate the symp-
toms of the other—that is, antipsychotics can exacerbate
obsessive-compulsive symptoms, and SRIs may exacer-
bate psychosis. Also, the choice of diagnoses made has
prognostic implications. (Rodriguez et al., 2010)

When a patient presents with the hallmarks of schizo-
phrenia—hallucinations, disorganized speech and behav-
iour, negative symptoms, and delusions (i.e., “erroneous
beliefs that usually involve a misinterpretation of percep-
tions or experiences” [DSM –IV-TR])—the diagnosis is
usually straightforward. Likewise, when a patient presents
with the hallmarks of OCD—obsessions (“recurrent or
persistent thoughts, impulses, or images...[that are]...
intrusive and inappropriate and that cause marked anxiety
or distress” [DSM-IV-TR]) and compulsions (“repetitive
behaviours...or mental acts...that the person feels driven
to perform in response to an obsession...[and]...are aimed
at... reducing distress or preventing some dreaded
event”[DSM-IV-TR])—and has good insight into the irra-
tionality of his or her thoughts and the link between his or
her thoughts and compulsions, it is clearly OCD. However,
in the patient who does not have hallucinations or disorganized speech but has psychotonic beliefs and repet-
titive behaviours, it can be a challenge to distinguish the
delusion of schizophrenia from the obsession of OCD if
the patient has poor or no insight. Another challenge in
some cases is to distinguish the repetitive behaviours of
schizophrenia from the compulsions of OCD. Neither of
the challenge is uncommon. In the absence of biomarkers
or behavioural tests that can distinguish these features,
careful attention to four aspects of the clinical phenotype
can help in evaluation. (Rodriguez et al. 2010; DSM-IV-
TR).

OBSESSIONS VERSUS DELUSIONS

A long-standing challenge facing investigators and
clinicians is the difficulty in differentiating an obsession
from a delusion when the 2 symptoms appear to be con-
ected. Obsessions and delusions are both thought distor-
tions. However, the content and character of the distor-
tions, as well as their relationship to repetitive behaviours,
can differ. In OCD, several common obsessive themes
have been described: contamination, symmetry or exact-
ness, forbidden thoughts (aggressive, sexual, religious, and
somatic), and hoarding. These obsessional themes are typ-
ically associated with corresponding compulsions: clean-
ing, ordering and arranging, checking, and hoarding. In contrast, the delusions seen in patients with schizophrenia include persecutory, referential, somatic, erotomanic, and grandiose themes. This is true even of the overvalued ideas seen in patients who are in a putative prodromal stage. Psychotic beliefs are more often “bizarre” (“clearly implausible and not understandable and do not derive from ordinary experiences”); however, bizarreness can be difficult to judge, especially across cultures. Although “somatic” themes overlap between the two disorders, somatic thoughts that are bizarre or represent loss of control over mind or body are more common in schizophrenia than in OCD with poor insight. Likewise, religious themes can occur in both, but in OCD, patients are overly concerned with sacrilege, blasphemy, or scrupulosity (i.e., excessive concern with right and wrong or with morality), whereas in schizophrenia, patients may more commonly have grandiose religious delusions (e.g., “I’m a divine messenger”). Furthermore, loss of control, or “agency” of thinking, more commonly occurs in schizophrenia. Patients with OCD often consider their obsessions as products of their own thinking, whereas patients with schizophrenia often believe that there is some external agency or cause to what they are experiencing and thinking. This distinction, however, becomes blurred when considering individuals with attenuated psychotic symptoms in a putative prodromal stage of schizophrenia or in patients with schizophrenia whose psychotic symptoms are partially remitted or residual. Also, a sense of permeation of ego boundary is more typical of schizophrenia than of OCD, although most patients with schizophrenia also have an intact sense of ego boundary. However, the problem with these distinctions is that they are less clear in prodromal or evolving stages of illness or with partial remission of symptoms during residual phases. For example, young people at heightened risk for schizophrenia have attenuated psychotic symptoms and can retain insight that their experiences are likely the product of their own imagination, although doubt may exist as to their source and nature. (Rodriguez et al., 2010; Bottas et al., 2005).

