

The psychotic spectrum: development and theoretical foundations

Lo spettro psicotico: definizione e fondamenti teorici

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Introduction

The Diagnostic and Statistical Manual (DSM-IV) ^{1,2} approach, using a neo-Kraepelinian view, has established reliable diagnostic criteria for mental disorders and has represented a step forward for psychiatric research methodology. Still, clinical evidence indicates that patients diagnosed with the same DSM-IV disorder may respond differently to psychiatric drugs or psychotherapy. Moreover, patients with different disorders may equally respond to a specific class of agents. For instance, subjects with schizophrenia, bipolar disorders and anxiety disorders may all respond to antipsychotics. The limited association be-

Summary

Background and aims

Evidence from epidemiological studies indicates that bipolar disorder (BP) and schizophrenia (SCHI) have each a lifetime prevalence of 1% across the world's populations. Recent family and linkage studies suggest that BP and SCHI share some genetic susceptibility and high familial risk. Other twin and adoption studies indicate that estimates of heritability are quite similar for these disorders (~70%). Moreover, evidence from clinical trials indicates that both disorders respond to atypical antipsychotics. Put together, these data challenged the DSM-IV classification of these disorders as separate syndromes and seem to favor alternative nosological approaches. Historically, various attempts have been made to group together syndromes sharing similar characteristics (the schizophrenic spectrum) or to define psychopathological dimensions, which could better describe the psychotic syndromes and, therefore, facilitate biological studies.

Typically, the afore-mentioned models overlook psychotic soft signs, low-grade symptoms, subthreshold syndromes, as well as temperamental and personality traits that may appear across all axis-I disorders, including anxiety disorders, and normal controls. We argue that a model encompassing the wide range of clinical and subsyndromal psychotic manifestations provides a useful approach to psychoses. For instance, isolated features belonging to the psychotic continuum might be prodromes of psychotic syndromes. We call this continuum, from psychotic soft signs to full-blown major psychoses, the "psychotic spectrum".

Method

In order to provide an operational definition of this concept, we have developed the Structured Clinical Interview for the Psychotic Spectrum (SCI-PSY) (Tables I, II). This paper reviews the hypotheses that have guided our conceptualization of the psychotic spectrum.

Conclusions

This approach has potential implications, in a clinical neuroscience perspective, for the characterization of behavioral phenotypes associated with the genotype, the neurobiological phenotype and the environment. These behavioral phenotypes could also be used to identify response groups and subjects with a higher likelihood of psychosis.

tween DSM-IV diagnoses and response to specific treatments suggests that the afore-mentioned diagnostic categories might not represent distinct phenotypes.

In addition to the poor characterization of clinically and therapeutically different phenotypes, the DSM-IV does not provide an adequate characterization of the full spectrum of manifestations related to each specific phenotype. According to the DSM-IV, psychiatric syndromes are deemed disorders only if their clinical significance is recognized, i.e., if they "cause clinically significant distress or impairment in social, occupational or other important areas of functioning". Consistent with the requirement of clinical signifi-

cance, the DSM-IV sets a threshold for the minimum number of symptoms to be endorsed by the patient presenting with the disorder. Clinical significance and symptom thresholds are likely to help the clinician in addressing most severe cases with prompt treatment. However, this approach overlooks isolated symptoms and precursors of full-blown major psychoses, and therefore limits the early characterization of each phenotype as well as the design and feasibility of secondary prevention strategies. Moreover, enduring paranoid ideation, interpretive attitudes, self-reference, the tendency toward isolation, difficulties in establishing relationships with others or bizarre behaviors are likely to interfere with the patient's social role and adaptation, even when criteria for an Axis-I or personality disorder are not fulfilled.

We argue that our approach has potential implications, in a clinical neuroscience perspective, for the characterization of behavioral phenotypes associated with the genotype, the neurobiological phenotype and the environment. These behavioral phenotypes could also be used to identify subgroups of subjects with a differential response to treatment.

The dimensional approach to psychosis

The approach of phenomenologists to the study of the schizophrenic/psychotic continuum was to extend the boundaries of schizophrenia towards potentially related syndromes. In the DSM-IV era, scientists have focused on the psychopathological/dimensional and biological approaches to identify common characteristics in schizophrenia and different DSM-IV disorders; the attempt being to define a cluster of disorders related to each other and to schizophrenia. Several attempts were aimed to define psychopathological dimensions, which could better describe the psychotic syndromes and, therefore, facilitate biological studies³⁻⁶.

