



The interrelationship between schizotypy, clinical high risk for psychosis and related symptoms: Cognitive disturbances matter

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ARTICLE INFO

Article history:

Received 3 April 2018

Received in revised form 13 December 2018

Accepted 20 December 2018

Available online 22 January 2019

Keywords:

Early detection

Schizophrenia

Cognitive basic symptoms

Structural equation modeling

ABSTRACT

Schizotypy and clinical high risk (CHR) criteria can identify individuals who are at increased risk for developing psychosis in community and patient samples. However, both approaches have rarely been combined, and very little is known about their associations. Therefore, we examined the factorial structure of CHR and related symptoms and schizotypy features as well as their interrelationship for the first time in a comprehensive approach. In a sample of 277 patients (22 ± 6 years) from two early detection services, structural equation modeling including confirmatory factor analysis was performed to test a theory-driven model using four Wisconsin Schizotypy Scales, 14 predictive basic symptoms (BS) of the Schizophrenia Proneness Instrument, and positive, negative, and disorganized symptoms from the Structured Interview for Psychosis-Risk Syndromes. The data fitted well to the six hypothesized latent factors consisting of negative schizotypy, positive schizotypy including perceptual BS, negative symptoms, positive symptoms, disorganized symptoms and cognitive disturbances. As postulated, schizotypy features were significantly associated with positive, negative and disorganized symptoms through cognitive disturbances. Additionally, positive and negative schizotypy also had a direct association with the respective symptom-domain. While the identified factorial structure corresponds well to dimensional models of schizotypy and psychoses, our model extends earlier models by indicating that schizotypy features are associated with positive, negative and disorganized symptoms directly or indirectly via subjective cognitive disturbances. This calls for more attention to subjective cognitive deficits in combination with heightened schizotypy in the early detection and intervention of psychoses – or even of an Attenuated Psychosis Syndrome.

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1. Introduction

To reduce the immense burden of psychotic disorders, such as schizophrenia (Olesen et al., 2012), their early detection and prevention are main targets of psychosis research based on a better understanding

of its underlying etiology (Fusar-Poli et al., 2013). Thereto, two main lines of research are followed to phenomenologically identify individuals at risk for psychosis; so far independently of each other and in different populations (Debbané et al., 2015). One targets the detection of a liability to schizophrenia-spectrum disorders via *trait*-like manifestations of schizotypy in the general population (Chapman et al., 1994; Mason et al., 2004; Kwapil et al., 2013) and the other targets the detection of a clinical high risk (CHR) *state* for psychosis in patient populations (Schultze-Lutter et al., 2015; Supplementary Text S1). This trait-state distinction of schizotypy assessments (*trait*) and CHR symptoms (*state*) was recently supported by a one-year follow-up study that showed significant changes in CHR symptoms but not in schizotypy assessments over time, with no significant correlation between changes in schizotypy and in CHR symptoms (Michel et al., 2019).

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Schizotypy research focuses on latent traits associated with psychosis- and/or schizophrenia-proneness (Miettunen et al., 2011), often using psychometric inventories like the Chapmans' psychosis-proneness scales (aka Wisconsin Schizotypy Scales [WSS]) in non-clinical samples (Kwapil et al., 2008; see also Supplementary Text S1.1. for more details on the schizotypy concept). Today, schizotypy is understood as a multidimensional construct that results from complex gene-environment interactions and is per se neither pathological nor identical with risk-for-schizophrenia. Instead, the co-occurrence of pronounced schizotypal traits is assumed to lead to taxon-like entities like schizophrenia, schizotypal personality disorder (SPD) or CHR (Barrantes-Vidal et al., 2015; Mason, 2014; Grant et al., 2018a). Factor-analytic studies suggest that schizotypy consists of the same three inter-related dimensions – positive, negative and disorganized – as schizophrenia (Table 1; Liddle, 1987; Vollema and van den Bosch, 1995), despite major differences in their conceptualization (Gross et al., 2014; Oezgen and Grant, 2018). Of these, disorganized schizotypy has frequently been neglected in studies and is not measured by the WSS, although this dimension might be essential to schizophrenia-liability (Grant et al., 2018a). Thus, effects of disorganized schizotypy may be misattributed to (especially) positive schizotypy in studies not assessing it (Grant and Hennig, 2018).

In clinical samples, negative schizotypy or corresponding schizoid features were associated with conversion to psychosis, particularly in the presence of CHR criteria or symptoms (Bang et al., 2017; Debbané et al., 2015; Flückiger et al., 2016; Schultze-Lutter et al., 2012a). In a non-clinical sample, both the positive and negative dimension of the WSS were found to be predictive of schizophrenia-spectrum disorders over ten years (Kwapil et al., 2013), with the positive dimension being specifically predictive of psychotic disorder and the negative dimension – with its emphasis on anhedonia – being more predictive of schizophrenia-spectrum disorder.

In CHR research, two early detection approaches currently prevail (Fusar-Poli et al., 2013; Schultze-Lutter et al., 2015): *basic symptom* (BS) (Schultze-Lutter et al., 2012b, 2016) and *ultra-high risk* (UHR) criteria (Yung and McGorry, 1996; Supplementary Table S1). They are associated with pooled conversion-to-psychosis rates ranging from 15% at one-year to 55% at four-year follow-up in clinical samples (Schultze-Lutter et al., 2015). The two symptomatic UHR criteria consist of brief intermittent (BIPS) and attenuated psychotic symptoms (APS). APS include positive features of SPD, which, however, have to have a clearly defined recent time of onset or worsening to be distinguishable from the enduring features that define SPD (Table 1). The third trait-state UHR criterion is defined by a genetic

Table 1

Comparison of latent schizotypy trait dimensions and their representing assessment scales, and trait abnormalities of schizotypal personality disorder (SPD) according to DSM-5 with the state features of clinical high risk and psychotic states, i.e., basic symptoms (BS) as well as attenuated (APS) and transient frank psychotic symptoms ((BI)PS).

