Studi sperimentali

Schizophrenia and obsessive-compulsive disorder: from comorbidity to schizo-obsessive disorder

Schizofrenia e disturbo ossessivo-compulsivo: dalla comorbilità al disturbo schizo-ossessivo

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SUMMARY. Current genetic, neurobiological, clinical-descriptive and pharmacological data about obsessive-compulsive symptoms (OCS) and/or obsessive-compulsive disorder (OCD) in schizophrenia hypothesize that schizophrenia combined with OCD is more than a mere comorbidity. To prove this hypothesis, “dimensional diagnosis”, based on the identification of a dysfunctional area common to different clinical cases, should replace “categorical diagnosis”, that focuses on discrete parameters that define specific disorders. It is our hope that the DSM-V will make reference to principles based on psychopathological “spectra” because these reflect the integration of pharmacotherapeutic, descriptive and etiopathogenetic aspects (genotypes common to various disorders, temperamental predispositions, neurobiological and chemical alteration). These three aspects explain how obsessive phenomena can develop into delusional phenomena.

KEY WORDS: schizo-obsessive disorder, psychopathological dimension, spectrum.

INTRODUCTION

Obsessive-compulsive symptoms were recently detected in psychotic subjects treated with atypical neuroleptics (1-6). It contributed to revive the interest in Axis I [according to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision, DSM IV-TR (7)] co-morbidity between obsessive-compulsive disorder and schizophrenia, and in the underpinning pathogenetic relationship between the two disorders. Today’s genetic (8), neuroimaging (9-13) and pharmacological (14-20) investigations allow to hypothesize a schizo-obsessive continuum and to identify delusions and obsessions as different manifestations of one syndromic construct, with familiarity and temperament (premorbid personality) acting as predisposing factors (8,21). Cerebral alterations are the shared biological correlators (13,22). Resistance to standard therapy (19,23,24) corroborates the diagnostic autonomy of this construct. A possible interrelation between obsession and delusion would certainly be of great interest. It actually poses a significant question, whose answer should be sought at the border between “to be” and “not to be”. Thought gives a sense to exist-
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tence; it processes what is perceived, it constitutes our memory and enables awareness of self, of the world, of the relations with the world. Thought is therefore the function of Ego which moves the will, drives action, and structures existence. “I think, therefore I am” (25). Thought alterations, although they deform perception, alienate reality and fragment memory, are the “best possible solution” (26) to give sense to existence. Transition from obsession to delusion is a progressive loss of safety in “staying in the world”. Such a remark reiterates the stance of classical pathology, according to which obsession is a form of defence from psychotic destructuring, and transition from obsession to delusion is failure to defend (27), resulting in regression towards earlier evolution phases. The clinical analysis of disorders dimensions is restrictive and restricting, if it is not integrated in an investigation of the constitutional dimensions of the psychic structure and their mutual interaction. Considering obsession and delusion simply as two disorders co-occurring in a given timeframe, according to the somatic-mutuated concept of co-morbidity (28,29), means losing sight of the whole psychic structure of patients. Modern psychiatry needs to integrate the categorical descriptive diagnosis with the dimensional, based on the functioning of the psychic structure. Such an approach allows assessing the personological background from which obsessive and delusion frames develop, and to reach an integrated treatment for patients as a whole.

EPIDEMIOLOGY

Over the last century, several authors have been observing obsessive-compulsive symptoms (OCS) associated with clinical cases of schizophrenia, and psychotic symptoms associated with obsessive compulsive disorder (OCD) (30). The incidence of OCS in schizophrenic patients ranges between 30% and 59% (31,32); the incidence of OCD is around 7.8% of cases (33). The rate of prevalence in OCD is around 20% for hospitalized schizophrenic patients (34). Research on OCD-affected patients shows (current or lifetime) psychotic symptoms in 14% of cases, with a rate of incidence of schizophrenia ranging from 4% to 12% (35-37). Further studies show that the rate of co-morbidity between OCD and schizophrenia is between 7% and 26% (33,38-41).

It should also be noted that the comparison between co-morbidity values and lifetime prevalence of each disorder (2-3% for OCD and 1% for schizophrenia) showed that the frequency of association of the two disorders is higher than the frequency attained by adding the frequency of each single disorder in the general population (31,36). Furthermore, the two disorders are homogenously distributed as to gender (male), age of onset (early) and development (chronic) (35).

