

SCHYZOTIPY: FROM PERSONALITY ORGANIZATION TO TRANSITION TO SCHIZOPHRENIA

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SUMMARY

The traditional medical model of schizophrenia assumes a categorical view of the syndrome. On the contrary, the dimensional approach to schizophrenia infers that schizophrenia is not a discrete illness entity, but that psychotic symptoms differ in quantitative ways from normal experiences and behaviours. Schizotypy comprise a set of inherited traits reflected in personality organization, which presents as qualitatively similar to schizophrenia. Schizotypy is in line with continuum hypothesis of schizophrenia where different combinations of genes and environmental risk factors result in a range of different phenotypic expressions lying on a continuum from normal through to clinical psychosis. We discuss evidences for the continuity of psychotic symptoms to normal experiences and theoretical and future research implications of such a continuum.

Key words: schizotypy - schizophrenia - genetics - development - personality

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INTRODUCTION

A whole range of evidence indicate that psychosis can be expressed well below its clinical manifestation and that there is a continuum of its severity rather than as an all-or-none phenomenon. A schizotypy is a continuous, but relatively stabile personality organization that confers a liability to schizophrenia spectrum disorder (Ettinger et al. 2014). However, it has attracted relatively little research attention especially from the psychiatrists (Grant et al. 2018). Instead, developmental research has proceeded to focus on the risk of conversion to schizophrenia focusing on high-risk state approach. However, although share similarities, schizotypy and other high risk-mental states approach conceptually differ.

Our aim in this article is to examine the schizotypy approach in more detail and focus on the overlap between schizotypy and schizophrenia. We provide an overview of the main models that explain schizotypy and similarities between the constructs of scizotypy and schizophrenia at the level of phenomenology, but also genetics and neurobiology. We argue on the basis of the current knowledge that schizotypal traits share not just superficial similarity with the signs and symptoms of schizophrenia, but appear related to the clinical disorder at multiple levels of analysis (Ettinger et al. 2014). Finally, we evaluate the advontages of this concept for the future research of schizophrenia.

MODELS OF SCHIZOTYPY

Schizotypy comprise a set of inherited traits reflected in personality organization, which presents qualitatively similar to schizophrenia symptoms and correlate

with schizophrenia liability. It is formally recognised as premorbid state of schizophereina and characterised as endophenotype for schizophrenia.

The construct of schizotypy was developed both within the individual differences and medical traditions, which has led to differences in its conceptualization.

Shizotypy as a term was fist introduced in the work of Rado (1953), to represent the schizophrenic phenotype implicated in the contium between schizophrenic and schizotypyc behaviour. Paul Meehl used this term to explain the structure of personality (Meehl 1989, 1990) and also introduced two new terms, he thought to be crucial for this kind of personality organisation: schizotaxia and hypokrisia. Schizotaxia was defined as neuro-integrative defficit and hypokrizia as neuronal level aberration that characterizes schizotaxia. Both refer on genetic predisposition for schizophrenia which he considered to be single-gen associated. He also presumed that about 10% of schizotaxic persons (and schizotypal) develop schizophrenia and that about 10% of schizotypes decompensate into schizophrenia (corresponding to the 1% lifetime prevalence of schizophrenia). Meehl's approach considers schizotypy as the subclinical expression of the symptoms of schizophrenia. This model is, thus, considered a *quasi*-dimensional because of the proposed clear demarcation between the healthy and schizotaxic brain.

Claridge's model is fully dimensional and evolved from the work of Eysenck capturing the underlying dimensional liability for all psychotic disorders. Eysenck conceptualised Psychoticism as an aspect of general personality capturing the underlying dimensional liability for all psychotic disorders. He considered psychotic disorders as extreme quantitative values in the trait Psychoticism, combined with individual expressions of Extraversion/Neuroticism (Eysenck & Eysenck 1991). This model,

however, did not manage to make a distinction between traits and clinical states and give explanation how traits lead to illness (Grant et al. 2018). Off note, the current conceptualization of the Eysenck Psychoticism scale bears little resemblance to “schizotypal” in comparisons with its older conceptualization (Eysenck 1952). Claridge proposed that schizotypy results from a combination of genetic, environmental and personality variations that are normally distributed in the general population and transition to illness is influenced by a wide range of biological and psychological factors (Claridge 1997). Like Meehl’s formulation, this fully dimensional model recognizes dimensionality of schizotypy in the clinical and subclinical ranges, but also argues for continuity of schizotypic traits that are part of normal individual differences expressed in the general population. It includes the pathological, quasi-dimensional components, but also encompasses healthy manifestations (e.g., creativity). The high prevalence of psychotic-like experiences in the general population is also in accordance with the fully dimensional approach.