	Schizotypy ^{a,b,c}	SPD	BS (SPI-A/SPI-CY)	APS (SIPS)	(BI)PS ^d
	Personality trait (not necessarily pathological)	An enduring pattern of long duration	A self-experienced disturbance of "normal" mental processes	Some insight into their abnormal nature; recent onset or worsening	No insight into their abnormal nature
Positive	Tendency to ascribe meaningfulness to the objectively irrelevant resulting in extrasensory, unusual or distorted perceptive experiences and unconventional, magical or delusional thought patterns and beliefs	Odd beliefs or magical thinking; suspiciousness or paranoid ideation; ideas of reference; unusual perceptual experiences	Derealization; decreased ability to discriminate between ideas and perceptions/memories; visual and acoustic perception disturbances (below APS-level in the SIPS)	P1 unusual thought content/delusional ideas; P2 suspiciousness/persecutory ideas; P3 grandiose ideas; P4 perceptual abnormalities/hallucinations; P5 disorganized communication	Delusions; hallucinations
Negative	Tendency to feel overwhelmed by (mainly external) stimuli resulting in diminished pleasure from, reduced drive to seek out or eschewing of social and/or physical stimulation as well as reduction in one's own verbal, behavioral and emotional expressiveness	Lack of close friends; excessive social anxiety associated with paranoid fears; inappropriate or constricted affect		N1 social withdrawal; N2 avolition; N3 expression of emotion; N4 experience of emotion & self; N5 ideational richness; N6 occupational functioning	Anhedonia (in social and other activities/situations); avolition; affective flattening; reduced intensity of emotional response; attentional impairment; alolia
Disorganized	Tendency towards disassociation both between (e.g., incongruence of cognition and emotion) as well as within mental functions (e.g., rapid emotional changes, simultaneous experience of divergent emotions or associative/-cognitive slippage); in measures based on SPD-symptomatology also the tendency towards oddness and eccentricity ^e	Odd thinking and speech; behavior or appearance that is odd, eccentric, or peculiar ^e		D1 odd behavior & appearance; D2 bizarre thinking; D3 trouble with focus and attention; D4 impairment in personal hygiene	Formal thought disorder/disorganized speech; disorganized or bizarre behavior; incongruous affect
Cognitive	Ambiguous meaning depending (mainly) on used measure: can refer either to the cognitive aspect of disorganization (i.e., related to formal thought disorder) or the cognitive aspects of positive schizotypy (i.e., related to delusional thinking)		Thought interference, blockage, pressure or perseveration; disturbances of abstract thinking, receptive or expressive speech; inability to divide attention; captivation of attention; unstable ideas of reference		

SIPS = Structured Interview for Psychosis-Risk Syndromes (McGlashan et al., 2010); SPI-A/SPI-CY = Schizophrenia Proneness Instrument Adult/Child & Youth version (Schultze-Lutter et al., 2007a; Schultze-Lutter and Koch, 2010).

^a According to Wisconsin Schizotypy Scales (Eckblad and Chapman, 1983; Chapman et al., 1978; Eckblad et al., 1982; Chapman et al., 1976).

^b According to Cognitive Slippage Scale (CSS; Miers and Raulin, 1987).

^c According to Schizotypal Ambivalence Scale (SAS; Kwapil et al., 2002).

^d According to Andreasen and Black (2000).

^e The disorganized dimension of SPD (and related scales) is suggestedly closer to positive schizotypy than "true disorganization" (Gross et al., 2014; Oezgen and Grant, 2018).

risk (having a first-degree relative with psychosis or meeting criteria of SPD), indicating the trait, along with a significant recent functional decline, indicating the state (Yung and McGorry, 1996). BS are self-experienced subclinical disturbances in mental processes, which are instantaneously perceived with full insight into their abnormal nature as deviations from one's normal mental processes. As such, BS are clearly different from the content-related, externalized and/or observable persistent positive features or symptoms described in schizotypy or APS/BIPS (Debbané et al., 2015; Table 1; see also Supplementary Text S1.4. for a detailed contrast of BS and schizotypy). A subgroup of 14 cognitive and perceptive BS forms two CHR criteria: Cognitive-Perceptive BS (COPER) and Cognitive Disturbances (COGDIS) (Schultze-Lutter et al., 2012b, 2015, 2016, 2018).

Based on a recent review, a theoretical model of the interplay between schizotypy, APS/BIPS, BS, manifest SPD and psychosis was proposed (Fig. 1, Debbané et al., 2015). This model assumes that APS/BIPS appear as a clinical manifestation or as an exacerbation of the underlying schizophrenia-liability (rather than unremarkable expressions of schizotypal traits “in action”; Debbané and Barrantes-Vidal, 2015) and might be triggered by neurobiological aberrations underlying schizophrenia-spectrum disorders that are experienced as BS as the most immediate expression of these abnormalities (Ettinger et al., 2014; Schultze-Lutter et al., 2016, 2018). This highlights the relevance of BS, especially cognitive disturbances, in the development of psychosis on the end of the assumed psychosis-continuum (Debbané et al., 2015) and delineates them from delusory/perceptual experiences that arise unrelatedly to schizophrenia-liability as state expressions of (positive) schizotypy (Mason et al., 2008; Barrantes-Vidal et al., 2013).