When the topic deals with comorbidity between schizophrenia and OCD clinically, we must distinguish among different conditions such as schematically:

- symptoms of “psychotic relevance” occur in patients already affected by OCD (42);
- schizophrenia occurs in patients whose first diagnosis has been OCD (36);
- OCSs occur or are boosted in patients already affected by schizophrenia (43);
- OCD occurs at the stage of remission of a psychosis (34);
- schizophrenia and OCD are in co-morbidity (schizoobsessive psychosis or delusional OCD) (44,45).

The data show that the rate of co-morbidity can be connected to a different phase of disease (46). They also validate the hypothesis of schizo-obsessive disorder as an autonomous diagnosis element which, in comparison to the corresponding mono-syndrome forms, is more serious regarding both to its development (more serious positive symptoms) and its prognosis (worse outcome and higher social isolation) (40,47-51).

In order to diagnose schizo-obsessive disorder, criteria for both OCD and schizophrenia need to be met. In these patients, as opposed to non OCD-affected schizophrenic patients (52):

a. family medical history is positive for obsessive-compulsive spectrum disorders;
b. relatives have the same risk to contract schizophrenic spectrum disorders and an increased risk to contract obsessive spectrum disorders;
c. association with other disorders of the obsessive-compulsive spectrum, such as tics or Impulse Control Disorders, is more frequent;
d. response to pharmacological therapy shows a low effectiveness of atypical nueroleptics, a favourable effect is reached when SSRIs are added;
e. prognosis is worse than in mono-syndromic patients.

HISTORICAL CONTEXT

Today’s psycho-biological knowledge shows that the relationship between OCD and schizophrenia develops in an area of clinical and pathogenetic interconnection without continuum solutions. Over the centuries, the
Kraepelien perspective, according to which transition from obsession to delusion seems impossible, has been denied at clinical and pathogenetic level by Bleuler (53) and Binswanger (54). They describe how obsessive ideas become temporary delusions in cases of patients at the apex of anancastic emotional states. Therefore the distinction between “obsessive neurosis” (defined by compulsion, egodosyntony and resistance to obsession) and “obsessive psychosis” (characterised by the lost of insight, egosyntony and reality distortion examination) is overcome. It is also clarified that the discriminant between delusion and obsession cannot be the level of insight alone. According to today’s literature, insight is not only a mental function, but also a psychological dimension, that is, a structure with its own consistency and internal stability. OCD entails different levels of insight and resistance: obsessive ideas can even become similar to repetitive and delusional ideas or can be so vivid as to develop into hallucination or pseudo-hallucination. Insel and Akiskal’s appellation for this clinic condition is “OCD with psychotic features” (42), recalling definitions like folie raisonnante, folie lucide, folie avec conscience (30). These terms imply a psychotic connotation of the obsession, which is also one of the elements of its psychopathology, as shown by the theories of will, intellect and emotion, popular in the 19th century. According to the theory of intellect, obsessions are an ideational dysfunction. Westphal states (55): “Obsessions are thoughts which come to the foreground of consciousness in spite of and contrary to the will of the patient; he/she is unable to suppress it, though recognizing them as abnormal and not characteristic of the Self”. His hypothesis is that obsessive and compulsive symptoms are either prodromes or a variety of schizophrenia. The theory of will considers obsession as a form of abulia. Esquirol (56) calls OCD an “instinctive monomania” and Schneider (57) and Jaspers (58) use the term “compulsion” to summarise that one’s will, though jeopardized, is still connected to the awareness (more or less complete) to be driven at level of thought, tendency and emotions (59). According to the theory of emotion, obsessions are distorted emotions and OCD is a disorder in emotion, linked to the awareness of a disease, as implied by the terms delire sans delire (60), folie lucide (61), folie raisonnante (62), folie avec conscience (63). The development of psychoanalysis entailed the need of overcoming these linguistic and conceptual paradoxes, going from well-defined nosological categories to constructs based on the psychic structure, which enable to distinguish psychotic disorders from neurotic disorders at the psychogenetic level. Freud (64) confers OCD the pathogenetic features typical of neurosis. When describing clinical pictures where classic psychotic symptoms – delusion, hallucination – and neurotic symptoms – obsessions and compulsion – coexist, he talks about “pseudoneurotic schizophrenia” or “concealed schizophrenia” (65). Abraham (66) has been the first author to clarify that the mechanisms leading to obsessive and delusion manifestations, and their relation of contiguity-continuity, are related to dynamics of psychosexual evolution/regression: certain obsessive-compulsive features can function at higher levels in subjects fixed at primordial stages of libido development and with a low maturity of the Ego. Abraham believes there is a “divided-line” between the first anal under-stage of expulsion (on top of which, he places the psychotic structures) and the second stage of retention (at the bottom of which, he places neurotic structures). Being located at the level of the “divided-line”, the obsessive structure can be considered on one hand as pre-organization of hysteria and, on the other hand, as linked to the paranoid structure – the least regressive psychosis (67). At this stage, the Ego functioning is not solid enough, thus leading to delusion when the weak Ego needs to tackle internal or external traumas. As to the onset of (temporary or persistent) delusional productive symptoms in course of OCD, Solyom et al. (68) identify an under-group of obsessive-compulsive patients where the disorder became manifest at an early age, its course is more severe and its prognosis is worse. Fear and Healy (69) describe obsessions as fixed and singular thoughts with unusual content, usually associated to emotional symptoms. Insel and Akiskal (42) talk about “obsessive psychosis” and highlight that such symptoms show the development of the disease itself, rather than co-existence with schizophrenia. Therefore the concept of obsessive-compulsive spectrum is replaced by the concept of co-morbidity. Eisen and Rasmussen (35) include the Schizotypal Personality Disorder in the continuum.