A first attempt to define psychopathological dimensions in psychoses was made by Andreasen⁷, who described impaired "functioning" as a dimension co-existing with both negative and positive schizophrenic symptoms. The same author postulated that impaired functioning appears at various levels in different disorders, and, therefore, represents the dimensional aspect that differentiates more severe psychoses. Similarly, social impairment, oddness and disorganization have been included together with positive and negative symptoms in a three-factor model to define schizotypal symptoms^{8,9}.

Wood et al.¹⁰ suggested that two specific dimensions, paranoid ideation and psychoticism, are risk factors for the development of psychosis in major depressive disorder. They also suggested that these dimensions might be more useful than the categorical classifica-

tion of delusional vs. non-delusional subtypes of major depressive disorder. In fact they found that a specific genotype, allegedly associated with the occurrence of full-blown psychotic syndromes, was also associated with paranoid ideation and psychoticism in major depressive disorder. Somatic and nihilistic delusions also showed neurobiological and neuropsychological mechanisms similar with paranoid delusions and auditory hallucinations¹⁰.

Starting from a dimensional model of psychosis dating back into the 19th Century (and more recently by Menninger et al.¹¹, Crow has proposed a unitary model in which psychosis is seen as a continuum extending from unipolar and bipolar affective illness and schizoaffective psychosis, to typical schizophrenia; with increasing degrees of severity and functional impairment. Crow based his continuum model on the assumption that genes predisposing to psychosis have a high degree of stability¹².

Interestingly, a recent genetic study seems to demonstrate that Schizophrenia and Bipolar Disorder share a down-regulation in the expression of different genes, involved in the oligodendrocyte cell fate determination and maturation¹³. Even if it is unknown whether these abnormalities correlate with specific psychopathological aspects, it can be hypothesized that their phenotypic expression might determine some clinical features, which appear both in Schizophrenic and Bipolar patients. Kendler et al.¹⁴, have challenged the aforementioned dimensional approaches proposing a qualitative approach to psychoses. Using a latent class analysis in probands with broadly defined schizophrenia and affective illness they identified a number of distinct psychotic syndromes that appeared to differ qualitatively from one another and were hardly explainable by a unitary approach that considers only quantitative variation among different syndromes¹⁴. Other authors have used latent variable models in order to delineate the underlying structure of psychosis¹⁵⁻¹⁷.

Peralta and Cuesta showed that five classes provided the best fit to the data (schizophrenia, psychosis, schizomania/schizobipolar, schizodepression and mixed psychosis)¹⁵. Murray et al., using the OPCRIT (operational criteria) analysis on patients with psychosis, identified four latent classes (depression, bipolar, reality distortion/depression and disorganization) that correspond well with DSM diagnoses but also reveal that diagnostic boundaries usually obscure groupings¹⁶. In another study, performing a latent factor analysis on patients with Schizophrenia and Schizoaffective disorders, the authors isolated a positive, a negative, a disorganized, an affective factor and a fifth factor representing early onset/developmental signs¹⁷.

Recently Peralta and Cuesta have performed a factor analysis of 23 diagnostic definitions for Schizophrenia, identifying three interpretable factors explaining

58% of the variance. Considering one of these factors as the most representative of the underlying structure of the different definition of schizophrenia, they demonstrate that it has a normal distribution within a psychotic population, with schizophrenia at one extreme of the continuum and affective and delusional disorders at the other. The authors concluded that the unitary schizophrenia construct seems to be better represented by a dimensional than by categorical ordering of typical schizophrenia-related variables¹⁸.

Psychotic features may also appear within Axis-I disorders, other than those belonging to the schizophrenic spectrum, and interfere with course of illness and treatment outcome¹⁹⁻²¹. Some authors have recently identified the existence of a continuum of delusions and hallucinations across normal controls, patients with anxiety/depression and patients with psychosis^{22, 23}. Psychotic symptoms have been reported in milder forms in the general population even if their role remains to be ascertained^{24, 25}.

Phenotypic differences between psychotic and “non psychotic” patients appear to be quantitative rather than qualitative for core dimensions of psychosis²². Therefore, a dimensional approach to the psychotic spectrum seems to be justified.