Only few studies have investigated the interrelationships between these concepts so far. Regarding CHR and schizotypal features, studies indicate that the negative dimension, particularly the WSS Physical Anhedonia, was related to UHR but not BS criteria (Flückiger et al., 2016) and to cognitive impairments (Brosey and Woodward, 2015). Another study found significant associations between schizotypal ideation and self-reported cognitive difficulties (Corcoran et al., 2013). Furthermore, examining the relationship between the four WSS plus two

disorganized schizotypy scales (Table 1) and questionnaire-assessed BS yielded a two-factor solution (Yon et al., 2009). Therein, the negative factor contained only Social and Physical Anhedonia, while all other five scales formed an extended positive factor including the disorganized features. The authors concluded that BS were significantly associated with the positive, but not negative schizotypy-dimension (Yon et al., 2009). Yet, questionnaire-assessed BS only poorly correspond to interview-assessed BS (Mass et al., 1997; Michel et al., 2017); and no study so far has included all criteria-relevant BS and analyzed single BS rather than only total scores. Moreover, no study to-date has integrated all concepts, i.e. schizotypy, APS/BIPS and BS, within one model to investigate their associations simultaneously.

Against this background, our aim was to examine the factorial structure of and associations between schizotypy-features, CHR and related symptoms (i.e. positive, negative, disorganized symptoms) in patients of two early-detection-of-psychosis services. In line with the proposed psychosis-continuum (Van Os et al., 2000, 2009) and based on factorial and longitudinal findings on the WSS and CHR symptoms (Gross et al., 2014; Kwapil et al., 2008; Michel et al., 2019; Wuthrich and Bates, 2006) as well as the theoretical model of Fig. 1, we assumed a separation between *trait*-features of schizotypy and *state*-phenomena, i.e. CHR and related symptoms. We hypothesized that negative schizotypy-features and negative symptoms will form separate factors and, analogously, we supposed a distinction between positive schizotypy-features and positive symptoms. Furthermore, we supposed that cognitive BS form a separate dimension while the non-cognitive BS join the positive schizotypy-dimension because of their phenomenological correspondence to schizotypal alienation and perception phenomena that are also assessed as fluctuating, potentially rare phenomena in the positive WSS. Additionally, we hypothesized that positive and negative schizotypy will be significantly associated with all three symptom-dimensions as the results of Flückiger et al. (2016) indicated that significant associations were not restricted to corresponding trait and state dimensions. Due to lack of disorganized schizotypy-scales, we postulated a disorganized symptom-dimension, but could not model a corresponding schizotypy-dimension. As BS are assumed to be an expression of underlying

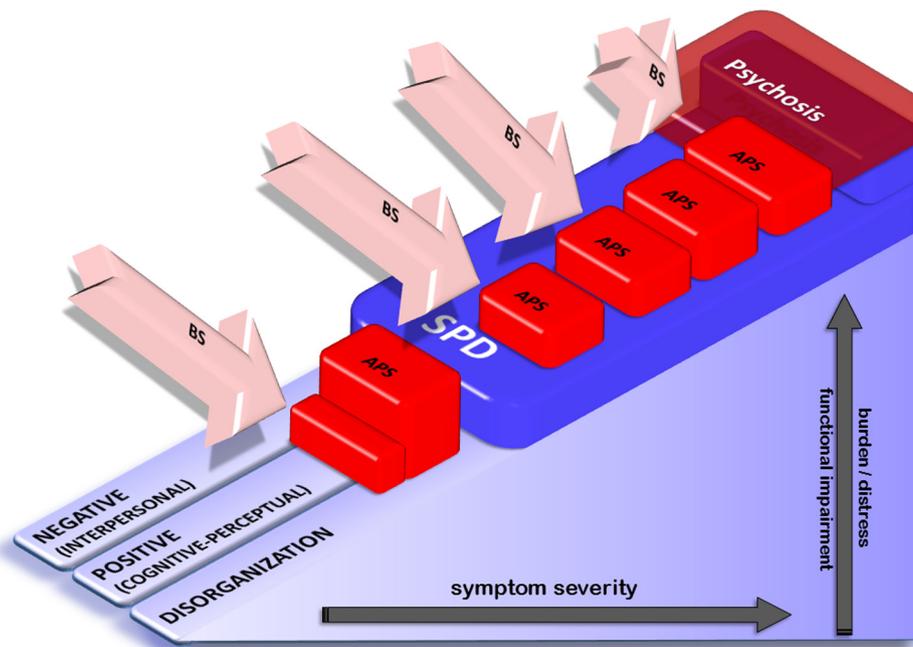


Fig. 1. Model of the relationship and interactions between schizotypy dimensions, clinical high risk of psychosis symptoms and psychosis (adapted from Debbané et al., 2015, with permission of the copyright owner). SPD = schizotypal personality disorder; BS = cognitive basic symptoms; APS = attenuated psychotic symptoms.

neurobiological abnormalities and as they were significantly associated with both schizotypy and APS/BIPS, cognitive BS were hypothesized to act as a mediator of the relationship between schizotypy and all symptom-dimensions.

2. Method

2.1. Participants

The sample comprised of 277 help-seeking, predominately young adult patients (including 28% minors <18 years; Table 2) from two early-detection-of-psychosis services in Cologne, Germany (n = 138), and Bern, Switzerland (n = 139). Exclusion criteria were: mental retardation or disorders that are related to a general medical brain-related condition (inflammatory, traumatic, and epileptic) or substance use. The patient cohort in Cologne also participated in a follow-up study (Schultze-Lutter et al., 2014), which included written informed consent for the scientific use of their clinical baseline data; all patients (and their guardians) in Bern also provided written informed consent for the scientific use of clinical data. The ethical committees of Cologne and Bern approved these procedures.

Table 2
Sociodemographic and clinical characteristics of the sample (N= 277).

