Schizotypy

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Summary

Schizophrenia is one of the most severe psychiatric disorders, often accompanied by long lasting symptoms and an invalidating outcome. Therefore preventive interventions are to be welcomed. Curative and preventive treatment is lacking, due to incomplete knowledge of the etiological and pathogenetical factors of the disease. One way to increase our understanding of the causal mechanisms of schizophrenia is to study the genetically determined vulnerability. The most elaborated theoretical model of this vulnerability is provided by Paul Meehl and is called 'the schizotypy model' (Meehl 1990).

In chapter 1 we presented the schizotypy model in detail. In sum, it is argued that during brain development a single dominant gene is held responsible for the development of subtle deviancies in neurochemical and neural functions. We are aware of current knowledge favoring multifactorial genetic models instead of single gene models. It is only relevant for this thesis that the schizophrenia origin is genetic. Whether it is multifactorial or not, is beyond the scope of this thesis. The neural malfunctions give rise to subtle deviancies in psychophysiological and neurocognitive functions. In particular, those functions are affected, in which complex integration of stimuli from different systems or finely tuned multiple control, is required. These subtle neurocognitive and psychophysiological deviancies almost always end up in a schizotypal personality. Meehl argued that cognitive slippage and aversive drift are at the the core of the schizotypal personality make-up. Neurocognitive deviancies and schizotypal traits are argued to be central to the vulnerability to schizophrenia. They form the necessary, but not sufficient, precondition for schizophrenia. It depends on protective and environmental factors whether a vulnerable subject will decompensate into full-blown schizophrenia.

In chapter 2 we explained the rationale of the thesis and we presented the outline. This study is mainly intended to contribute to our understanding of the vulnerability to schizophrenia. From Meehl's model and the widely accepted notion that schizophrenia, schizotypal personality disorder and schizotypy are genetically related, it follows that schizotypy and schizophrenia share the vulnerability to schizophrenia. The constructs differ in degree of compensation. Investigating schizotypy in healthy subjects (either subjects from the normal population or biological relatives of schizophrenia patients) has the potential to clarify underlying pathogenetical mechanisms of schizophrenia. The use of these subjects, instead of patients, for research into the vulnerability has many methodological advantages, because they are mainly healthy individuals (e.g. motivated and capable, without psychiatric medication and hospitalisation, without psychotic or negative symptoms).
This thesis is focused on the psychological components of the vulnerability to schizophrenia, viz. schizotypal personality traits, neurocognitive functions and their interrelatedness. We have chosen a broad range of schizotypal traits, because the construct of schizotypy is still open. Therefore we included, next to the traits outlined by Meehl, also traits and signs outlined by Kendler et al. (1989) and the DSM-IV.

The central part of the thesis is divided into two parts. Part I is about the assessment of schizotypy and includes chapters 3, 4, 5 and 6. The main questions to be addressed in Part 1 are: 1) Which and how many dimensions of schizotypy are to be distinguished?, 2) Is it possible to assess the schizotypal features with a sufficient level of test-retest reliability?, and 3) Is schizotypy equally assessed with a self-report questionnaire and a structured interview?
Part II is about the neurocognition of schizotypy and includes chapters 7 and 8. The main questions to be addressed in Part II are: 1) The dimensions of schizotypy, are they related to dimension-specific neurocognitive dysfunctions?, and 2) Are the patterns of neurocognitive correlates of dimensions of schizotypy similar across samples of normal subjects and first-degree relatives of schizophrenia patients?

In chapter 3 we presented an overview of self-report scales for measuring schizotypy and a review of exploratory factor analytical studies of these scales. These studies with normal subjects show that schizotypy is a multidimensional construct consisting of three or four dimensions. Positive Schizotypy, Negative Schizotypy, Nonconformity and possibly Cognitive Desorganisation/Social Anxiety. Clinical and external validation studies seem to support the construct validity of Positive Schizotypy and Negative Schizotypy dimensions, but as yet fail to support Nonconformity and Desorganisation/Social anxiety dimensions.
In accordance with this multidimensional structure, the scales for measuring schizotypy can be classified as dimension-specific scales. We considered the striking similarities between the multidimensionality of schizotypal traits and the multidimensionality of schizophrenic symptoms. We also looked at the similarities and the differences between schizotypy and normal personality traits. Some practical and theoretical implications of these relationships were discussed.