The psychotic spectrum model and the Structured Clinical Interview for the psychotic spectrum

The psychotic spectrum identifies psychopathological dimensions which appear in schizophrenia, delusional psychosis, organic psychosis and mood disorders with psychotic symptoms, together with traits and features that may appear also in non-psychotic mental disorders such as panic disorder, obsessive-compulsive disorder, social anxiety, eating disorders and body dysmorphic disorder.

Our approach differs from previous dimensional approaches because it considers the threshold and sub-threshold phenomena of psychosis, such as isolated signs or symptoms or clusters of symptoms; we also focus on atypical aspects of psychosis as well as behavioral patterns, temperamental and personality traits.

In order to operationally define the psychotic spectrum, we have developed and validated the Structured Clinical Interview for the Psychotic Spectrum (SCI-PSY). The SCI-PSY, based on the spectrum concept of Cassano and colleagues²⁶, is structured into core symptoms of Axis-I psychotic syndromes, the related atypical and subthreshold phenomenology, as well as psychotic behavioral patterns and temperamental traits. The instrument was developed at the Department of Psychiatry, Pharmacology and Biotechnologies of the University of Pisa by the members of the “Spectrum Project Collaborative

Group” that include experienced psychiatrists and psychologists with a long-standing experience with psychotic patients from Pisa, Columbia University, New York, the University of Pittsburgh and the University of California in San Diego.

The instrument includes 164 items, exploring lifetime symptoms and behaviors organized into five domains: “interpersonal sensitivity”, “paranoid”, “schizoid”, “misperceptions”, and “typical psychotic symptoms”. Within each domain more specific subdomains were identified, that explore hypertrophic self-esteem, strict thinking, superstition, fanaticism, relations with others, interpretive attitude, suspiciousness, anger/overreactivity, hypervigilance, schizoidism/autism, mistrust, jealousy, rage and anger, unusual and odd thoughts, “illusions”, “depersonalization/derealization”, “delusions”, “hallucinations” and “catatonia”. Item responses are coded in a dichotomous way (yes/no) and domain scores are obtained by counting the number of positive answers. In order to increase the face validity and the reliability of responses the items have been arranged by conceptual domains and by increasing levels of severity. Item assignment to domains and subdomains was based on their content validity (Table I).

The validation study has provided evidence of the validity and reliability of the SCI-PSY. Study participants were enrolled at 11 Italian Departments of Psy-

Table I. Domains and subdomains of the SCI-PSY. *Domini e sottodomini dello SCI-PSY.*

	# Items
<i>Interpersonal sensitivity</i>	10
<i>Paranoid</i>	
Hypertrophic self-esteem	9
Strict thinking	8
Superstition	6
Fanaticism	10
Relations with others	8
Self-reference	6
Interpretive attitude	8
Suspiciousness	18
Anger/overreactivity	8
Hypervigilance	11
<i>Schizoid</i>	
Schizoidism-autism	12
Unusual and odd thoughts	6
<i>Misperceptions</i>	
Illusions	6
Depersonalization/derealization	5
<i>Typical psychotic symptoms</i>	
Delusions	23
Hallucinations	8
Catatonia	2

chiatry located at 9 sites and included 77 consecutive patients with schizophrenia or schizoaffective disorder, 66 with borderline personality disorder, 59 with psychotic mood disorders, 98 with non-psychotic mood disorders, 57 with panic disorder and a comparison group of 102 unselected controls.

The study has demonstrated that the instrument is able to discriminate patients with mental disorders from unselected controls and patients with and without psychotic disorders; moreover, the SCI-PSY is able to detect psychotic spectrum features in patients without psychotic DSM-IV disorders. The internal consistency of domains and subdomains has proved to be substantive with all the Kuder-Richardson coefficients exceeding the minimum standard of 0.50 and all the domains and 12 out of 16 subdomains exceeding the 0.70 standard for individual comparisons. Correlation between domains were all positive and significant, with Pearson's r ranging between 0.39 and 0.77 ($p < 0.01$)²⁷.

In patients with borderline personality disorder, the SCI-PSY has permitted to identify a relationship between the lifetime manic and depressive components of mood disorders and specific psychotic spectrum features both in patients with and without comorbid mood disorders²⁸.