Age (years) ^a		
Mean (±SD)	22.0	(±5.9)
Median (range)	21.2	(9.1–40.6)
Gender, male n (%)	165	(59.6)
Partnership, n (%)		
Single	259	(93.5)
Married/steady partner	12	(4.3)
Divorced	6	(2.3)
Graduation / vocational education, n (%)		
Early school leaver (ISCED0)	1	(0.4)
Still in school / training	185	(66.7)
Finished school, but no vocational occupation	27	(9.7)
Finished vocational education	64	(23.1)
Apprenticeship (ISCED level 3b)	44	(68.8)
Foreman certificate / master of workman (ISCED level 5b)	5	(7.8)
University / college of advanced studies (ISCED level 5a)	14	(21.9)
other	1	(1.6)
Current occupation, n (%)		
No work / education	46	(16.6)
Sheltered position / employment	6	(2.2)
Regular occupation incl. education	225	(81.2)
Clinical characteristics ^{b,c}		
Any current ICD-10 diagnosis, n (%)	187	(67.5)
F2 Schizophrenia, schizotypal and delusional disorders ^c	35	(12.6)
F3 Mood (affective) disorders	77	(27.8)
F4 Neurotic, stress-related and somatoform disorders	40	(14.4)
F5 Behavioural syndromes associated with physiological disturbances and physical factors ^d	3	(1.1)
F6 Disorders of adult personality and behaviour	5	(1.8)
F9 Behavioral and emotional disorders with onset occurring in childhood and adolescence	13	(4.7)
Other lifetime or axis II-diagnosis, n (%)	14	(5.1)
Any current CHR criteria, n (%)	150	(54.2)
BS criteria only	41	(14.8)
UHR criteria only	26	(9.4)
BS & UHR criteria	83	(30)

ISCED = International Standard Classification of Education; CHR = clinical high risk for psychosis; BS = basic symptoms; UHR = ultra-high risk.

[§] multiple group membership possible.

^a age groups: ≤15 years, n=39 (14%); 16–20 years, n=92 (33%); 21–25 years, n=75 (27%); ≥26 years, n=71 (26%).

^b 99 (35.7%) only clinical diagnosis; 88 (31.8%) risk and clinical diagnosis; 62 (22.3%) only risk; 28 (10.1%) just help-seeking.

^c schizophrenia (71.4%), schizophreniform (8.6%), delusional disorder (2.9%), bipolar (2.9%), anxiety (2.9%), obsessive-compulsive disorder (2.9%), polymorph (2.9%), not otherwise specified (5.7%).

^d only eating disorders.

2.2. Assessments

CHR and related symptoms were assessed using semi-structured interviews (Table 1; Supplementary Table S1). BS were assessed using the Bonn Scale for the Assessment of Basic Symptoms (BSABS; Gross et al., 1987) until 06/2000 and, thereafter, the Schizophrenia Proneness Instruments versions for adults or minors (SPI-A/SPI-CY; Schultze-Lutter et al., 2007a; Schultze-Lutter and Koch, 2010). APS/BIPS were assessed using the five positive (P) items of the Structured Interview for Psychosis-Risk (SIPS; McGlashan et al., 2010); the negative and disorganization symptoms were assessed using the six negative (N) and four disorganization (D) items of the SIPS, respectively. All assessments were performed by trained psychologists and psychiatrists and supervised by F.S.L. Good inter-rater reliabilities (McGlashan et al., 2010; Michel et al., 2014; Schultze-Lutter et al., 2012b) and good test-retest reliability across short periods of time (Michel et al., 2014) were reported for the assessment of CHR criteria according to these interviews.

Schizotypy was assessed psychometrically using the German versions of the WSS (Burgdörfer and Hautzinger, 1987; Meyer and Hautzinger, 1999, 2002; Scherbarth-Roschmann and Hautzinger, 1991): Physical Anhedonia (PhyAnh; 50 items), Social Anhedonia (SocAnh; 40 items), Perceptual Aberration (PerAb; 21 items), and Magical Ideation (MagicId; 20 items), for which either endorsement (true) or negation (not true) was rated as a positive response (Table 1). The German translations have good internal consistencies ($\alpha > 0.81$; Bailer et al., 2004; Oezgen and Grant, 2018).

2.3. Data analyses

Data were analyzed using SPSS v24 and Mplus v8 (Muthen and Muthen, 1998–2011) with the weighted least squares means and variance adjusted (WLSMV) estimator for categorical variables. Model fit was assessed using the following indices: χ^2 -test, Comparative Fit Index (CFI), Root-Mean-Square Error of Approximation (RMSEA), and Weighted-Root-Mean-Square Residual (WRMR). The non-normally distributed schizotypy-scales and SIPS-items were treated as ordinal variables; BS were included in the analyses as binary categorical variables (0 = absent; 1 = present), i.e., in the rating format of BSABS. Missing items (0.92%) were replaced by group-means.

As recommended (Anderson and Gerbing, 1988), we used a two-step approach: First, we conducted *confirmatory factor analysis* (CFA) to test measurement-models to assure that all latent factors are assessed reliably before testing the structural relationships between these latent factors. To generate measurement-models, latent variables were formed as follows: a “Negative schizotypy”-dimension consisting of PhyAnh and SocAnh and a “Positive schizotypy”-dimension consisting of MagicId, PerAb and the four non-cognitive BS (visual and acoustic perception disturbances, derealization, and decreased ability to discriminate between fantasy and perception/true memories). The remaining ten cognitive BS were used as indicators for the “Cognitive disturbances”-dimension. According to the SIPS (McGlashan et al., 2010), the “Negative symptoms”-dimension consisted of the six negative SIPS-items (N1–N6), the “Disorganized symptoms”-dimension of four disorganized SIPS-items (D1–D4) and the “Positive symptoms”-dimension of five positive SIPS-items (P1–P5). Before the CFA, items and scales were excluded from further analyses when Spearman’s Rho (ρ) was <0.3. Additionally, to control for possible age-effects, we re-calculated the CFA twice, in participants ≥16 years (n = 238) and in adults ≥18 years (n = 199).