In chapter 4 we tested the hypothesis that schizotypy is composed of multiple dimensions. All studies into the multidimensionality of schizotypy, as reviewed in chapter 3, used common factor analysis of scales (exploratory). We argue that with respect to research into the multidimensionality of schizotypy with dichotomous item responses on questionnaires (as is the case with the Schizotypal Personality Questionnaire; SPQ, Raine et al. 1991) a lot can be learned using Generalized Multidimensional Rasch Models (GMRM). The GMRM requires a priori postulated models of schizotypy, which can be tested in confirmatory analyses.
We hypothesized four competing models of schizotypy, based on the literature and on clinical impressions, viz. two two-dimensional models and two three-dimensional models. We also hypothesized that items differ in the degree they are indicative for a particular dimension of schizotypy. The sample consisted of 418 psychiatric in- and outpatients, with moderate levels of psychopathology, which filled in the SPQ. Both three-dimensional models yielded a much better fit to the data than both two-dimensional models. Our revised three-dimensional model yielded the best fit. This three-dimensional model was a revision of the model put forward by Raine et al. (1994) and Gruzelier (1996). It consisted of Positive Schizotypy (including magical ideation, unusual

perceptual experiences, delusional mood, paranoid ideation and referential thinking), Desorganisation (including odd speech and odd behavior) and Negative Schizotypy (including paranoid ideation, referential thinking, constricted affect, no close friends and social anxiety).
The results strongly suggest that schizotypy, as measured with the SPQ, is a three-dimensional construct.

In chapter 5 we investigated the reliability of the Structured Interview for Schizotypy-Revised (SIS-R). The original interview (SIS) was developed by Kendler. We revised the SIS, primarily by standardizing the rating procedures. We introduced operational definitions, a four-point scale and provided clear criteria for rating severity of symptoms and signs (frequency, duration and level of conviction). We divided schizotypal signs of global affect and global organization of speech into three separate signs of affect and five separate signs of thinking and speech.
The main goal of this study was the assessment of test-retest reliability of the SIS-R. A robust test-retest design with different interviewers at both times, with an interval of 19 days, was used. The sample consisted of 42 almost all personality disordered psychiatric patients. The strong linear weighted kappa statistic was used to evaluate reliability.
The first conclusion is that most of the schizotypal symptoms can be reliably assessed with the SIS-R. The second conclusion is that most of the schizotypal signs do not reach sufficient levels of reliability.
After excluding unreliable items the shortened SIS-R is a reliable research instrument for measuring schizotypal features (as far as it concerns our mixed samples) and it covers all three dimensions of schizotypy.

In chapter 6 we examined in 63 first-degree relatives of schizophrenia patients, whether a questionnaire (SPQ) and an interview (SIS-R) assess the dimensions of schizotypy equally. In a multitrait-multimethod design we used confirmatory factor analysis in order to test the hypothesis that the data are best described using three latent trait factors (Positive, Negative and Desorganisation Schizotypy) and two latent method factors (questionnaire and interview). This five factor model did not fit the data. A four factor model, including two trait factors (Positive and Negative Schizotypy) and the two method factors, had a good fit to the data. It showed that questionnaire and interview measures of Positive and Negative Schizotypy equally assess these dimensions (that is had similar levels of variance due to traits and methods and unexplained variance). Questionnaire and interview ratings of Desorganisation were highly unequivalent (that is they had no shared trait variance and questionnaire Desorganisation even loaded on the Positive dimension). It is very likely that for this reason we failed to confirm the five factor model. The results imply that questionnaire and interview measures for Positive and Negative Schizotypy can be used interchangeably. They also imply that the questionnaire is not a valid measure for Desorganisation. Whether the interview will qualify as a valid measure is to be expected, but remains to be seen.

