Anomalous self-experiences in subjects with increased risk of developing psychosis

Tor Gunnar Værnes

TIPS Sør-Øst, Division of Mental Health and Addiction, Department of Research and Innovation, Oslo University Hospital

Dr. philos. thesis submitted to the Faculty of Medicine, University of Oslo

Oslo, Norway, 2021

© Tor Gunnar Værnes, 2022

Series of dissertations submitted to the
Faculty of Medicine, University of Oslo

ISBN 978-82-348-0079-5

All rights reserved. No part of this publication may be
reproduced or transmitted, in any form or by any means, without permission.

Cover: Hanne Baadsgaard Utigard.
Print production: Graphics Center, University of Oslo.

Contents

Acknowledgements

The studies reported in this thesis were carried out at TIPS Sør-Øst, Early Intervention in Psychosis Advisory Unit for South-East Norway, Department of Research and Invention, Division of Mental Health and Addiction at Oslo University Hospital, and were part of the Thematically Organized Psychosis research (TOP) study at NORMENT, University of Oslo and Oslo University Hospital. I am grateful to a number of people who have contributed in several ways to this thesis. First, I would like to thank the participating patients in the study. I am very grateful to you all for your participation in the thorough, in-depth assessments. Your willingness to share your experiences and to endure the lengthy assessments have been impressive and indispensable. My main supervisor, MD, Dr. Med. Paul Møller, Head of Mental Health Research Dept. at Vestre Viken Hospital Trust, and my co-supervisor and project leader of the studies in this thesis, Professor Jan Ivar Røssberg at Oslo University Hospital and University of Oslo, have been invaluable in helping me carrying out the work with this thesis. To Paul, I am very grateful for sharing of your deep knowledge and clinical and research expertise regarding phenomenological perspectives on schizophrenia and prodromal conditions. Your thorough and wise supervision, and continuous encouragement and patience have been an immense support. I am equally grateful to Jan Ivar for your extensive and wise supervision, helping me to understand the research process and guiding me all the way in the work with this thesis with your encouragement, helpful advice and great sense of humor. I am also very grateful to you, as a former leader of TIPS Sør-Øst, for giving me the opportunity to carry out this research project as part of my position at TIPS Sør-Øst.

My sincere gratitude also goes to the current leader of TIPS Sør-Øst, MD, Dr. Med Kristin Lie Romm. This thesis could not have been carried out without your patience and support, and your contributions as a co-author have been very helpful. Next, I would like to thank Professor Ole Andreassen, Head of NORMENT, and Professor Ingrid Melle, co-director of NORMENT, for letting me take part in the TOP study, and for all helpful support and advice. I would like to give a special thanks to the TOP administrative staff, in particular Thomas Bjella and his assistants, for handling my data files, and to the research assistants at NORMENT, as well as to Dag Skjelstad at Vestre Viken Hospital Trust, for contributions regarding data collection. My sincere thanks also go to Ingrid Melle and to Professor Barnaby Nelson at Orygen and Melbourne University for very helpful contributions and advice as co-authors. A special appreciation goes to all my current and former colleagues at TIPS Sør-Øst for all advice, support and valuable discussions. I am very pleased to be part of such a highly

competent, enthusiastic team, which is also great fun to work with. I am also very grateful to the personnel at the clinical units I have recruited patients from for their cooperation in this recruitment process. In particular, I would like to thank the personnel at TIPS Ung at BUP Oslo South, the TIPS-team at DPS Oslo South and TIPS, Asker DPS. I would also like to thank Petter Lohne and other members of the former study group on phenomenological perspectives on psychosis for stimulating and very interesting discussions. In addition, I am grateful to all other clinicians and researchers I have met and discussed this research project with during the last years. Your interest in this field of research, and your comments and advice have been very helpful. Last, but not least, I wish to thank my wife Hege and my children, Lars, Emil and Ida for all invaluable emotional support and love.

P.S. The paper on study 4 was accepted for publication, but not published, in European Archives of Psychiatry and Clinical Neuroscience when this thesis was submitted to University of Oslo, Faculty of Medicine in October 2021. This paper was published in November 2021:

Værnes, T.G., Røssberg, J.I., Melle, I. *et al.* Basic self-disturbance trajectories in clinical high risk for psychosis: a one-year follow-up study. *Eur Arch Psychiatry Clin Neurosci* (2021). https://doi.org/10.1007/s00406-021-01349-6

Summary

The overall aim of this thesis was to investigate the presence, severity and quality of anomalous self-experiences in subjects with increased risk for psychosis, and the cross-sectional and prospective relationships between these phenomena, other clinical symptoms and functioning, and background factors.

These anomalies are assumed to reflect a 'basic self-disturbance', involving an abnormality in *subjectivity*, i.e. the spontaneous, implicit sense of "ownership" to experiences and actions. Such anomalies are characteristic features of schizophrenia spectrum disorders, and assumed to constitute a common ground for psychosis symptom formation and articulation in these conditions. They have also been shown to characterize the prodrome of schizophrenia, in retrospective studies. However, prospective studies investigating anomalous self-experiences in subjects at clinical high-risk of psychosis are sparse. Such studies are important to investigate whether these experiences may function as prospective clinical markers of conditions associated with elevated risk for psychosis, schizophrenia spectrum disorders or other adverse clinical outcomes.

The first aim of the thesis was to investigate anomalous self-experiences with the Examination of Anomalous Self-Experience (EASE) in a clinical high-risk sample of 38 patients, aged 15-29 years, and cross-sectional associations with other symptoms, present and childhood psychosocial functioning and childhood trauma. Total levels of these experiences were in line with findings in other clinical high-risk studies, and were particularly enhanced in subjects with schizotypal personality disorder or with cognitive disturbances according to the basic symptom concept (COGDIS). Each of the four most frequent EASE-items were present in 66-82% of the sample. We found significant correlations between anomalous self-experiences and negative and disorganization symptoms, but only negative symptoms explained a significant amount of the variance in the total levels of these experiences.