Second, structural equation modeling (SEM) was used to estimate the hypothesized relationships between the measurement-models. Significance of mediated, indirect effects was tested by calculating bootstrapped, bias-corrected confidence intervals (CIs) of the indirect effect (Preacher and Hayes, 2004). Finally, sensitivity

analyses were conducted with regard to the whole sample and the sample without individuals with a psychotic disorder.

3. Results

3.1. Measurement-models of schizotypy-features, CHR, and related symptoms

Spearman rho (ρ) correlations revealed that two BS had to be excluded from further analyses for $\rho < 0.3$, i.e., “captivation of attention by details of the visual field” and “disturbance of abstract thinking”, which were both reported by $\leq 5\%$ of patients (Supplementary Table S3).

The measurement model of the remaining 31 items (i.e., 12 BS, 15 SIPS-items, and four WSS; Supplementary Table S4) yielded a moderate model fit and all indicators had significant path coefficients on the respective latent factor. Modification indices suggested that the SIPS-item D2 “bizarre thinking” serves better as an indicator of the “Positive symptoms”-dimension and P5 “disorganized communication” better as an indicator of the “Disorganized symptoms”-dimension. A respective modification resulted in an improved good model fit ($\chi^2_{(419)} = 781.960$, $p < .001$; CFI = 0.930, RMSEA = 0.056 [90% CIs = 0.050, 0.062], WRMR = 1.151) (Table 3) with significant path coefficients for all indicators. Additional analyses supported that “Negative schizotypy” and “Negative symptoms”, “Positive schizotypy” and “Positive

symptoms” as well as “Cognitive disturbances” and “Disorganized symptoms” are better represented as separate dimensions than as single dimensions (Supplementary Tables S5–S11). Consequently, these measurement-models were used in all subsequent analyses. When measurement-models were estimated separately in participants aged ≥ 16 years and ≥ 18 years, the proposed model of the interplay between schizotypy, BS and CHR and related symptoms was confirmed.

3.2. Structural equation model

The hypothesized SEM-model yielded a good model fit (Fig. 2). All indirect effects were significant ($p < .05$). Standardized estimates of the indirect effects were: from “Negative schizotypy” to “Negative symptoms” 0.180 (95% CIs: 0.104, 0.256), and to “Positive symptoms” of 0.073 (95% CIs: 0.001, 0.146), and to “Disorganized symptoms” of 0.250 (95% CIs: 0.147, 0.352). The standardized estimates of the indirect effects from “Positive schizotypy” to “Positive symptoms” were 0.117 (95% CIs: 0.027, 0.206), to “Negative symptoms” with 0.286 (95% CIs: 0.182, 0.390), and to “Disorganized symptoms” with 0.396 (95% CIs: 0.269, 0.523). In addition to the mediated effects through “Cognitive disturbances”, “Positive schizotypy” and “Negative schizotypy” were also significantly associated with the respective symptom-dimension but not with “Disorganized symptoms”. To prevent our model from being unfairly rejected due to the large sample size, the significant chi-square was disregarded. Sensitivity analyses revealed stable results with and without participants with psychosis.

Table 3
Measurement models of latent variables.

Latent variable	Indicators	Stand. Est. ^a	S.E. ^b	p-value
Negative symptoms	Social withdrawal (N1)	0.779	0.031	.000
	Avolition (N2)	0.773	0.027	.000
	Expression of emotion (N3)	0.816	0.027	.000
	Experience of emotion and self (N4)	0.726	0.038	.000
	Ideational richness (N5)	0.790	0.031	.000
Negative schizotypy	Occupational functioning (N6)	0.691	0.036	.000
	Physical anhedonia (WSS)	0.684	0.060	.000
Positive schizotypy	Social anhedonia (WSS)	0.922	0.071	.000
	Perceptual aberration (WSS)	0.398	0.072	.000
Positive symptoms	Magical ideation (WSS)	0.411	0.074	.000
	Acoustic perception disturbances (BS)	0.770	0.090	.000
	Visual perception disturbances (BS)	0.906	0.097	.000
	Derealization (BS)	0.373	0.107	.006
	Discrimination of ideas & perception, fantasy & true memories (BS)	0.586	0.119	.000
	Unusual thought content / delusional ideas (P1)	0.922	0.030	.000
	Suspiciousness / persecutory ideas (P2)	0.786	0.035	.000
Disorganized symptoms	Grandiose ideas (P3)	0.427	0.086	.000
	Perceptual abnormalities / hallucinations (P4)	0.625	0.049	.000
	Bizarre thinking (D2)	0.677	0.045	.000
Cognitive disturbances	Odd behaviour and appearance (D1)	0.774	0.044	.000
	Trouble with focus and attention (D3)	0.647	0.037	.000
	Impairment in personal hygiene (D4)	0.728	0.046	.000
	Disorganized communication (P5)	0.822	0.033	.000
	Thought interference (BS)	0.803	0.054	.000
Disorganized symptoms	Thought pressure (BS)	0.628	0.070	.000
	Disturbance of receptive speech (BS)	0.884	0.044	.000
	Unstable ideas of reference (BS)	0.740	0.059	.000
	Thought blockages (BS)	0.740	0.051	.000
	Disturbance of expressive speech (BS)	0.815	0.058	.000
	Thought perseveration (BS)	0.917	0.056	.000
	Inability to divide attention (BS)	0.825	0.061	.000

BS = basic symptoms; P1–P5 = positive symptom items; N1–N6 = negative symptom items; D1–D4 = disorganized symptom items; WSS = Wisconsin Schizotypy Scales.

^a standardized estimator.

^b standard error.