CLINICAL IMPLICATIONS OF CO-MORBIDITY BETWEEN SCHIZOPHRENIA AND OCD: THE SCHIZO-OBSESSIVE SPECTRUM

The diagnosis framework of schizo-obsessive pathology is its main difficulty. Indeed obsessive-compulsive symptoms can variously associate with psychotic symptoms. Specifically, they may lead to whip psychosis, be prodromes of schizophrenia, show in their florid phase or be iatrogenic. When dealing with co-morbidity, obsessions should be distinguished from delusions. For this purpose, the following semiological criteria have been recently proposed (5):
1) Obsessions and compulsions detected in schizophrenia are phenomenologically similar to those detected in sheer OCD, as described in DSM-IV.

2) Repetitive actions should be considered compulsion only if they are a consequence of obsessions, and not if they follow a psychotic ideation.

3) Recurrent, intrusive and ego-dystonic thoughts should not be considered obsession when featured by delusion themes only.

4) Obsessive-compulsive symptoms may be difficult to detect when occurring with thought formal disorders; therefore their re-assessment may be necessary once the thought form has normalized.

5) Primary obsessive slowness may be confused with prodromes of schizophrenia or thought disorders. Certain patients may not be able to explain their obsessions or may not show compulsions.

6) When it is not possible to decide whether thought and behaviour alterations in presence of psychosis are actually obsessive-compulsive symptoms, empirical treatment with a neuroleptic and a reuptake serotonin inhibitor is recommended (i.e. OCD standard treatment).

The following remarks corroborate the hypothesis according to which co-occurrence of obsessions and delusions is more than a mere manifestation of chronic psychosis:

- conventional anti-psychotic treatment is of little use in OCS therapy for schizophrenia (70);
- OCSs continue even at the remission of psychotic symptoms (48);
- SSRIs are effective in treating OCS in schizophrenic patients (24,71,72).

The concept of spectrum may be helpful for a more thorough explanation. As for categorical diagnosis, each disorder is to be considered as “independent” from the others and characterized by a series of signs and symptoms (discrete variables). Nevertheless, most clinical pictures are complex and multiple, thus requiring a comorbidity diagnosis. On the other hand, the dimensional perspective recognises that alterations of different intensity (continuous variables) can be associated with one or another thus creating more complex clinical pictures, in whose continuum we can also find low-insight OCD and schizo-obssessive disorder. Frank et al. (73) picture the spectrum as an iceberg, with its top portion representing the “core symptoms” and its underwater portion corresponding to personality factors and copying styles.

Our hypothesis of a schizo-obssessive spectrum is based on the epidemiological and clinical data. A recent study by Guillem et al. (74) reveals a strong positive relationship between delusion and obsession such as between auditory hallucination and compulsion. These results suggest that they share common mechanisms. The inverse relationship between somatic obsession and disorganization and between hoarding/collection compulsion and delusion or auditory hallucination validates the protective effect of obsessive compulsive symptoms against disorganization and psychotic symptoms.