Accounts of anomalous self-experiences from subjects with schizophrenia spectrum conditions seem to have many similarities with certain depersonalization and derealization phenomena in conditions assumed to be outside the spectrum. Accordingly, the second aim of the thesis was to explore similarities and differences in the descriptions of anomalous self-experiences in two clinical high-risk cases, one with DSM-IV schizotypal personality disorder and one with DSM-IV depersonalization disorder. In both cases, descriptions reflected central dimensions of basic self-disturbance, i.e. diminished self-affection/self-presence and

hyperreflexivity, as well as prototypical depersonalization phenomena. In contrast to the depersonalization disorder case, the schizotypal case was more inclined to attribute the experiences to an external (unknown) force. The externally triggered onset of anomalous self-experiences in the depersonalization disorder case (episode of cannabis use and panic anxiety) differed from the more insidious, childhood onset in the schizotypal case, with no clear triggers. These findings might be accounted for by an updated model of self-disorders, proposing that anomalous self-experiences have a reactive-defensive character in depersonalization disorder, less likely to develop in to psychotic symptoms. In schizophrenia spectrum conditions however, we may find a combination of "primary" anomalies in self-experience (associated with neurodevelopmental disturbances) and "secondary", reactive anomalies in self-experience, rendering the affected subjects more vulnerable for a psychotic decompensation.

The third aim of the thesis was to investigate the relationship between basic self-disturbance at baseline and the clinical and functional outcome one year after the baseline assessments, in a sample comprising 32 clinical high-risk patients (the same sample as in study I, except six drop-outs). We found that higher total levels of anomalous self-experiences at baseline were associated with symptomatic and functional non-remission, more severe negative and disorganizations symptoms, and predicted more severe positive (attenuated) symptoms and lower level of functioning, all at follow-up. Symptomatic and functional non-remission was also associated with higher baseline levels of negative symptoms and lower level of functioning.

The fourth and final aim of the thesis was to investigate whether and how levels of anomalous self-experiences changed from baseline to follow-up, and associations with other clinical and functional characteristics at baseline and follow-up. Total levels of these experiences decreased significantly in the sample as a whole (n = 32), but individual trajectories varied considerably. High follow-up levels were associated with more severe negative symptoms and cognitive disturbances at baseline, and correlated strongly with more severe positive, negative, disorganization and general symptoms, and with lower level of functioning, at follow-up. Total levels of anomalous self-experiences at follow-up were also significantly higher in subjects with a schizophrenia spectrum disorder diagnosis at follow-up (9 of 12 with schizotypal personality disorder). Increasing levels of these experiences from baseline to follow-up were associated with higher baseline levels, and with more severe clinical and functional status at follow-up.

In conclusion, these studies have demonstrated that anomalous self-experiences may constitute important clinical markers in clinical high-risk conditions for the prospective identification of adverse (and more beneficial) clinical and functional outcomes. Subjects with high levels of anomalous self-experiences, more severe negative symptoms, and a lower level of functioning seem to be particularly vulnerable for symptomatic and functional non-remission. At follow-up, high levels of anomalous self-experiences were strongly associated with a more severe symptomatic and functional profile, irrespective of psychosis transition, pointing to a consolidation of a clinical gestalt as the time passed. In addition to constituting an important prognostic tool, phenomenologically oriented assessment of (anomalous) self-experience may have strong implications for clinical understanding and therapeutic interventions, relating symptomatic manifestations to a subjective, experiential level.

List of papers

Study 1

Værnes TG, Røssberg JI, Møller P. Anomalous self-experiences are strongly associated with negative symptoms in a clinical high-risk for psychosis sample. *Compr Psychiatry* 2019; 93: 65-72, doi: 10.1016/j.comppsych.2019.07.003.

Study 2

Værnes TG, Røssberg JI, Møller P. Anomalous self-experiences: markers of schizophrenia vulnerability or symptoms of depersonalization disorder? A phenomenological investigation of two cases. *Psychopathology* 2018; 51(3):198-209, doi: 10.1159/000488462.

Study 3

Værnes TG, Røssberg JI, Møller P, Melle I, Nelson B, Romm KL, Møller P: Basic self-disturbance in subjects at clinical high risk for psychosis: Relationship with clinical and functional outcomes at one year follow-up. *Psychiatry Research* 2021

Study 4

Værnes TG, Røssberg JI, Møller P, Melle I, Nelson B, Romm KL, Møller P: Basic self-disturbance trajectories in clinical high-risk for psychosis: A one year follow-up study. *Eur Arch of Psych and Clin Neurosc* 2021 (accepted for publication October 2021)

Abbreviations

ASE(s)	Anomalous Self-Experience(s)
APS	Attenuated Psychotic Symptoms
AUDIT	Alcohol Use Disorder Identification Test
BIPS	Brief Intermittent Psychotic Symptoms
BSABS	Bonn Scale for the Assessment of Basic Symptoms
BSD	Basic Self-Disturbance
CAARMS	Comprehensive Assessment of At-Risk Mental States
CDSS	Calgary Depression Scale for Schizophrenia
CHR	Clinical High Risk (for psychosis)
CMS	Cortical Midline Structures
COGDIS	(High-risk criterion) Cognitive Disturbances
COPER	(High-risk criterion) Cognitive-Perceptual disturbances
COPS	Criteria of Prodromal Syndromes
CTQ-SF	Childhood Trauma Questionnaire - Short Form
DMN	Default Mode Network
DPD	Depersonalization Disorder
DSM	Diagnostic and Statistical Manual (III, IV or 5)
DUDIT	Drug Use Disorders Identification Test
EASE	Examination of Anomalous Self-Experience
GAF	Global Assessment of Functioning
S-GAF	Global Assessment of Functioning – split version
GAF-F	Global Assessment of Functioning – Functioning scale
GAF-S	Global Asssessment of Functioning – Symptom scale
GRD	Genetic Risk and Deterioration Syndrome
ICD-10	International Statistical Classification of Diseases and Related Health Problems 10^{th} version
JIR	Jan Ivar Røssberg
PAS	Premorbid Adjustment Scale
PM	Paul Møller
POPS	Presence of Psychotic Syndrome
SCID-I	Structured Clinical Interview for DSM-IV Axis I disorders