Interpersonal sensitivity domain

The interpersonal sensitivity domain describes the tendency to avoid the others due to the fear of being misunderstood or criticized or to vague perceptions of hostile attitudes of the others. This tendency may sometimes extend beyond the limits of interpersonal sensitivity and subjects may lose insight in it. We decided, therefore, to include within the SCI-PSY some items exploring the loss of insight in sensitive patients. Indeed, these subjects may refer to friends or even to the physician they are able to tell "immediately when someone thinks badly about them or is against them". They are also likely to overreact and feel not only rejected but also betrayed because of criticism²⁹.

Paranoid domain

The paranoid domain covers the spectrum features encompassing mild hypervigilance, diffidence, suspiciousness, interpretive attitude and paranoid self-reference. The subject is asked if he/she has ever thought to be the center of attention or felt that others are "too interested" in what he/she does. Diffidence can be expressed by paranoid subjects through radical statements such as "it is good to be distrustful of anyone who is too friendly" or "my own words can be turned against me". The interpretive attitude

can present as the subject looking for hidden meanings in words. Thinking that "nothing happens by chance" or "circumstances are not what they seem to be" are also typical cognitive styles of interpretive subjects. Several behaviors are put in place to cope with these beliefs. For instance, subjects may try to live and act in such a way to avoid being blackmailed and may avoid keeping a diary because someone might read it. Moreover, they may spend a lot of time searching for proofs of their suspicions. In our interview, the tendency to defend ideals or behaviors has been considered as varying from rigidity of thought to fanaticism, aggressiveness, querulomania. Paranoid subjects may hardly ever change their mind about things or people and not be able to compromise. They also tend to strongly defend their opinions, even if it means risking their safety or getting into a fight or losing friendships. They may become jealous and think, if male, that "they are not the father of their children", and, if women, that their husband "might have kids somewhere else"³⁰.

Schizoid domain

The "Unusual and odd thoughts" subdomain explores religiosity, superstition, magical and odd thoughts. The subject is asked whether he/she has ever been convinced that spirits, the evil eye, dark forces, spells or magic could influence people lives. Other odd beliefs are also explored, for instance that some people may have paranormal powers (for example psychics or clairvoyants), as well as several avoidant behaviors related to fears of bad luck, such as avoiding black cats, and the fear of spilling salt and breaking a mirror. Magical thoughts could also present with "protective" behaviors, typically carrying a good luck charm, crossing fingers or knocking on wood to avoid bad luck. In the same domain we included unusual, odd thoughts like the fear of being contaminated or of being influenced by invisible negative or positive forces or even exposed to X-rays or magnetic waves and bizarre behaviors associated with such beliefs. Other schizotypal items included the feeling of being a "puppet in a game, which everybody knew about, except the person". Finally, lack of emotional resonance, difficulty in showing feelings, being unemotional and unromantic, the tendency to be isolated, which is typical of autism and schizoidism, were considered in the schizoidism-autism subdomain³¹⁻³³.

Misperceptions domain

The domain of misperceptions includes some borderline manifestations as well as the full-blown phe-

nomenology of hallucinations and delusions. We also explored the presence of dissociative phenomena with partial or no insight such as experiencing sudden changes of the environment, without being able to specify which ones; feeling that everything around is changing and becoming unfamiliar and unreal, perceiving sounds as unbearable and amplified, or recognizing in the background indistinguishable voices, or feeling the body or the reality as suddenly changed or strange. Some of these sudden experiences, accompanied by an emotional turmoil, similar to the so-called *Wahnstimmung phenomena*, have been considered part of an acute prodromal state of schizophrenia by German psychiatrists³⁴ or as a syndrome that may precede acute psychosis^{35,36}. Similarly, one should also consider Huber's basic neuro-vegetative symptoms³⁷, as precursors preceding the development of Schneiderian full-blown psychotic symptoms. Some of the items explored could be related to co-occurring panic symptoms; nevertheless, the meaning the person attributes to them is unrealistic. For instance, sensing the presence of someone behind and recognizing voices in the background noise and doubting about the nature of these experiences. See also Table II.