The endophenotype studies suggest that schizo-OCD may not only be a distinct clinical entity from pure OCD and schizophrenia, but it may also be characterized by distinguishable neurophysiologic pattern. Pallanti et al. (75) investigated cognitive event related potentials (ERP) measured during a discriminative response task (DRT) in schizo-OCD patients, compared with patients with OCD without psychotic features, patients with schizophrenia without OCD, and healthy controls. When comparing the ERP results between groups, the schizo-OCD group was found to exhibit a unique abnormal pattern compared with the OCD only, schizophrenia only, and healthy control groups.

We recognize that there are different relevant dimensions in the schizo-obssessive spectrum, such as:

1) insight;
2) impulsivity/compulsivity;
3) temporality: disorganization of the Self.

Insight

The dimensional analysis of schizophrenia and OCD clearly shows that insight is the most used parameter to detect obsessions and to distinguish them from delusions. Similar remarks allow distinguishing obsessions from thought insertions. The difference is based on three judgement criteria, namely: thought attribution (self vs. others), the sense of agency (own vs. alien) and Ego-boundary (intact vs. pervaded) (76). The aforementioned definitions refer to insight in dichotomic terms like “everything/nothing”, focusing on a sheery cognitive model according to which a patient is either fully-aware or fully-unaware of his/her disorder. Modern psychiatry considers such a conception as reductive and in conflict with clinical significance of a transition/overlapping between obsessive and delusional thought. Hence, defining insight as a multidimensional construct appears more relevant and exhausting (77). Over time, several elements have been progressively identified as constitutional dimensions of the continuum. Namely: “Disease awareness” (78), acknowledging the need for treatment and possible hospitalization; ability to detect and label as abnormal
phenomena like delusions and hallucinations (79); identifying effects of pharmacological therapy; last, Amador and Strauss (80) encompassed anosodiaphoria (patient’s indifferent attitude towards the aspects of his/her mental disorder and specific symptoms) in the lack of insight. On the basis of the aforesaid, the following components are identified in the insight construct: a “cognitive” component (81,82) (awareness and acknowledgement of the meaning of disease); an “emotional” component (conditioning, for instance, resistance towards an obsessive idea); a “time” component (featured by the ability to perceive time gone by since the onset of the disease), which is not usually detected in psychotic patients (83). Owing to the use of dichotomic parameters, lack of insight has so far been almost exclusively associated to psychotic manifestations, either autonomous or cross-sectional with other categorical disorders. Hence difficulty in differential diagnosis between obsession and delusion, above all because OCD is traditionally distinguished from psychotic disorders on the basis of ego-dystony (condition which implies the presence of insight). Difficulty in distinguishing between delusion and obsession lies in the fact that a lack of insight and the consequent “absurdity of thought” are considered founding parameters of delusion. As demonstrated by a study carried out by Meduri et al. (23), such parameters are limitative and misleading. This latter study shows that obsessive ideas found in the sample of schizophrenic patients refer to two main kinds: obsessive ideas with content other than delusional forms and, more frequently, delusional ideas which shed their delusional traits to become obsessive. Insight is usually kept in obsessive patients, whereas delusional patients lose conscience of the absurd and impossible nature of such ideas. It was observed that delusional ideas are kept as to their content, yet they acquire the formal features of repetitiveness, intrusivity and ego-dystony, typical of obsessive thought. These hybrid symptoms, obsessive as to their form and delusional in their content, are called “obsessive delusion” by Spitzer (84). They are correlated to various degrees of insight deficiency. Lelliott et al. (85), studying OCD-affected patients with typical features, detected a threefold ideas fixity:

a) How much patients believe in consequences of not-performing rituals.
b) Evaluate why others do not share their beliefs.
c) How firmly they keep believing, in spite of contrary evidence.