4. Discussion

Our first-time comprehensive dimensional study of schizotypy-features and CHR and related symptoms, on the one hand, confirmed a structure of these features and symptoms, which closely resembles the main dimensions that define schizotypy (Vollema and van den Bosch, 1995; Oezgen and Grant, 2018) and psychoses, i.e., the positive, negative, and disorganized dimensions, as well as a related cognitive dimension in psychosis (Barch et al., 2013; Heckers et al., 2013; Potuzak et al., 2012). On the other hand, it gave first empirical support to the hypothetical model of Fig. 1 and the mediating role of subjective cognitive disturbances between the distinct, yet corresponding trait-like schizotypy-feature and state-like symptom dimensions that might inform preventive and etiological research.

The distinction between “Positive schizotypy” and “Positive symptoms” supported the proposed trait-state-distinction into two different stages on the assumed psychosis-continuum within a greater positive symptom dimension. The “Positive schizotypy” dimension consists of the two positive WSS complemented by those BS that score per definition below the APS-severity-threshold in the SIPS and resemble some positive schizotypy-features. In line with other studies (Klaassen et al., 2011; Hawkins et al., 2004), “Positive symptoms” exclusively consisted of positive SIPS-items and the dependent item D2, which is used to rate the degree of bizarreness of and illogical thinking expressed by unusual thought contents (P1–P3). A similar distinction was supported for the two negative dimensions: Expectedly, “Negative symptoms” consists exclusively of all six negative SIPS-items, and the “Negative schizotypy” dimension of only the two anhedonia WSS. A similar distinction between schizotypy-features and symptoms can be expected for the disorganized dimension, yet, for lack of assessment of disorganized schizotypy-scales could not be examined in our study.

Although the distinction between positive and negative schizotypy and between positive, negative and disorganized symptoms generally supports the current dimensional models of schizotypy (Gross et al., 2014; Kwapił et al., 2008; Wuthrich and Bates, 2006) and psychosis (Potuzak et al., 2012), it only partly supports the assumption of a phenomenological continuum of psychosis. Since this distinction could also be attributed to differences between trait- and state-phenomena, it could also be caused by differences on the psychopathological level,

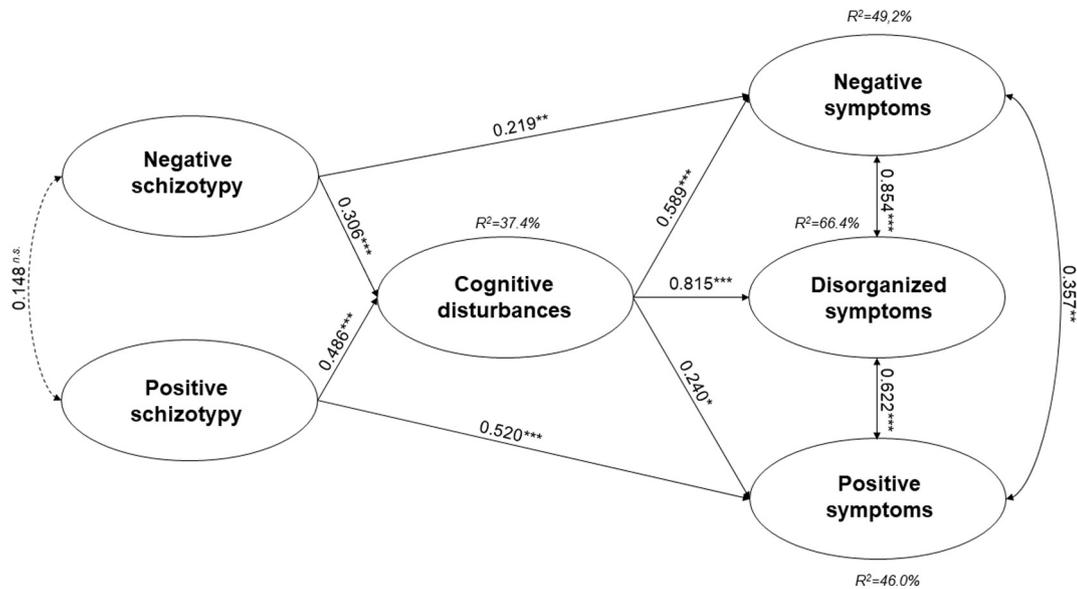


Fig. 2. Structural equation model depicting the hypothesized cross-sectional interrelations between schizotypy features, CHR for psychosis and related symptoms. Model fit indices: $\chi^2_{(423)} = 774.022$, $p < .001$; CFI = 0.933, RMSEA = 0.055 [90% CIs = 0.049, 0.061], WRMR = 1.154. n.s., non-significant, * $p \leq .05$, ** $p \leq .01$, *** $p \leq .001$.

particularly with respect to the two negative dimensions. For example, social anhedonia is defined by the diminished experience of pleasure from interactions with others, irrespective of the quantity of such interactions; the negative symptom social withdrawal (N1) and its counterpart on the level of SPD, “lack of close friends”, are defined by a reduced or deficient number of interactions, rather than by the affective experience of such social encounters (Flückiger et al., 2016; Table 1).

Extending the three-dimensional model of schizotypy and psychosis, and the related assumption of a common cognitive-disorganized dimension (Ettinger et al., 2014; Nelson et al., 2013; Vollema and van den Bosch, 1995), our data support a four-dimensional model as depicted in Fig. 1 with separate disorganized and cognitive dimensions. As expected, the disorganized dimension included the disorganized SIPS-items “odd behavior and appearance” (D1), “trouble with focus and attention” (D3) and “impairment in personal hygiene” (D4) and was complemented by the positive SIPS-item “disorganized communication” (P5); the cognitive dimension, “Cognitive disturbances”, comprised exclusively BS. With this, our results differ from the finding of Yon et al. (2009) of a broad positive dimension including disorganized symptoms and cognitive BS and from the assumption of a common dimension of negative schizotypy and cognitive BS (Brosey and Woodward, 2015). Rather, they support the notion of a fourth “impaired cognition”-dimension in psychosis (Heckers et al., 2013).