In chapter 7 we presented a meta-analytical review of 33 studies into the neurocognitive correlates of dimensions of self-report schizotypy in normal subjects. The goal was to explore and arrange the neurocognitive correlates of each schizotypal dimension. This descriptive review may be of use in generating future studies and may contribute to the refinement of neurocognitive theories.
The results provide evidence for the construct validity of multiple dimensions of schizotypy. The main conclusions are that self-report Positive Schizotypy (PS) in normal subjects is associated with abnormalities in Smooth Pursuit Eye Movements, Continuous Performance Task, Wisconsin Card Sorting Test, Visual Backward Masking, Latent Inhibition and possibly Span of Apprehension performance. Self-report Negative Schizotypy (NS) in normal subjects is associated with abnormalities in Smooth Pursuit Eye Movements, Continuous Performance Task, Visual Backward Masking and Wisconsin Card Sorting Test performance. PS is more strongly related than NS to SPEM and CPT, NS is more strongly related than PS to WCST. These findings suggest that in the development of Positive and Negative Schizotypy different neurocognitive mechanisms are the main determinants.
Nonconformity and Desorganisation Schizotypy, however, were seldomly investigated in these neurocognitive studies.
The findings have several implications. First, the findings with respect to Positive and Negative Schizotypy in normal subjects can serve as hypotheses for future studies into causal mechanisms. Second, the findings (with respect to the neurocognitive correlates of Positive Schizotypy in normal subjects) are hard to reconcile with the findings from schizophrenia studies, almost always showing a lack of neurocognitive correlates of the Positive dimension. This divergency points to sample-differences. Finally, the findings with respect to Positive Schizotypy are hard to reconcile with the hypothesis that temporal-limbic dysfunctions (only) underly Positive Schizotypy. The findings with respect to Negative Schizotypy in normal subjects do converge with findings from schizophrenia studies, and support the hypothesis that mainly prefrontal dysfunctions underly Negative Schizotypy.

In chapter 8 we examined the neurocognitive correlates of dimensions of schizotypy in 63 healthy first-degree relatives of schizophrenia patients in order to test hypotheses from chapter 7 and from the neurodevelopmental model by Walker and Gale (1995). Neurocognitive measures of attention, verbal memory and prefrontal functioning were related to self-report and interview measures of schizotypy. The main findings are as follows. State-psychopathology (anxiety and depression) was a strong predictor for Positive (PS) and Negative Schizotypy (NS). PS was only slightly correlated to verbal memory, which is weak support for the hypothesis of temporal-limbic malfunction underlying PS. NS was not correlated to prefrontal measures and therefore no support was found for the hypothesis of prefrontal malfunction underlying NS. Desorganisation Schizotypy (DS) was strongly correlated to the false alarm variable of the Continuous Performance Test (CPT), probably supporting the hypothesis of orbitofrontal malfunction underlying DS.

The correlational pattern of DS in this study agrees well with two schizophrenia studies reporting a strong relationship between formal thought disorder and the false alarm CPT-variable. This similarity between first-degree relatives and schizophrenia patients can be considered as evidence that false alarms on the CPT and (subtle) problems in goal-directedness of thinking are indicators of the genetically determined vulnerability to schizophrenia.

In the final chapter we discussed the main findings and their implications for theoretical models, assessment and future research. The main conclusions from this thesis are that 1) schizotypy consists of at least three dimensions, 2) schizotypal symptoms can be rated with higher reliability than signs, 3) the dimensions of Positive and Negative Schizotypy are equally assessed with either SPQ or SIS-R; Desorganisation Schizotypy is unequally assessed with SPQ and SIS-R, 4) schizotypy has dimension-specific neurocognitive correlates, and 5) these neurocognitive correlates are sample dependent.
The findings are in favor of genetic models of schizotypy and schizophrenia by showing similarities of neurocognitive patterns of schizotypal dimensions between first-degree relatives and schizophrenia patients, and discongruencies of these patterns between relatives and schizotypy in normal subjects. The findings support Meehl's model of schizotypy by showing a rather strong relationship between two different outcomes of the genetic vulnerability, viz. a lack of inhibition during sustained attention and subtle formal thought (or speech) disorder. It is likely that these two features are at the core of the genetic vulnerability to schizophrenia. They may represent the psychological heart of schizophrenia. The findings warn against the uncritical use of normal subjects in schizotypy research. It is likely that due to the use of questionnaires too many false positives have been included (and probably too many false negatives have been excluded) in the studies using normal subjects (as reviewed in chapter 7).
Future studies may confirm the hypothesis that Desorganisation and CPT-false alarms are at the core of the genetic vulnerability. These studies should be directed at a further exploration of the psychological components of the vulnerability. Future studies may also be directed to protective factors in order to facilitate the development of psychological preventive interventions.