Currently, there are numerous terms that are used to describe similar phenomena: schizotypy, schizotypal personality disorder, psychosis proneness, psychotic-like experiences, anomalous experiences, as well as broad labels such as subclinical psychotic symptoms. In recent years, this terminology has expanded with descriptors of clinical vulnerability for schizophrenia, such as the prodrome, basic symptoms, at risk mental states for psychosis. Concept of attenuated psychotic symptoms syndrome recently is introduced in Diagnostic and Statistical Manual of Mental Disorders (DSM)-5 (Heckers et al. 2013), as a condition for future research. Many of these newer syndromes are based upon attenuated forms of positive symptoms and in order to help evaluate the risk of transition into psychosis. According to dimensional model of schizotypy these phenomena or constructs can be viewed as manifestations along schizotypy continuum. The differences in conceptualization of schizotypy models and interchange usage of similar concepts in research may hinder our ability to integrate findings across studies.

Schizotypy can be assessed in the general population using clinical interviews (such as the Structured Interview for Schizotypy (Kendler et al. 1989) or psychometric self-report questionnaires. Most often used instruments are: Multidimensional schizotypy Scale (Gross et al. 2018), Schizotypal Personality Questionnaire (SPQ) (Reine 1991; Reine 2006), the Oxford–Liverpool Inventory of Feelings and Experiences (O-LIFE (Mason & Claridge 2006), the Rust Inventory of Schizotypal Cognitions (RISC) (Rust 1988), the Community Assessment of Psychic Experiences (CAPE) (Stefanis et al. 2002), the Delusions Inventory (PDI) (Peters et al. 2000), the Eysenck Psychoticism (P) Scale (Eysenck & Eysenck 1991). These scales are constructed based on one of former concepts of schizotypy.

Schizotypy is a multidimensional construct composed of three dimensions extracted, although the fourth dimension has also been described. These are positive dimension also known cognitive-perceptual dimension. It includes odd beliefs, unusual perceptual experiences, suspiciousness, aberrant perceptions and beliefs. There is also a negative dimension described also as interpersonal dimension, characterised by the loss of emotional, physical, and social functions such as pleasure, volition, interest in social contacts and emotionality. The third is disorganised or conceptual disorganisation dimension, which includes formal thought disorder and eccentric behaviour (Tarbox & Pogue-Geile 2011). Vollema also described an asocial/non-conformity dimension as part of schizotypy (Vollema & van den Bosch 1995). The dimensions of positive, negative and disorganisation symptoms reported in schizophrenia are comparable to similarly constructed dimensions in schizotypy (Kemp et al. 2020; Vollema & Hoijtink 2000; Vollema & van den Bosch 1995, Ettinger et al. 2014).

In an attempt to distinguish individuals in the general population who show relatively normal variations in schizotypy from those who manifest clinically relevant levels of schizotypal traits, schizotypy entered the diagnostic systems as schizophrenia personality disorder (Esteberg & Compton 2009). It is classified in a section of personality disorders in DSM 5, but as a part of Psychosis related disorders chapter in ICD-10 (APA 2013, WHO 2004).

SCHIZOTYPY AND SCHIZOPHRENIA, EPIDEMIOLOGICAL DATA

Large and continuously growing body of evidence suggests that certain aspects of the phenomenology of schizophrenia are also traceable in the general population, beyond the diagnostic borders of the current nosological systems ICD and DSM (APA 2013, WHO 2004). Several epidemiologic studies showed much higher prevalence rates of reported psychotic experiences than diagnosable psychotic illnesses in the general population. The data reported from the NIMH Epidemiologic Catchment Area Program (ECA) carried out in the US between 1980–1984 in the sample of 18,572 community residents showed the lifetime prevalence of hallucinations (not related to drugs or medical problems) in this sample was 10% for men and 15% for women (Tien 1991). The National Comorbidity Survey found that 28.4% of respondents from the general population endorsed one or more queries exploring psychotic symptoms (Kendler et al. 1996).

Family studies have shown that schizotypy cooccurs with schizophrenia in the same family more often than would be expected by chance (Kendler et al. 1993; Kendler et al. 1995). This suggests that the same social and/or genetic factors that contribute to schizophrenia also contribute to schizotypy, i.e. that the two conditions are at least in part aetiologically continuous.