SIPS	Structured Interview for Prodromal Syndromes (Structured Interview for Psychosis-risk Syndromes in post-2010 versions)
SOPS	Scale of Prodromal Symptoms (Scale of Psychosis-risk Symptoms in post-2010 versions)
SPD	Schizotypal Personality Disorder
SPI-A	Schizophrenia Proneness Instrument, Adult version
SPI-CY	Schizophrenia Proneness Instrument, Child & Youth version
SPSS	Statistical Package for the Social Sciences
SSD(s)	Schizophrenia Spectrum Disorder(s)
TGV	Tor Gunnar Værnes
UHR	Ultra-High risk

"I can suddenly feel that I don't know who I am… seeing myself from the outside, not feeling any connection to myself…"

"Eva" – participant in the present study

1. INTRODUCTION

In a qualitative study in Norway, retrospectively examining subjective experiences during the prodromal phase in patients with schizophrenia or schizophreniform disorder (shortly after their very first psychotic episode), almost all described profound and painful disturbances in the experience and perception of themselves. In most cases, this was accompanied by a preoccupation of metaphysical, philosophical or supernatural ideas, and a withdrawal to an inner world (Moller & Husby, 2000). Very similar descriptions of prodromal self-disturbances were collected from first-admission patients with schizophrenia in a study in Denmark (Parnas, Jansson, Sass, & Handest, 1998). These two studies, conducted in the 1990's, sparked a rebirth of phenomenologically oriented international interest in self-disturbances in the schizophrenia spectrum. Many studies have followed during the last two decades, demonstrating that such disturbances indeed characterize the schizophrenia spectrum disorders (SSDs), e.g. (Handest & Parnas, 2005; Haug, Lien, et al., 2012; Nordgaard & Parnas, 2014; Parnas, Handest, Jansson, & Saebye, 2005; Parnas, Handest, Saebye, & Jansson, 2003; Parnas et al., 2011; Raballo, Saebye, & Parnas, 2009).

A self-disorder model of schizophrenia was launched, postulating a *disorder of the basic sense of self* as a core feature of schizophrenia, also termed an *'ipseity disturbance'* or a *'basic self-disturbance'* (BSD) (Nelson, Parnas, & Sass, 2014; Nelson & Raballo, 2015; L.A. Sass & Parnas, 2003). The development and phenomenological manifestations of the seemingly disparate positive, negative and disorganization symptoms, typically present in schizophrenia, were considered to be rooted in a common connectedness to this self-disorder. Accordingly, self-disorders/BSD have been suggested as important vulnerability factors for psychosis development, particularly with respect to schizophrenia and other schizophrenia spectrum disorders (Nelson & Raballo, 2015; L.A. Sass & Parnas, 2003).

Hence, early detection of these disturbances in the basic sense of self may be of considerable value in the early identification of subjects at particularly high risk of these adverse clinical outcomes. However, the validity of BSD as a vulnerability factor cannot fully rely on

retrospective studies of the prodrome of schizophrenia or cross-sectional studies in subjects with established schizophrenia or other psychotic disorders. Studies are needed which investigate BSD in subjects at clinical high-risk (CHR) of psychosis, and associations between BSD and concomitant and future clinical symptoms, functioning and background factors. When planning this thesis, no CHR studies had yet been published investigating BSD and other clinical features longitudinally. Hence, we saw a need to set up such a study. Prospective studies (also including investigations of cross-sectional relationships) may reveal whether BSD indeed constitute a marker of clinical and functional outcomes in CHR for psychosis, including (but not restricted to) schizophrenia spectrum disorders.

Additionally, it is important to explore these phenomena in their own right, as they usually have a significant impact on the afflicted person (Parnas & Handest, 2003), and are known from other studies to be associated with personal suffering, increased suicidality (Haug, Melle, et al., 2012; Skodlar & Parnas, 2010) and social dysfunction (Haug et al., 2014). Self-disturbances are regularly very difficult for the afflicted individual to communicate (Moller & Husby, 2000), and a guided, qualitative, phenomenologically oriented exploration of these phenomena by an interviewer who is familiar with these phenomena, may have an important therapeutic value for the patient (Škodlar & Henriksen, 2019).

The overall aim of this thesis was to investigate BSD in subjects with increased risk for psychosis, and the cross-sectional and prospective relationships between self-disturbances, other clinical symptoms and functioning, and background factors.

1.1. Clinical high risk for psychosis, the prodrome and related terms

1.1.1. The schizophrenia prodrome and the ultra-high risk for psychosis approach

In the research literature on psychosis-risk conditions, the CHR concept (also referred to as the CHR-P concept (Fusar-Poli, 2017)) is used in mainly two ways. First, it exclusively refers to the so-called ‘ultra-high risk’ (UHR) for psychosis criteria (Jean Addington et al., 2017; T. Y. Lee et al., 2014; Piskulic et al., 2012a), originally introduced by Yung and colleagues (Yung et al., 2003). Second, it is used as a broader term to cover the two main approaches in the field of early identification of subjects at increased risk for psychosis. These are the

mentioned UHR approach, and the 'basic symptoms' high-risk approach (Fusar-Poli, Borgwardt, et al., 2013; Schultze-Lutter et al., 2015). In this thesis, the CHR concept will refer to this broader use of the term, if not otherwise specified.