Typical psychotic symptoms domain

The fifth domain includes the typical DSM-IV symptoms of psychosis. The lifetime presence of delusions (e.g. persecution, reference, guilt, ruin, megalomaniac and erotomaniac), auditory hallucinations, (e.g. noises or whispering voices or voices talking together) and visual and somatic hallucinations is explored in this domain. Catatonia is described by three items including, along with inhibition of psychomotor activity also the extreme forms of hyperactivity of manic patients.

Conclusions

Diagnostic systems, such as the DSM-IV, assign psychotic patients to different categories according to their clinical presentation, course of illness and outcome. Nevertheless, diagnostic categories sometimes proved to have poor therapeutic and research usefulness³⁸⁻⁴³. Recent studies have shown that similar neurobiological and neuropsychological mechanisms underlie different types of psychotic symptoms¹⁰. Moreover, familial liability to psychosis extends

Table II. Items derived from the Misperceptions domain and the Interpretive Attitude subdomain of the Structured Clinical Interview for the Psychotic Spectrum (SCI-PSY). *Items del dominio "dispercezioni" e del sottodominio "interpretatività" dell'Intervista Clinica Strutturata per lo Spettro delle Psicosi.*

Misperceptions

Illusions

Have you sometimes:

Perceived low sounds as amplified and unbearable (e.g. cannot bear the buzz of florescent blub or the hum of traffic on the highway)?

Perceived voices in background noises?

Seen threatening and indistinct images in shadows or dim light?

Had the sensation that your thoughts are occurring as an inner voice different from your own?

Sensed that your, body was changed, for example, heavier or lighter than usual, floating, strange?

Viewed the world outside as unfamiliar, unreal and threatening?

Heard the voices of others as suddenly sounding strange and frightening?

Sensed a presence behind you and find no one was there?

Interpretive attitude

Have you often thought that ...

... things were not what they seemed?

... words had hidden meanings or that people say one thing but mean another?

... people were making secret agreements behind your back?

... it is good to be distrustful of anyone who is too friendly?

... things don't happen by chance?

... people are rude without any reason?

Has it ever happened that ...

... you thought that there was a hidden reason for apparently trivial events?

... you understood many things that others did not?

across several syndromes¹⁴. Overall, psychotic full-blown manifestations could be better conceptualized as the extreme poles of dimensional traits instead of all-or-none phenomena, as implied by classic nosography^{44,5,6}, and that the two approaches to psychosis, the categorical and the dimensional one, could be integrated in a “polydiagnostic-multidimensional paradigm”⁴⁵. In the last decades, several authors have attempted to refine psychopathological dimensions describing psychotic syndromes^{3,4}. The psychotic spectrum approach, differently from any other dimensional approach, includes, in addition to typical psychotic symptoms, the wide phenomenological halo characterized by signs, symptoms, behavioral patterns and personality traits that may precede and/or appear during the course of a psychotic disorder. Lifetime manifestations of psychosis that may appear within a non-psychotic axis-I disorder, within a personality disorder and even in normal subjects are considered as well. In order to recognize these features, we have designed a structured clinical interview for lifetime psychotic spectrum. Our interview was developed by reviewing symptoms included in the Axis I and II DSM-IV categories of Schizophrenia and other psychotic disorders, Mood disorders with psychotic symptoms and Cluster A Personality Disorders and examining existing instruments de-

signed to assess psychotic symptoms such as the Schizotypal Personality Questionnaire⁴⁶, the Peters Delusions Inventory (PDI)⁴⁷ and its simplified versions, the CAPE⁴⁸. Some items were derived from our clinical experience on psychotic patients. The SCI-PSY differs from existing instruments in the measurement model, the type of administration and the overall content. In particular the SCI-PSY explores the presence/absence of hypertrophic self-esteem, anger/overreactivity, superstition, fanaticism, self-reference and hypervigilance, aspects frequently seen in clinical patients with paranoid ideation and not assessed by the other instruments.

This approach could help defining behavioral phenotypes, characterized by different course, outcome and treatment response, in line with the research agenda for DSM-V². Ultimately, it could allow tailoring specific treatments to the patient. Precursors and prodromes of full-fledged psychosis could be better identified using the lifetime spectrum approach, and help preventing severe and disrupting psychoses. Residuals, which could lead to persistent chronic impairment, could be more easily detected as well, and subsequently addressed by specific treatments. The spectrum model could help identifying dimensions with substantial heritability for molecular genetic studies of psychotic syndromes.

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