There are also data from longitudinal studies to support these associations. In the 10-year longitudinal follow-up the both positive and negative schizotypal dimensions predicted development of schizophrenia spectrum disorders. Positive dimension was associated with mood and substance use disorders and mental health treatment. In the same study, negative schizotypy was associated with schizoid symptoms and social impairment at the follow-up (Kwapil et al. 2013). Follow-up studies of subjects with elevated schizotypy scores have demonstrated high rates of clinical psychosis and related disorders (Chapman et al. 1994; Racioppi et al. 2018; Johns & van Os 2001). A large study of a birth cohort of children from New Zealand showed that children who had reported psychotic symptoms at age 11 years had a more than 16-fold higher risk of developing schizophreniform disorder by the age of 26 (Poulton et al. 2000). This suggests that lower states on the continuum are a risk factor for more severe states, and that transitions over the continuum occur with time (Johns & van Os 2001).

Studies showed that the severity of positive symptoms in psychotic patients were associated with the level of positive schizotypy in the relatives, as well as negative symptoms with negative schizotypy (Fanous et al. 2001).

The observation of individual psychotic symptoms and the description of subclinical schizotypal traits in the general population have led to the concept of the schizophrenia spectrum.

SCHIZOTYPY AND SCHIZOPHRENIA: GENETIC AND NEUROBIOLOGICAL DATA

Studies provide strong support for similarities between schizotypy and schizophrenia across multiple domains of research. Due to large number of studies this report is not comprehensive.

There are plenty of results that connect findings from genetics and epigenetics studies with schizophrenia and schizotypy. Part of these results are associated with psychosis proneness concept which is not necessary the same as schizotypy. Schizotypy enhances the power of genetic and endophenotype studies that previously omitted subclinical cases or misclassified them as nonaffected (Barrantes-Vidal et al. 2015).

Genetic and environmental studies

About 8300 independent polymorphisms confer schizophrenia risk (Ripke et al. 2013). A large number of contributing alleles supports the assumption of a continuous nature of schizotypy which does not preclude the existence of a functional discontinuity between high schizotypy and schizophrenia.

Several dopamine-related genes show associations with schizotypy. It has been consistently associated with rs4680 (COMT val158met), as well as with DRD2, SLC6A3 and MAOA (Grant et al. 2013). Genes like

NRG1, RGS4, PRODH, BDNF, and ZNF804A that have also been implicated in the etiology of schizophrenia were also associated with schizotypy (Ma et al. 2007, Barantes-Vidal et al. 2015, Walter et al. 2017). However, the latest Genome-Wide Association Study (GWAS) did not confirm associations of many of the aforementioned genes (with the exception of DRD2 and ZNF804A) with schizophrenia (Schizophrenia working group 2014). This GWAS did not control sample for schizotypy implicating the schizotypy persons with sharing genetics were in the control groups.

Grant (2017) has suggested that there are at least 2 groups of genetic factors. The first group mainly explains schizotypy variance and increases proneness for psychosis. The second group, which marks the risk of transition between high but healthy schizotypy and clinical schizophrenia, is probably independent of schizotypy, but reflects unspecific neuronal resilience. For instance, highly polygenic risk scores for schizophrenia are inversely associated with positive dimensions of schizotypy in healthy individuals (Hatzimanolis et al. 2018, Grant et al. 2013). Some genetic (or environmental) factors that are different from those conferring susceptibility to schizophrenia, such as frontal lobe reserve or general intelligence, may decrease the impact of genetic susceptibility to schizophrenia and allow high schizotypy individuals to be more resistant (Rosell et al. 2014; Barrantes-Vidal et al. 2015).

In addition to genetics, environmental risk factors are also known to play an important role in the etiology of schizophrenia. Heritability studies estimate that genetic factors explain about 50% of schizophrenic, but also schizotypic variance. A number of pre- and perinatal complications have been associated with schizotypy (Lahti et al. 2009; Barrantes-Vidal et al. 2015). A large study found that mothers' exposed to influenza in the second trimester, maternal diabetes and lower APGAR score presented with higher schizotypy as adults (Zammit et al. 2009). Others found effects of lower birth and/or placental weight as well as head circumference, but only in women and limited to positive schizotypy traits (Lahti et al. 2009), as well as winter or spring birth (Konrath et al. 2016).