The UHR criteria were first developed and defined by an Australian research group who set up a research agenda and established a research clinic (the "Personal Assessment and Crisis Evaluation (PACE) Clinic") in 1994. Central aims were to identify features associated with increased risk of psychosis, improve understanding of the psychopathology of psychosis development, and to develop and evaluate interventions (P. D. McGorry, Yung, & Phillips, 2003; Yung et al., 1996; Yung et al., 2003). Interventions were aiming to ameliorate, delay or hopefully prevent the onset of psychotic disorders, but also to reduce current symptoms (P. D. McGorry et al., 2003; Yung et al., 2003; Yung, Phillips, Yuen, & McGorry, 2004).

In this endeavor, they questioned the utility and clinical implications of the schizophrenia 'prodrome' concept. The 'prodrome' (derived from Greek 'prodromos', meaning the forerunner of an event (Yung & McGorry, 1996)), is a term commonly used in medicine and mental health to denote early signs and symptoms indicating the onset of a disorder. With respect to psychotic disorders, the prodrome had been defined accordingly, e.g. by Beiser, who defined it as the period from the first noticeable symptoms to the first prominent psychotic symptoms (Beiser, Erickson, Fleming, & Iacono, 1993). The prodrome of schizophrenia was described early in the history of psychiatry, mainly through retrospective reconstructions of this phase, based on interviews with patients and other information sources (e.g. by Bleuler and Conrad) (Bleuler, 1950; Conrad, 1958).

Before the 1990s, most investigations of the prodrome were of an anecdotal nature or based on non-standardized interview techniques (Yung & McGorry, 1996). The majority of frequently identified prodromal features in these investigations were quite non-specific, e.g. depression, anxiety, irritability, sleep disturbances, reduced drive and motivation, social withdrawal, disturbances in concentration, suspiciousness and deterioration of role functioning (Yung & McGorry, 1996). More specific symptoms associated with disturbances in subjective experiences were also identified, e.g. by Chapman. He claimed that certain characteristic disturbances in the ability to filter out irrelevant sensory stimuli could underlie other specific subjective symptoms, more unspecific neurotic symptoms and later development of psychotic symptoms (Chapman, 1966). Early studies indicated a large

variability in the length of the prodrome, from months to several years (Yung & McGorry, 1996).

A list of prodromal features was included in the DSM-III-R as criteria for a prodromal syndrome (American Psychiatric Association, 1987). This list primarily included behavioral symptoms, in line with the operationalistic trend characterizing the invention of DSM-III (Andreasen, 2007; Parnas, Sass, & Zahavi, 2013). Symptoms mainly subjective in nature were not included, due to the difficulties in reliably measuring these (Yung & McGorry, 1996), e.g. the attentional disturbances emphasized by Chapman and McGhie as fundamental symptoms (Chapman, 1966; McGhie & Chapman, 1961). The DSM-III-R prodromal list was not included in DSM-IV and in ICD-10, due to concerns about the validity and reliability of the criteria (Yung & McGorry, 1996).

Yung and McGorry highlighted the need for more methodologically sound studies of the prodrome of psychotic disorders (Yung & McGorry, 1996). There were difficulties in pinpointing the onset of the prodromes, and there was some conceptual confusion, e.g. through extended use of the concept by some authors to include early warning signs of relapse (Herz & Melville, 1980; Norman & Malla, 1995; Subotnik & Nuechterlein, 1988). Symptoms characterizing the initial prodrome were often treated as the first manifestations of a disorder already in progress (Chapman, 1966). Yung and colleagues argued that we cannot know beforehand whether certain signs and symptoms signify the inevitable development of schizophrenia or other psychotic disorders. Hence, the prodrome concept should be reserved for retrospective considerations. They suggested the '*at-risk mental state*' as a more appropriate term to denote the clinical presentation of subjects considered to have a heightened vulnerability for psychosis development (Yung et al., 1996).

Aiming for a prospective identification of putatively prodromal subjects, they developed and operationalized the so-called UHR criteria. These criteria defined three groups of at-risk subjects. These were (1) the *Attenuated Psychotic Symptoms (APS)* group, (2) the *Brief Limited Intermittent Psychotic Symptoms (BLIPS)* group, characterized by experiences of recent short-lasting, spontaneously abating frank psychotic symptoms, and (3) the *Genetic Risk and Deterioration (GRD)* group, characterized by a presumed genetic vulnerability (schizotypal personality disorder or having a first degree relative with a psychotic disorder) combined with a significant decrease in functioning within the past year (P. D. McGorry et al., 2003; Yung et al., 2003). Overlaps between these groups were possible. As most first episodes of psychosis occur in young adults or adolescence (Häfner, Maurer, Löffler, &

Riecher-Rössler, 1993; Solmi et al., 2021), these criteria only pertained to help-seeking youth (14-30 years) (Yung et al., 2003).

With these criteria they aimed to detect subjects at incipient risk of psychotic disorders (within the next 12 months), and to maximize the predictive power (to avoid engaging "false positives", i.e. subjects never developing psychotic disorders). They chose the UHR term to differentiate this approach from traditional genetic risk studies relying on family history of psychosis as the primary inclusion criterion, e.g. the Copenhagen Schizophrenia High-Risk Project (Cannon & Mednick, 1993). The problem with the genetic risk approach from an early intervention perspective was the low predictive value and high false positives rate (the majority of cases with schizophrenia have no first-degree relative with schizophrenia) (P. D. McGorry et al., 2003). The predictive target was first episode psychosis rather than schizophrenia, because a significant minority of transitioning cases develop psychotic disorders outside of the schizophrenia spectrum (P. D. McGorry et al., 2003). In this thesis, the UHR criteria constituted main inclusion criteria.