The authors also concluded that fixity of obsessions was closely correlated to ideas eccentricity, thus demonstrating that the meaningless nature of ideas is not an essential feature of obsessions, nor is it always acknowledged. Therefore, in the light of today’s clinical data, insight cannot be used as a parameter to discriminate between obsessive and delusional ideas. Actually, empirical data demonstrate that criticism or adherence, resistance or acceptance of ideas content are not easily detectable in certain OCD-affected patients, to the extent that distinguishing between obsessive, prevailing and delusional ideas is actually impossible. Certain patients present a condition of fluidity, where variations in insight enable a direct transition from obsession to delusion. In conclusion, insight is a construct of reference in schizo-obsessive pathology only if it is considered in its multidimensional nature. Insel and Akiskal (42) note that “emotional” and “intellectual” aspects of insight may be variously compromised in obsessive patients; many of these patients are aware that their obsessive ideas are actually absurd, but they are not equally convinced about the possibility of not performing their compulsions. Divergence of the two aspects of insight has twofold consequences: on one hand, patients show a certain resistance to their obsessive ideas, on the other hand it contributes to determine a “delusional atmosphere” with extremely low anxiety levels (42,86). Hence, developing more adequate assessment instruments to investigate insight in anxiety disorders is required.

Impulsivity/compulsivity

According to the DSM-IV-TR (7), the following are considered impulse-control deficiency disorders:

- intermittent explosive disorder;
- kleptomania;
- pyromania;
- pathological gambling;
- trichotillomania;
- NAS impulse control disorders;
- paraphilia;
- substance use disorders;
- antisocial personality disorder and borderline personality disorder.

DSM-IV-TR (7) considers the following as compulsivity-featured disorders:

- obsessive-compulsive disorder,
- body dysmorphic disorder,
- hypochondria,
- depersonalization disorder,
- anorexia nervosa,
- Tourette syndrome,
- obsessive-compulsive personality disorder.
Intrusive thoughts and compulsive behaviour are the core of these disorders, featuring them as disorders of the schizo-obsessive spectrum. The dimensional approach to OCD and to impulse-control disorders enables placing each feature in a compulsive-obsessive continuum, whose extension is modulated on the basis of the “risk evaluation” concept. Hollander (87), on the basis of Cloninger’s personological “harm-avoiding” and “novelty seeking” dimensions (88), placed compulsivity and impulsivity at the opposite ends of a continuum. This continuum includes the tendency to “risk overestimation” and “risk avoiding” (at compulsive end) and a low “perception of danger” (of certain behavior) and high “risk seeking” (at impulsive end). Inability to delay or inhibit repetitive behaviour is found at both ends, respectively. McElroy et al. (89) suggested that, although compulsivity is ego-dystonic and impulsivity is ego-syntonic, they share many features such as: anxiety decrease, persevering responses disturbing goal achievement. The personality characteristic “impulsivity” has many clinical implications, as highlighted by its significant relations with several mental disorders. Correlations between impulsivity and personality traits in anxiety-disorders-affected subjects are relevant to understanding how serious the psychopathological picture is. Clinicians should focus on borderline and schizotypal traits in anxious patients, as a possible source of impulsivity-related conditions (for instance, aggressiveness and substance abuse). Correlation between impulsivity, borderline personality disorder and comorbidity with various Axis I psychiatric disorders deserves particular attention.

Temporality: disorganization of the Self

Most recent studies clarify that the main requirement for an idea to be featured as obsessive is the intrusive and repetitive way in which it manifests itself. Janet (90) was the first to detect an alteration of the time dimension (regulating according to the principle of lasting) in obsessions. To feature a psychic phenomenon as obsessive, classical psychopathology, along with the criteria of impulses and representation intrusiveness, has always attached much importance to features like “recurrence” (periodically recurrent ideatic content) and “persistence” (constant and continuous over time). Janet opposed OCD pathogenesis to emotional and self-assertiveness modalities in healthy subjects. “Duration” implies the idea of “beginning” and “cessation” of certain activities and leads to successful evolution. Initial (or cessation) difficulties (owed to inertia, avoidance of new situations and responsibility, will-deficiency or abulia) develop to the extent that obsessive patients feel incomplete and faulty. It leads to their need to procrastinate, repeat and control thus not concluding anything, losing themselves in details and preambles. According to Janet, they are beleaguered by a constant sense of “psychological imperfection” and suffer frequent drops in “psychological tension”. It prevents them from using their intelligence and their physical and motor potential to change actions and amplify their effectiveness, in order to reach innovative results with less effort. Since the affected aspect is the sense of continuity of the Self, the most recurrent clinical manifestation is not obsession but psychotic disorganization. Liotti (91) uses the attachment disorganization model to explain the loss of the self-continuity sense, as a cross-sectional condition for various Axis I and Axis II disorders. Attachment disorganization is a “unitary and interpersonal mental process”, corresponding to Kernberg’s notion of splitting (92), “leading both to a multiple and incoherent self-representation and to disorders in regulation and perception of mental states, mainly of emotions” (93). The attachment disorganization dimension defines a psychopathological continuum featured by dissociation and disorganization of personal meanings (of different degree and type compared to what is observed in schizophrenia) (94). Conditions like borderline personality disorder or dissociative disorders may belong to this continuum, as well as various disorders of the impulsive or obsessive-compulsive spectrum (disorganization and dissociation occur when rituals are prevented).