COMPULSION VERSUS REPETITIVE BEHAVIOURS

In adults with OCD, compulsive behaviours are typically performed in response to an obsession and to reduce distress or prevent a dreaded event. In contrast, in schizophrenia, repetitive behaviours are often independent of thought content. The presence of compulsions linked to obsessions may be a useful guide in diagnosing comorbid OCD in patients with schizophrenia. (Rodriguez et al., 2010; Bottas et al, 2005)

TIME OF ONSET OF SYMPTOMS

Age at onset is similar for both OCD and schizophrenia, with 50% of OCD cases starting by age 19 and 20%–40% of first psychotic symptoms in schizophrenia starting by age 20. In both disorders, subsyndromal symptoms can start in adolescence. However, the time of symptoms onset in relationship to changes in medication can exclude diagnoses. For example, if the first evidence of obsessive-compulsive symptoms or an exacerbation of existing symptoms occurs after initiating antipsychotic treatment for psychosis, one should consider the possibility that the symptoms are medication induced. Similarly, if psychotic symptoms worsen after initiating or titrating an SRI, one should consider the possibility of medication-induced psychosis (Rodriguez et al., 2010).

FAMILY HISTORY

Family history can help inform the differential diagnosis. Although both schizophrenia and OCD are heritable disorders, with higher concordance rates in monozygotic twins than in dizygotic twins, they do not appear to cosegregate. Families of patients with schizophrenia are more likely to have members with schizophrenia spectrum disorders, such as schizoaffective disorder and schizotypal personality disorder. In contrast, families of patients with OCD are more likely to have what are called “OCD spectrum disorders” (including tic disorder, Tourette’s syndrome, skin picking) and comorbid mood and anxiety disorders. (Rodriguez et al., 2010)

DEVELOPMENTAL PSYCHOSOCIAL FUNCTIONING

Both schizophrenia and OCD can lead to significant functional impairment in the work, family, and social domains. However, in contrast to OCD, social dysfunction is a core feature of schizophrenia and functional impairment is one of the DSM-IV criteria required for diagnosis. In schizophrenia, this social dysfunction is evident early. It is first expressed subtly during the premorbid period in childhood as difficulty in establishing relationships and social overreactivity (social anxiety, “acting out”) in boys and underreactivity (withdrawal) in girls. Likewise, adolescents at genetic risk for schizophrenia have poor peer engagement and unpopularity with peers. Active social withdrawal is a feature of the putative prodromal period in schizophrenia. Lack of interpersonal relatedness (i.e., diminished capacity for others to feel engaged and relate well to the individual) may also be characteristic of schizophrenia. In addition to social dysfunction, negative symptoms (e.g., flat affect, avolition, and alogia) are a key clin-
SUGGESTIONS FOR IDENTIFYING OCS IN THE PRESENCE OF PSYCHOSIS

1. The types of obsessions and compulsions observed in schizophrenia are phenomenologically similar to those present in pure OCD.

2. A repetitious act should be considered a compulsion only if it occurs in response to an obsession and not if it occurs in response to psychotic ideation (e.g., repetitive checking in response to paranoid fears does not constitute a compulsion).

3. A recurrent, intrusive, ego-dystonic thought should not be considered an obsession if it involves exclusively around current delusional themes (e.g., violent images, which constitute a common type of obsession in OCD, may represent an entirely different phenomenological entity in the context of psychosis). In the acute psychotic phase it may be necessary to exclude questionable “obsessions” and reassess for these after the psychotic symptoms have been treated.

4. OCS may be difficult to distinguish in the presence of thought form disorder; it may therefore be necessary to reassess for OCS once thought form has normalized.

5. Primary obsessional slowness may be mistaken for prodromal schizophrenia or thought disorder; such patients may be unable to articulate any obsessions and may exhibit no compulsions.

6. At times it may not be possible to determine if apparent OCS in the presence of psychosis represent real OCS, in which cases empiric treatment with a neuroleptic and a serotonin reuptake inhibitor (the standard treatment for OCD) may be necessary. (Bottas et al, 2005)

NEUROPSYCHOLOGICAL PROFILE OF OBSESSIVE-COMPULSIVE SCHIZOPHRENIA

OC-schizophrenia patients possess a distinct clinical and neuropsychological profile that differs from that of their non-OC schizophrenic counterparts. This profile includes a worse clinical course with poor treatment response, lower functioning levels, and greater impairment of functions primarily subserved by the frontal lobes. (Hwang et al. 2000). Co-occurrence of schizophrenia and OCS reflects the presence of both the structural and functional abnormalities associated with schizophrenia and OCD. Accordingly, it has been suggested that individuals with schizophrenia and OCS/OCD may represent a group of persons with particularly severe cognitive and functional deficits. Research supporting this hypothesis includes studies linking OCS with deficits in several domains of executive function, including abstract reasoning and abstract flexibility (Lysaker et al., 2002, Kumbhani et al, 2009, Niendam et al, 2008)