1.1.2 The basic symptoms approach

In contrast to the UHR-criteria, which largely focused on behavioral and other observable "attenuated" psychotic symptoms, the more phenomenologically oriented German 'basic symptoms' approach focused on subjectively experienced phenomena, which were not directly observable. These included subtle, sub-clinical disturbances, particularly cognitive and perceptual, but also phenomena related to drive, stress tolerance, affect, speech, and motoric function (Klosterkotter, 1992; Schultze-Lutter, 2009). Gerd Huber coined the 'basic symptoms' term, considering these symptoms as the earliest neurobiological manifestations of schizophrenia, i.e. the "basis" of the disorder (Gross, 1989; Huber & Gross, 1989). The basic symptoms could be present in every stage of the illness, i.e. in the initial prodrome, before relapse to a new psychotic episode, or even during a psychotic episode. During the prodrome, the basic symptoms were assumed to gradually increase in number and severity until they in most cases developed into psychotic symptoms (triggered by stressful situations and demands) (Schultze-Lutter, 2009). In some cases they would spontaneously remit and not develop into psychotic symptoms (the so-called "outpost syndromes") (Huber & Gross, 1989). Basic symptoms were first operationalized in the Bonn Scale for the Assessment of Basic Symptoms (BSABS) (Gross, Huber, Klosterkkotter, & Linz, 1987) and in the Frankfurt Complaint Questionnaire (Süllwold & Huber, 1986a, 1986b).

Some basic symptoms have been demonstrated to be more specific to psychosis development (particularly in schizophrenia), and include cognitive and perceptual disturbances, e.g. thought interference, thought pressure, captivation of attention by details, and derealization (Klosterkotter, Hellmich, Steinmeyer, & Schultze-Lutter, 2001; Schultze-Lutter, 2009). These symptoms are currently included in two prodromal or high-risk basic symptoms sets, the cognitive-perceptual basic symptoms (COPER) and the high-risk criterion cognitive disturbances (COGDIS). There is a considerable overlap between these sets, but the COGDIS criterion has been demonstrated to be more precise with respect to the prediction of schizophrenia, and to reflect a more imminent risk of psychosis (Schultze-Lutter, Addington, Ruhrmann, & Klosterkotter, 2007; Schultze-Lutter, Ruhrmann, & Klosterkotter, 2006).

1.1.3 Assessment of CHR conditions

The Australian research group behind the definitions of the UHR criteria developed the Comprehensive Assessment of At-Risk Mental States (CAARMS) for the reliable assessment of risk factors assumed to indicate imminent development of a psychotic disorder, and to determine if an individual met the UHR criteria. The instrument displayed good to excellent reliability and high predictive validity (Yung et al., 2005). Following its development, the CAARMS has been extensively used in Australia, Asia and Europe.

In the USA, Thomas McGlashan, Tandy Miller, and colleagues at the Prevention through Risk Identification, Management and Education (PRIME) prodromal research team at Yale University, designed another instrument for risk identification of the three UHR syndromes, and to quantitatively rate the presence and severity of prodromal symptoms. This was the Structured Interview for Prodromal Syndromes (SIPS), which also included the Scale of Prodromal Symptoms (SOPS) to assess the presence and severity of (attenuated) positive symptoms, negative symptoms, disorganization symptoms and general symptoms (Miller et al., 2003; Miller et al., 1999; Rosen, Woods, Miller, & McGlashan, 2002). The SIPS and SOPS was revised and renamed in 2009-2010 as the Structured Interview for Psychosis-risk Syndromes and the Scale of Psychosis-risk Symptoms (Thomas H. McGlashan, Walsh, & Woods, 2010) The CAARMS and the SIPS/SOPS address the same UHR criteria, but their operationalization differs in several ways (Fusar-Poli, Cappucciati, Rutigliano, et al., 2016). The SIPS has also been demonstrated to have excellent interrater reliability among trained raters (Miller et al., 2003), and to identify UHR subjects and predict future psychosis at similar rates as the CAARMS (Fusar-Poli et al., 2012; Fusar-Poli, Cappucciati, Rutigliano, et

al., 2016; Schultze-Lutter et al., 2015). The SIPS is also widely used around the world in research and clinical settings.

High-risk basic symptoms, including COPER and COGDIS criteria are assessed with the Schizophrenia Proneness Instrument, Adult (SPI-A) (F. Schultze-Lutter et al., 2007) or Child & Youth version (SPI-CY) (Fux, Walger, Schimmelmann, & Schultze-Lutter, 2013). This instrument is based on the Bonner Scale for the Assessment of Basic Symptoms (BSABS) (Gross et al., 1987), which has been demonstrated to possess good interrater reliability (Vollmer-Larsen, Handest, & Parnas, 2007). The SPI-A has also been demonstrated to display good inter-rater reliability (Schultze-Lutter, Klosterkötter, Picker, Steinmeyer, & Ruhrmann, 2007). A meta-analysis revealed that the conversion rates for COGDIS positive samples ranged from 25.3 % after one year to 61.3 % at >4 years. This was not significantly different from the conversion rates in CAARMS and SIPS samples at 6 months, one and two years, but conversion rates for COGDIS samples were significantly higher thereafter (Schultze-Lutter et al., 2015). In this thesis, assessment of UHR criteria with the SIPS/SOPS was supplemented with assessment of COGDIS criteria.