Overall, findings indicate associations of schizotypy with cannabis use (Compton et al. 2009) and earlier age of initiation of its use (Skinner et al. 2011). The individuals who inherit a schizotypal personality may be more likely to take drugs such as cannabis to try to alter an unhappy internal psychological state. Their genetic liability renders them more prone to exposure to a factor e.g. cannabis to which they are genetically susceptible (McDonald & Murray 2000).

A substantial body of work has shown that a range of social and interpersonal environmental factors are associated with schizophrenia and schizotypy, with evidence appearing to be more robust for the positive dimension (Brown 2011, Barrantes-Vidal et al. 2015).

Psychosocial factors are not mere triggers of a genetic vulnerability but rather coparticipating factors in the psychosis continuum. Specifically, it has been suggested that epigenetic mechanisms might mediate environmental effects on gene function by 'switching' on and off gene transcription throughout development, constituting a mechanism for rapid genome adaptations to the environment (VanWinkel et al. 2013). Increased rates of psychotic phenomena and schizotypy in ethnic minority individuals were also described as well as growing up in an urban area (Binbay et al. 2012; Mimarakis et al. 2018). Considering microenvironmental risk factors, a plenty of studies showed that parental communication pattern as well as personal attachment style is associated with psychotic disorders and schizotypy traits. Childhood abuse, neglect, and bullying have all been linked to schizotypy (Meins et al. 2008; Giakoumaki et al. 2013; Velikonja et al. 2018).

Neurobiological studies

In structural neuroimaging studies, prefrontal cortex alterations were the most consistently reported finding in young relatives of schizophrenia patients defined through the concept of schizotaxia (Thermenos et al. 2013). Several fMRI studies of schizotypy personality disorder showed reduced activations in fronto-parietal area during the retention interval of a visuo-spatial working memory task (Koenigsberg et al. 2005). Auditory discrimination, a measure also known to be impaired in schizophrenia, was associated in schizotypy personality disorder with hyper-responsive neuronal processing of deviant tones in temporal and parietal areas (Dickey et al. 2020). Interpersonal and disorganized schizotypy are associated on fMRI with neural correlates of mentalizing in brain regions that are involved in self-processing and mentalizing (Acosta et al. 2019). These brain regions have also been linked to mentalizing in schizophrenia and have been associated with schizophrenic-like patterns of cognitive impairment (Vivano et al. 2018). The association between schizotypal personality traits and striatocortical functional connectivity was found for positive schizotypy in a sample of healthy adults providing support for dimensionality from schizotypy to clinical disorder (Wang et al. 2018). Left temporal volume reductions have been regularly seen in nondisordered schizotypy, schizotypal personality disorder and schizophrenia, suggesting common genetic vulnerability, whereas striatal and frontal lobe abnormalities are not consistently present in high schizotypy and schizotypal personality disorder, suggesting that they may represent compensatory or protective factors (Rosell et al. 2014, Barrantes-Vidall et al. 2015).

Neurological soft signs connected with schizophrenia were found mainly to correlate with negative, but also with positive and disorganized schizotypy (Machri et al. 2010; Barrantes-Vidal et al. 2015). Also, dermatoglyphic anomalies have been associated with positive and negative schizotypy as well with schizophrenia spectrum

disorders (Donde et al. 2018, Soler et al. 2017, Barantes-Vidal et al. 2015). It was found that high schizotypy is associated with a reduction in the P100 amplitude during a working memory task, suggesting the existence of early information processing deficits (Koychev et al. 2010), as well as a reduction in P300 amplitude in participants with higher overall schizotypy, similar to what had previously been found in schizophrenia (Klein et al. 2009, Ettinger et al. 2014). All these findings add to the understanding that schizotypy also shares a common biological continuum with schizophrenia.

CONCLUSION

In this article we concentrated on data that showed associations between schizotypy and schizophrenia in genetics and neurobiology, but there are range of studies that showed associations in environmental factors and cognitive functioning between the two. Schizotypy is in line with continuum hypothesis of schizophrenia where different combinations of genes and environmental risk factors result in a range of different phenotypic expressions lying on a continuum from normal through to clinical psychosis. Schizotypy provides a promising, useful, and integrative construct for capturing pathological and subclinical variation across this continuum. It also provides a useful construct for studying gene-environment effects avoiding misclassifications of schizotypy as healthy controls and enhances identification of protective mechanisms by including the nondisordered members of the schizophrenia spectrum phenotype. It offers an important tool for increasing the power of genetic studies but also studies on schizophrenia spectrum in general.

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