In line with previous dimensional studies on BS (Schultze-Lutter et al., 2008, 2012b, 2016), our data supported the assumption of cognitive and perceptive BS as separate constructs. Further, cognitive BS were separated from “derealization” and “decreased ability to discriminate between fantasy and true perceptions/memories”, which both can be conceptualized as reflecting a changed experience of the environment rather than a cognitive disturbance. Thus, their content, rather than their common subjective nature, defined group-membership of BS within the common schizotypy-psychosis (risk) space. So, expectedly but in contrast to their definition as state-symptoms, rather than trait features, the non-cognitive BS were significantly associated with “Positive schizotypy”. This might highlight the subtle, sub-clinical character that non-cognitive BS, particularly when infrequent, share with milder expressions of positive schizotypy and items of MagicId and PerAb, respectively, that relate to infrequent, non-persistent perceptual disturbances and/or alienation.

With regard to the interrelation between the six schizotypy- and symptom-dimensions, our analysis additionally delivered new

important insights. Broadly confirming the hypothetical model of Fig. 1, negative and positive schizotypy as underlying vulnerability were associated with (attenuated) positive, negative, and disorganized symptoms through an increase in “Cognitive disturbances”, which functions as a mediator of this relationship. Interestingly, the positive, negative, and disorganized symptom-dimensions were significantly associated with each other, while there was no such association between the positive and negative schizotypy-dimensions. Based on conflicting findings (Chan et al., 2015; Gross et al., 2014; Kwapił et al., 2008; Smith et al., 2016), the correlation between negative and positive schizotypal-dimensions was suggested to be related to SocAnh cross-loading on both. Such a cross-loading, however, was missing in our data. Another reason for the lack of a significant correlation between the positive and negative schizotypy-dimension might be the differences in their mean expression in our sample. Although at 6.0 and 3.9, the two positive WSS had mean scores well within the range reported for non-clinical samples (ranges of mean scores: MagicId: 3.0–8.5; PerAb: 1.5–7.0), while, at 20.5 and 16.6, the two negative WSS had mean scores well above those reported from non-clinical samples (ranges of mean scores: PhyAnh: 5.6–15.4; SocAnh: 5.4–11.2) (Bailer et al., 2004; Blanchard et al., 2001; Chapman et al., 1976; Clementz et al., 1991; Fonseca-Pedrero et al., 2010; Meyer and Hautzinger, 1999; Tandon et al., 2012). Contrary to non-clinical samples, high negative schizotypy (but not high positive schizotypy) in clinical samples was related to frank psychosis and CHR (Debbané et al., 2015; Flückiger et al., 2016). Further, it was proposed that negative schizotypy better reflects the underlying *Krankheitswert* in ‘unhappy schizotypes’ (Grant, 2015) and, consequently, must be assumed to accumulate in clinical samples and translates “into a type of ‘shutting down’ that would manifest by diminished expression that is so often central to the diagnosis of schizophrenia” (Xie et al. 2018; p. S552).

In line with Fig. 1, our model indicates that the relationship between corresponding schizotypy- and symptom-dimensions is partly mediated by the presence of “Cognitive disturbances”. This suggests that a genetic liability to psychosis, as reflected by heightened WSS-scores, increases the probability of aberrant neurobiological processes and, consequently, of developing cognitive BS as their most immediate psychopathological expression (Huber, 1995; Klosterkötter, 1992; Schultze-Lutter, 2009), which then increase the probability for APS/BIPS or psychosis – possibly via inadequate coping (Schultze-Lutter et al., 2018). Neurobiological correlates of trait-schizotypy resemble

those described for schizophrenia, albeit less pronounced (Corlett and Fletcher, 2012; Ettinger et al., 2014; Modenato and Draganski, 2015), and also BS were related to a variety of neurobiological aberrations also found in psychoses (Schultze-Lutter et al., 2016).

The relationship between schizotypy and *subjective* cognitive disturbances in terms of BS has not been investigated in detail in previous studies despite the evidence that cognitive dysfunctions act as vulnerability marker for psychosis (Bora et al., 2014; Mollon et al., 2018; Snitz et al., 2006); yet, high schizotypy was related to more self-reported, subjective cognitive complaints, mainly related to memory functions, in a healthy college sample (Chun et al., 2013) and questionnaire-assessed BS increased risk-for-conversion to psychosis in the presence of pronounced PhyAnh (Bang et al., 2017) that, in turn, predicted presence of UHR but not BS-criteria (Flückiger et al., 2016). Similar to studies of BS (Schultze-Lutter et al., 2007b), however, cross-sectional findings showed little associations between elevated schizotypy and cognitive deficits in terms of *objective* neurocognitive impairments (Bora et al., 2014; Chun et al., 2013; Ettinger et al., 2015). Objective neurocognitive impairments that fall within the definition of the “impaired cognition”-dimension of psychosis (Barch et al., 2013; Heckers et al., 2013) were considered as too unspecific to reliably distinguish patients with (schizophrenic) psychosis from healthy persons or patients with other psychiatric disorders (Barch et al., 2013). In contrast, cognitive BS as included in COPER/COGDIS seem to rarely appear in other disorders, in healthy relatives of patients with psychosis, or in healthy controls (Klosterkötter et al., 1996, 1997) and were infrequent in the general population (Schultze-Lutter et al., 2017a). Thus, for the evaluation of the “cognitive impairment”-dimension suggested for psychosis, the assessment of subjective cognitive deficits in terms of cognitive BS in clinical interviews might be a veritable and advantageous completion of neurocognitive measures in clinical practice (Barch et al., 2013; Chun et al., 2013).