1.1.4 CHR for psychosis – targeted interventions and ethical concerns

A major reason for the introduction of operationalized criteria for the identification of subjects at putative high risk of psychosis was the increased possibilities for targeted interventions (P. D. McGorry et al., 2003). The prevention or at least postponement of psychosis has been, and still is, a primary target for interventions in CHR conditions, as well as preventing delays to accessing mental health services and diminishing the duration of untreated psychosis in the case of transition. However, in recent years CHR interventions have focused more broadly on a range of both current and future clinical and functional needs, reflecting the heterogeneity of clinical trajectories and risk factors (Fusar-Poli et al., 2019; Mei et al., 2021; Schmidt et al., 2015).

Recommendations for interventions in CHR are mainly focusing on psychosocial interventions like cognitive behavioral therapy (CBT), psychoeducation, family interventions, case management, cognitive and social skills training, and supported education/employment (Schmidt et al., 2015; E. Thompson et al., 2015; Woodberry, Shapiro, Bryant, & Seidman, 2016). A staged approach is favored, tailored to the individual needs of the patient, with the least restrictive service approach offered as the first choice (P.D. McGorry et al., 2009; Schmidt et al., 2015). Antipsychotics are in general not recommended in CHR conditions, but

some international guidelines recommend short-term treatment with second generation, low-dose antipsychotics if psychosocial interventions have proved ineffective, and symptomatology is severe and progressive (J. Addington, Addington, Abidi, Raedler, & Remington, 2017; Schmidt et al., 2015). Meta-analyses of treatment effects have found marked reductions of transition rates at one year following targeted interventions (54% reduction (van der Gaag et al., 2013), 43% reduction (Mei et al., 2021)). CBT was the only intervention more efficient than control conditions in reducing the transition rates in the most recent of these studies (Mei et al., 2021). However, a Cochrane meta-analysis and an umbrella review (a review of meta-analyses) found no clear evidence that any specific interventions (including CBT, other psychological, pharmacological and psycho-social interventions) were significantly more effective than others, including control treatment conditions ("treatment as usual") (Bosnjak Kuharic, Kekin, Hew, Rojnic Kuzman, & Puljak, 2019; Fusar-Poli et al., 2019). Likewise, no specifically targeted interventions were more successful with respect to other treatment targets, e.g. social and general functioning, depression and distress, quality of life, or the severity of positive and negative symptoms (Fusar-Poli et al., 2019; Mei et al., 2021). The lack of significant treatment effects may be due to low statistical power and the high heterogeneity of CHR populations, the latter highlighting the need to tailor interventions according to the specific needs and level of risk in each person (Fusar-Poli et al., 2019).

Ethical concerns have been raised regarding the identification and treatment of CHR conditions, which may or may not develop into psychosis, e.g. with respect to the introduction of the Attenuated Psychosis Syndrome as a diagnostic category in DSM-5 (Fusar-Poli, Carpenter, Woods, & McGlashan, 2014; Heinssen & Insel, 2015; Moritz, Gawęda, Heinz, & Gallinat, 2019; Yung, Nelson, Thompson, & Wood, 2010). Among these concerns have been findings of significant side effects (e.g. weight gain) in CHR individuals treated with antipsychotics, and uncertain or not significant preventive effects (T.H. McGlashan et al., 2006; Schmidt et al., 2015; Stafford, Jackson, Mayo-Wilson, Morrison, & Kendall, 2013). However, as previously noted, antipsychotics are not part of the recommended treatment of CHR conditions in most countries (but in some countries, e.g. the USA, antipsychotics seem to be prescribed more often) (Yung et al., 2019). Another concern has been the fear and stigma related to being defined as belonging to a high-risk of psychosis group (Heinssen & Insel, 2015; Moritz et al., 2019). This has been countered by pointing out that CHR services are carefully designed to diminish stigma, e.g. by conveying a message that improvement and

recovery is possible, and by not situating these services in "traditional" mental health institutions (Yung et al., 2019).

In light of the more broad focus of CHR interventions during the last years, we were in this thesis interested in the identification of clinical characteristics and needs in addition to conventional psychosis-risk symptoms. In particular, this included anomalous self-experiences, which may be associated with clinical suffering (including suicidality), deficits in functioning and more severe symptom development (Haug, Melle, et al., 2012; Haug et al., 2014; L.A. Sass & Parnas, 2003; Skodlar & Parnas, 2010).

1.1.5 CHR for psychosis – current challenges

Since the introduction of the UHR and the basic symptoms high-risk criteria, many studies have investigated the predictive value of these criteria. A meta-analysis from 2013, including 27 studies published between 1996 and 2011, found a transition rate of 22% at 1 year, 29% at 2 years and 36% after three years (Fusar-Poli et al., 2012). In recent years, transition rates have decreased (Fusar-Poli et al., 2012; Schultze-Lutter et al., 2015; Wiltink, Velthorst, Nelson, McGorry, & Yung, 2015), and a review of meta-analyses published after 2013 (only including UHR studies) found a transition rate of 22% after three years (Fusar-Poli et al., 2020). Most UHR subjects meet the APS criteria (APS: 85%, BLIPS: 10%, GRD: 5%), and transition rates differ considerably between the three UHR subgroups (BLIPS: 39% at 2 years, APS: 19% at 2 years, GRD: 3%) (Fusar-Poli, Cappucciati, Borgwardt, et al., 2016). This has led to suggestions that the UHR concept should be restricted to APS and BLIPS, due to the low transition rates in the GRD group (e.g. not higher than in clinical control groups) (Fusar-Poli, Cappucciati, Borgwardt, et al., 2016; Schultze-Lutter et al., 2015). An even more radical approach has been suggested, restricting the UHR concept to the APS subgroup only (Cornblatt & Carrión, 2016). In addition to the low predictive validity of the GRD group, the validity of the BLIPS criteria has been questioned, due to concerns that subjects meeting these criteria are already in a psychotic state (Cornblatt & Carrión, 2016; Fusar-Poli, Cappucciati, Borgwardt, et al., 2016). Two-thirds of subjects meeting BLIPS criteria have been found to simultaneously meet criteria in the ICD-10 for an "Acute and Transient Psychotic Disorder" (Fusar-Poli, Cappucciati, et al., 2017) .