NEUROBIOLOGY

Considerable work has been done to elucidate the neurobiologic basis of both schizophrenia and OCD. Serotonin and dopamine have most consistently emerged as the principal neurotransmitters of interest in both disorders. In schizophrenia, the dopamine hypothesis has long been regarded as the fundamental neurochemical premise; this is most strongly supported by successful treatment of the disorder with dopamine receptor antagonists. However, the superior efficacy of the serotonin–dopamine receptor antagonists in the treatment of schizophrenia additionally supports the importance of the serotonergic system in the pathophysiology of this disorder and may reflect the modulation of dopaminergic systems by serotonin. Conversely, in OCD a somewhat opposing picture has emerged with respect to neurotransmitter involvement. The serotonin hypothesis of OCD is supported by successful treatment of the disorder with serotonin reuptake inhibitors. Pharmacologic challenge studies with serotonin agonists and cerebrospinal fluid neurotransmitter metabolite studies have provided further evidence for the involvement of the serotonergic system in OCD. However, not all studies support a singular role for serotonin in OCD. Typically only 40%–60% of patients with OCD exhibit response to monotherapy with selective serotonin reuptake inhibitors, and the magnitude of response is often modest. This observation suggests the involvement of other neurotransmitter systems in the pathophysiology of OCD, and evidence supporting the role of the dopaminergic system in this disorder has led to a proposed dopamine-serotonin hypothesis of OCD. Several lines of evidence implicate the dopaminergic system in the pathophysiology of OCD, including the role of dopamine in stereotypic behaviours in animal models, the etiologic role of dopamine in Tourette’s disorder (which is frequently comorbid with and shares neuroanatomic substrates with OCD), preclinical evidence of dopamine’s reciprocal modulatory effects on the serotonin system and successful treatment of refractory OCD with dopamine receptor antagonists and serotonin–dopamine receptor antagonists. The latter observation (of the therapeutic utility of antipsychotic medications in OCD) is difficult to interpret, given numerous reports of...
the emergence of de novo OCD or exacerbation of pre-existing OCD in patients with schizophrenia who have been treated with atypical antipsychotics. Such paradoxical findings are a testimony to the extreme complexity of the neurotransmitter systems involved in each disorder. (Bottas et al., 2005; Poyurovsky et al 2007, Hwang et al. 2000)

NEUROANATOMY AND NEUROCIRCUITRY

Several investigators have hypothesized that similarities in the neurocircuitry and specific anatomic structures implicated in each disorder may account for symptom co-expression. The functional circuitry involved in the pathophysiology of OCD is generally believed to involve a corticostriatal-thalamic-cortical circuit. Specific structures involved in this pathway include the basal ganglia, orbitofrontal cortex and anterior cingulate cortex. In schizophrenia, the dorsolateral prefrontal cortex circuit contains anatomic substrates similar to those of the OCD orbitofrontal circuit. Thus, the specific neuroanatomic sites identified by structural and functional neuroimaging studies performed in each of these disorders independently show considerable overlap in implicated structures, including the basal ganglia, thalamus, anterior cingulum, orbitofrontal cortex and regions of the temporal cortex, although some of these findings are controversial. (Bottas et al., 2005; Poyurovsky et al 2007)

NEUROIMAGING STUDIES

Neuroimaging studies suggest that there may be a specific pattern of neuroanatomic dysfunction in the comorbid subgroup. Aoyama et al performed MRI in subjects with juvenile-onset schizophrenia and OCS and found significantly smaller left hippocampi in this group than in subjects who had schizophrenia without OCS and in control groups. These researchers also found an inverse correlation between illness duration and frontal lobe size in the group with both schizophrenia and OCS, but not in the group with schizophrenia only. In another MRI study of patients with juvenile-onset schizophrenia, investigators demonstrated significant enlargement of the anterior horn of the lateral ventricle and the third ventricle in patients with OCS relative to those without OCS. In a study of functional MRI performed on patients with schizophrenia and various degrees of OCS, one subgroup exhibited a negative correlation between activation of the left dorsolateral prefrontal cortex and OCS severity. Taken together, these findings suggest specific neuroanatomic abnormalities in the overlap group that differ from what is observed in each disorder individually. (Bottas et al., 2005)