Our sample included patients between 9 and 40 years-of-age, roughly a quarter of them being minors. Because APS/BIPS (Schimmelmann et al., 2015; Schultze-Lutter et al., 2017b), BS (Schultze-Lutter et al., 2018) and schizotypy (Bora and Arabaci, 2009; Fonseca-Pedrero et al., 2008) have shown an impact of age with higher prevalence rates of APS/BIPS and BS in youth compared to adulthood, and an increase of schizotypy-severity across adolescence with a subsequent decrease in adulthood, we had conducted sensitivity analyses to test for age effects on our latent variables. These indicated that these are valid across age groups and not dependent on the different developmental trajectories of CHR-symptoms and schizotypy-features.

If the interrelations of our model can be replicated in future cross-sectional and longitudinal studies, our findings have significant clinical implications. They suggest that very-early interventions to prevent development or progression of positive, negative and disorganized symptoms should focus on both schizotypy and cognitive disturbances to disrupt the detrimental cascading effect as early as possible. To this aim, schizotypy and cognitive disturbances should be assessed and monitored carefully and targeted if necessary. In doing so, subjective cognitive disturbances might be a central target of interventions due to their mediating role. Regarding the definition-inherent immediate recognition of BS as disturbances in one's own mental processes, however, cognitive therapies that are frequently used for APS to increase reality testing and generate more adequate explanatory models (Bentall et al., 2007; French et al., 2007) might not be the first method of choice. Rather, a stress-reducing approach with educational and behavioral elements was suggested for BS in patients with schizophrenia (Süllwold and Herrlich, 1990, 1992). Recently, significant stress reduction in UHR-patients was also achieved using non-directive reflective listening (Stain et al., 2016), which consequently might also be another viable BS intervention option. Furthermore, with regard to their assumed close relationship to the neurobiological aberrations underlying psychotic disorders, they may help to target such aberrations more specifically, e.g. by new pharmacological approaches (Schultze-Lutter et al., 2016, 2018).

4.1. Strengths and limitations

The current study has several strengths including the large sample size, first-time common assessment of schizotypy-features as well as CHR and related symptoms, the low number of missing data, symptom-assessment in clinical interviews, and the estimation of an age-effect. However, some limitations of the current study should also be noted. First, disorganized schizotypy-scales were not assessed. This is especially important, as the schizotypy-dimensions are not wholly independent, wherefore effects of (unassessed) disorganization might be misconstrued as apparent effects of positive or negative schizotypy (Grant and Hennig, 2018). Second, the cross-sectional design of the study did not allow testing of the temporal relationship between dimensions. Future studies with longitudinal data are highly needed to examine if and how changes in the three symptom-dimensions relate to changes in “Cognitive disturbances” over time. Third, in light of the first and second limitation, the prediction of states (like CHR-symptoms) by traits (schizotypy-dimensions) (Barrantes-Vidal et al., 2013) might appear across schizotypy-dimensions; e.g., levels in disorganized (but not positive) schizotypy best predicted experiment-induced changes in positive states – induced by both psychological intervention (Grant et al., 2018b) and social stress (Grant and Hennig, personal communication). Thus, our findings support the assumption of the distinction between schizotypy as a personality construct and risk-for-schizophrenia (Grant et al., 2018a) in that BS are not merely reflections of the corresponding trait “in action”, but manifestations of a schizophrenia-liability core.

4.2. Conclusions

Our model broadly confirmed the hypothesized model in Fig. 1 with three underlying dimensions, highlighting the important function of cognitive BS as a fourth dimension, and, thus, emphasizing etiological models of schizophrenia and other psychoses beholding impaired neurocognition as a core element (Insel, 2010). Our study did, however, challenge the view that schizotypy-features and (attenuated) psychotic symptoms mainly differ in severity, rather than quality. Importantly, this was the first study about the relationship of schizotypy-features, CHR, and related symptoms in one model to emphasize the important (and most likely crucial) role of subjective cognitive symptoms in both development of (attenuated) psychosis and early intervention.

Conflict of interest

All authors declare no conflicts of interest regarding the topic of this article.

Contributors

Rahel Flückiger: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Visualization, Writing - original draft. **Chantal Michel:** Data curation, Project administration, Writing - review & editing. **Phillip Grant:** Conceptualization, Validation, Writing - review & editing. **Stephan Ruhrmann:** Data curation, Resources, Writing - review & editing. **Kai Vogeley:** Data curation, Resources, Writing - review & editing. **Daniela Hubl:** Data curation, Resources, Writing - review & editing. **Benno G. Schimmelmann:** Data curation, Resources, Writing - review & editing. **Joachim Klosterkötter:** Data curation, Resources, Writing - review & editing. **Stefanie J. Schmidt:** Conceptualization, Data curation, Formal analysis, Methodology, Writing - review & editing. **Frauke Schultze-Lutter:** Conceptualization, Funding acquisition, Investigation, Methodology, Project administration, Supervision, Visualization, Writing - original draft.

Role of funding source

The early detection of psychosis services in Bern is a cooperation between the University Hospitals of Child and Adolescent Psychiatry and Psychotherapy, and of Psychiatry and Psychotherapy of the University of Bern, and the Soteria Bern. The “Predictive accuracy of criteria for inclusion into prodromal studies in the clientele of the Cologne Early Recognition Centre, FETZ” study of patients of the early detection of psychosis service in Cologne, including baseline data collection, was supported following ethical approval included in the review process by a grant from the Koeln Fortune Program/Faculty of Medicine, University of Cologne (grant numbers 8/2005, 27/2006) to Prof. Schultze-Lutter (no additional protocol number provided). The study's sponsor had no role in study design, data collection, or analysis, or in interpretation, writing, or submission of the report. The use of the clinical data after written general consent of the patients (and their legal guardians)

for research purpose was granted by the ethical committee of the University of Bern (protocol number 139/2014).

Acknowledgement
None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.schres.2018.12.039>.

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