In light of the varying transition rates, CHR approaches (particularly the UHR approach) have been criticized for overemphasizing the predictive validity of these criteria (Moritz et al., 2019; van Os & Guloksuz, 2017). Central to this critique is that transition rates are

significantly affected by differences in risk enrichment of samples *before* being defined as belonging to a CHR group (Fusar-Poli, Yung, McGorry, & van Os, 2014). A meta-analysis from 2016 revealed that the pretest risk for psychosis in help-seeking patients selected to be assessed according to CHR criteria was 15 %, with high heterogeneity (95% CI: 9%-24%) between the included studies (Fusar-Poli, Schultze-Lutter, et al., 2016). This heterogeneity probably reflects widely differing, opportunistic sampling strategies (Fusar-Poli, Schultze-Lutter, et al., 2016).

Epidemiological studies have revealed that attenuated psychotic symptoms are not that uncommon in the general population (van Os, Linscott, Myin-Germeys, Delespaul, & Krabbendam, 2009; Werbeloff et al., 2012), and even more frequent in non-psychotic disorders (Hanssen et al., 2003; Varghese et al., 2011). However, the yearly transition rate in population based samples with attenuated psychotic symptoms is low (0.56%, in a meta-analysis (Kaymaz et al., 2012)). As most UHR patients meet criteria for the APS syndrome (Fusar-Poli, Cappucciati, Borgwardt, et al., 2016)), it is obvious that transition to psychosis cannot be dependent on the presence of these symptoms alone. The longitudinal development from an attenuated psychotic state to a psychotic disorder is assumed to be driven by an interaction between genetic and environmental factors, impacting on a state characterized by both non-psychotic psychopathology (particularly affective dysregulation) and sub-threshold psychotic symptoms (van Os & Linscott, 2012). According to this model, attenuated psychotic symptoms are *trans-diagnostic phenomena*, which may be markers of multidimensional psychopathology rather than "schizophrenia light" symptoms (Fusar-Poli, Yung, et al., 2014; van Os & Linscott, 2012). These symptoms may only develop into a psychotic disorder in the context of a complex interplay with other risk factors (van Os & Linscott, 2012; van Os et al., 2020).

What may constitute pretest risk enrichment factors in CHR samples? First, CHR samples are comprised of help-seeking, distressed individuals, which more often than not are afflicted by affective psychopathology, particularly anxiety, depression and high perceived stress (Fusar-Poli, Nelson, Valmaggia, Yung, & McGuire, 2014; Fusar-Poli, Tantardini, et al., 2017). A range of other personal and environmental risk factors are also more common in CHR than in controls, e.g. disturbances in childhood and adolescent functioning, male gender, obstetric complications, childhood trauma and social disadvantages, e.g. unemployment (Fusar-Poli, Tantardini, et al., 2017). Several factors have also been identified which are more frequent in transitioning than in non-transitioning CHR individuals. These include negative and/or

disorganization symptoms (Demjaha, Valmaggia, Stahl, Byrne, & McGuire, 2012; Piskulic et al., 2012b; Ryan et al., 2017; Valmaggia et al., 2013; Velthorst et al., 2009), neurocognitive impairments (Jean Addington et al., 2017; Bolt et al., 2019; De Herdt et al., 2013), abnormalities in frontal and temporal brain regions (Niznikiewicz, 2019), social functioning (Jean Addington et al., 2017) and childhood trauma (Mayo et al., 2017).

Given complexities like these, when planning this thesis we were aware of and concerned about the specificity issue of the CHR criteria (particularly the APS criteria) as markers of risk for psychosis. Through phenomenological explorations of subjective experiences of the self and the world, we aimed to investigate whether BSD could be a useful supplementary characteristic of CHR conditions. We wanted to investigate whether BSD could affect future clinical outcomes and thus add to the predictive validity of the CHR criteria. During the first year of the data collection to this thesis, findings from a prospective study were published demonstrating that BSD indeed was significantly more common in a UHR sample than in healthy controls, and predicted transition to psychosis (Nelson, Thompson, & Yung, 2012). The findings of this study underlined the need for further investigations of BSD in CHR and associations with future outcomes.

However, studies of outcomes in CHR should not be restricted to transition to psychosis. First, the binary transition concept has been criticized with respect to validity and reliability. Transition implicates a qualitative shift from a non-psychotic to a psychotic state, dependent on quantitative shifts on continuous positive symptoms scales (Fusar-Poli, Yung, et al., 2014; van Os & Guloksuz, 2017). The concept is also somewhat arbitrarily defined, with different definitions in CAARMS and SIPS compared to definitions in the diagnostic manuals (ICD-10, DSM-IV) (Fusar-Poli, Yung, et al., 2014). Second, other factors than a worsening of positive symptoms may be more important for long-term clinical and functional outcomes (van Os & Guloksuz, 2017). Many non-transitioning individuals are not in clinical remission from attenuated psychotic symptoms for several years following the initial CHR assessment, and in a recent review the majority of these individuals were found to struggle with other non-psychotic mental disorders and functional deficits (Beck, Andreou, et al., 2019). Hence, in the present thesis we were interested in investigating clinical and functional outcomes more broadly, also focusing on the clinical and functional outcomes in non-transitioning subjects. With respect to the psychopathological understanding of different CHR trajectories, we suspected that longitudinal investigations of BSD in CHR could be of considerable relevance.