PRESENT DEFICIENCIES AND FUTURE SKILLS IN CHILDREN WITH ASPERGER SYNDROME

A few studies have addressed how to treat patients with both schizophrenia and OCD. Based on these studies, OCD treatment guidelines suggest that these patients should first be stabilized on a second-generation antipsychotic and the obsessive-compulsive symptoms subsequently treated by the addition of an SRI. Whether these patients require SRIs at the high doses needed in patients with OCD without a comorbid psychotic disorder is unclear: obsessive-compulsive symptoms in the context of psychotic disorder have been found to respond to lower doses of fluvoxamine (100–200 mg/day) than typically used in treatment of OCD (250–300 mg/day). Poyurovsky and colleagues proposed that those who do not respond to the steps above be switched to another SRI or clomipramine, to another second-generation antipsychotic, or to a first-generation antipsychotic with an SRI or clomipramine. If these strategies are ineffective, they propose clozapine at a low dosage (75–300 mg/day), SRI augmentation of clozapine, and finally ECT. Combining antipsychotics and SRIs (e.g., fluvoxamine and clozapine; clomipramine and clozapine; paroxetine and risperidone or a phenothiazine) requires careful monitoring for drug-drug interactions and for possible exacerbation of obsessional or psychotic symptoms. In patients with co-occurring schizophrenia and OCD or obsessive-compulsive symptoms, if antipsychotic medication induces obsessive-compulsive symptoms, there are several options: waiting for spontaneous resolution (4–6 weeks), gradually reducing the dosage of antipsychotic, switching to another antipsychotic, adding an SRI to target the obsessive-compulsive symptoms (e.g., fluvoxamine, clomipramine, sertraline), or attempting a trial of exposure and response prevention. The evidence base for these approaches is limited. Some patients with both schizophrenia and OCD, remain symptomatic despite the treatment recommendations listed above. Recent data have implicated glutamatergic abnormalities in the pathophysiology of schizophrenia, OCD, and depression. Lamotrigine is an anticonvulsant typically used for seizure disorders and maintenance treatment in bipolar disorder. In addition to its varied mechanisms of action, lamotrigine inhibits glutamate release. In schizophrenia, there is preliminary evidence that lamotrigine (at dosages of 200 mg/day and higher) might be effective for psychotic symptoms when added to clozapine but not when added to antipsychotics other than clozapine. In OCD, an open-label study found that one of eight patients responded to lamotrigine augmentation of an SSRI (although the lamotrigine dosage was only 100 mg/day), and there has been a case report of marked improvement with lamotrigine augmentation (150 mg/day) of clomip-
ramine. Although no randomized clinical trials have yet been conducted to evaluate the efficacy of lamotrigine for patients with comorbid OCD and schizophrenia, these preliminary data suggest that glutamate modulators may be an area of interest for treatment-resistant patients with both psychotic and obsessive-compulsive symptoms. There are as yet no consensus guidelines for the treatment of the putative schizophrenia prodrome. Olanzapine has unclear efficacy and problematic side effects and one study reported efficacy with risperidone when administered in combination with CBT. It remains unknown whether treating obsessive-compulsive symptoms in a putative schizophrenia prodrome has an effect on the natural course of either of these illnesses (Rodriguez et al, 2010).

CONCLUSIONS

Despite the growing evidence supporting the existence of an epidemiologic and biologic relation between OCD and schizophrenia, the association remains poorly understood. Although the distinction between obsessions and delusions is often unclear, clinical evidence suggests that OCS in schizophrenia represents more than just an expression of enduring psychosis. The epidemiologic data suggest a unique relation between these 2 disorders, given the marked degree of comorbidity that has been observed. Furthermore, the neurobiologic data on each disorder suggest the involvement of common brain regions and neurotransmitter systems. In patients with both schizophrenia and OCD more severe impairment was generally revealed than among patients who have schizophrenia and not OCD (and patients who have OCD and not schizophrenia), which suggests a specific and active interaction between these 2 disease processes. Further research focusing specifically on this overlap group is essential and should clarify the nature of this putative entity in the years to come.

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