Borderline Personality Organization: Premorbid Personality of the Schizo-obsessive Disorder?

Borderline personality organization and obsessive-compulsive spectrum disorders share the dimension of impulsivity; similarly, borderline organization and psychotic spectrum disorders have the time dimension and a low sense of continuity of the Self as their common feature (92). Borderline is therefore an area where the psychotic spectrum and the obsessive spectrum intersect. Actually, the term “borderline” has often been used to gather “diagnostic labels” like “impulsive character” (95), “atypical schizophrenia” or “schizoeffectual schizophrenia” (96), “personality like the Self” (97), “latent psychosis” (98), “pseudoneurotic schizophrenia” (65), “psychotic character” (99) and “abandonic personality” from the French school. For a long time, borderline psychopathology could not
find a precise nosographical collocation, on the edge between psychosis and neurosis. Therefore it was variously identified as “pseudoneurotic syndrome”, “borderline” or “marginal syndrome” (100). Bleuler (53) introduced the concept of “latent schizophrenia” referring to special clinical conditions where psychotic latency seems to play a key role in ostensible neurotic or behavioural clinical pictures. Ey (101) called these clinical pictures as “schizoneurosis”, considering them as an evolution from neurosis to psychosis. Other authors considered borderline states as proper mental disorders, with their own stability and internal consistency, thus implying autonomous diagnosis (102). Classical psychiatric nosographies define borderline conditions as syndromic pictures including:

1. Intense, prolonged and pervasive anxiety symptoms.
2. Neurotic symptoms (obsessions, phobias, hysteria, neurasthenia, etc.).
3. Psychotic symptoms (reference ideas, paranoid ideas, etc.).
4. Temporary cognitive disorders with occasional episodes of mental confusion.
5. Impulsive and aggressive behaviour, typical of psychopathic personalities.

The core of psychopathology in borderline patients is the concept of disorganization, in a broader sense compared to psychotic de-structuring, to refer to Kernberg’s concept (92) of structuring of faulty and weak identities. Such a form of disorganization expresses itself through various symptoms which affect several areas, namely:

- behaviour (impulsivity, uncontrolled anger);
- emotional (mood instability, dysphoria);
- relational (sudden swings from idealization to de-evaluation of the significant other, abandonment anguish).

Results of neurobiological research (alteration in gratification circuits including the prefrontal cortex) (103-106), conclusions of classical psychopathology and phenomenological observations suggest that borderline organization is a predisposition to obsessive-psychotic decompensations (schizo-obsessive pictures). Hence the importance of investigating the personological background to reconstruct the diagnostic and existential meaning underpinning such a complex symptom, with an aim towards prevention or treatment of the fracture of Self which patients try to hide behind their obsessions or to fill with their delusions.

**CONCLUSION**

Many questions still lack a response; first of all sensitive and specific diagnostic methods and the creation of syndromic constructs whose consistency and validity enable a clearer definition of the matrix of the spectrum. Much has been discussed about insight; specifically whether insight alone is a discriminant parameter. That is why clinics’ attention must be moved from the variable “symptom” to the variable “patient as a whole”. Low insight, reduced resistance to compulsions and obsessions, pervasive obsessive-compulsive symptoms and obsessive control in interpersonal relations have been described as characteristics of OCD in borderline personality disorder patients (107). Nevertheless, only few studies investigate the relation between insight and Axis II disorders. Transition from obsession to delusion can better be understood only by overcoming theories which distinguish between healthy and unhealthy functions, thus driving research towards the definition of psychopathological spectra which integrate descriptive with pharmacotherapy and etiopathogenetic aspects (i.e. genotypes shared by several disorders, temperamental predisposition, neurobiological and neurochemical alterations). Guidelines including aspects of symptomatic continuity in the framework of premorbid personality are desirable in DSM-V.

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