1.2. Self-disorders, basic self-disturbance and related terms

1.2.1. Phenomenology and early conceptualizations of self-disorders in schizophrenia

1.2.1.1 From Kraepelin to Blankenburg

Disorders of the self in schizophrenia have been described since the beginning of the 20th century. Emil Kraepelin considered that the fundamental features of 'dementia praecox' (later renamed as schizophrenia by Eugen Bleuler (Bleuler, 1950)) were disruptions in the unity of consciousness and a disorder of the will ("orchestra without a conductor") (Kraepelin, 1896). Bleuler considered schizophrenia to be characterized by a splitting of psychic functions which could manifest as a disunity of personality in marked cases (involving a "loosening of associations", referring to dissociations in the persons psyche, i.e. not a purely cognitive term) (Bleuler, 1950; Moskowitz & Heim, 2011). An Austrian psychiatrist, Joseph Berze, suggested that schizophrenia was characterized by subtle alterations in self-awareness (Parnas & Handest, 2003), and Hans Gruhle (one of Karl Jasper's colleagues at Heidelberg) allegedly coined the term self-disorder in 1915: "Tentatively, I call this passivity – the nonparticipation in one's own experience – a self-disorder…" (p. 874, translated quote) (A. Mishara et al., 2016).

Bleuler also considered *autism* as a fundamental feature of schizophrenia, however driven by, and secondary to, the loosening of associations. He defined this feature as a detachment from reality coupled with a predominance of an inner (fantasy) life (Bleuler, 1950). A French psychiatrist and pupil of Bleuler, Eugène Minkowski, reconceptualized this Bleulerian autism concept. He considered autism as the *phenomenal core* and the *"trouble gènèrateur"* (generative disorder) of schizophrenia. He defined this core feature as a *loss of "vital contact with reality"*, involving a deficit in the spontaneous, pre-reflective attunement ("lived synchronism") between the person and the world. The automatic, spontaneous feeling of being a living, vital, existing subject, embedded in, and interacting with, a "lived" and felt world, was severely disturbed (Minkowski, 1987; Parnas & Bovet, 1991; Parnas, Bovet, & Zahavi, 2002). The loss of this vital contact with reality further implied a fundamental disturbance in the natural, self-evident sense of "how to live" as a human being in the social and physical world, and a diminishment of the ability to be affected by the world, and to empathize with others. Typical manifestations of this disturbance were what later have been named negative symptoms, as well as compensatory efforts, e.g. "morbid rationalism"

(considering all human behavior as driven by purely logical rules) (Parnas & Bovet, 1991; Parnas et al., 2002; L. A. Sass, 2001). Symptoms were not considered by Minkowski as separate entities, but as intimately connected phenomena, emerging from, and shaped by, the "trouble gènèrateur" (Parnas et al., 2002).

These ideas about the schizophrenic autism were later elaborated by the German psychiatrist Wolfgang Blankenburg with his concept *'loss of natural self-evidence'*, first introduced in an article published in 1969 (translated version in reference) (Blankenburg & Mishara, 2001; L. A. Sass, 2001). The term 'natural self-evidence' referred to the normally unquestioned, pre-reflective 'common sense' orientation to the world, in which everyday situations and events are taken for granted. The loss of the common sense attitude to the world was considered as a basic disorder ('Grundstörung'), involving a qualitative alteration of the foundations of experience and consciousness. This 'Grundstörung' was leading to a profound *perplexity* in the encounters with the world, and was considered to underlie the typical symptoms in schizophrenia (particularly the negative or 'deficit' syndrome). It was also often accompanied by an exaggeration of self-awareness (hyperreflexivity) where "everything is just an object of thought" (as one of Blankenburg's patients "Anne" described her condition) (L. A. Sass, 2001). Normally unnoticed sensations and experiences became objects for an intense, analytical scrutiny, which involved monitoring and objectification of one's own experiences and actions, and an alienation both with respect to the world and the self (Parnas, 2011; L. A. Sass, 2001). In the current thesis, these kind of experiences were among the clinical features we were particularly interested in exploring in CHR conditions.

1.2.1.2 Phenomenology – history and definitions

Minkowski is considered as one of the founders of *phenomenological psychiatry* (along with Ludwig Binswanger), and the works of Blankenburg is also a main contribution to this tradition (L. A. Sass, 2001). While Minkowski himself was not considered to be a disciple of any phenomenological school of philosophy, this strain of psychiatry has been heavily inspired by phenomenological philosophers like Husserl, Heidegger, Merleau-Ponty, Henry and Polanyi (L. A. Sass, 2001; L.A. Sass & Parnas, 2003). Phenomenological psychiatry is particularly concerned with "grasping the *essential structures of human experience and existence*, both normal and abnormal" (L.A. Sass & Parnas, 2003)(p. 429). This tradition has fostered a strong interest in the disorders of the self in schizophrenia by a range of authors, including Jaspers (Jaspers, Hoenig, & Hamilton, 1997a, 1997b), Schneider (Schneider, 1959)

and others, e.g. Mayer-Gross (Mayer-Gross, Slater, & Roth, 1960), Laing (Laing, 1965) and Kimura (Kimura, 2001). It should be noted that the term *'phenomenology'* has been used in different ways. It has its roots in the term *'phenomenon'*, which in ancient Greek refers to the appearance of something. In contemporary Anglo-American psychiatry, phenomenology simply refers to the wide variety of manifestations of symptoms and signs related to a psychiatric disorder, amenable for description by an objective observer (L.A. Sass & Parnas, 2003). The use of the phenomenology term in this thesis is in accordance with its use in the strain of psychiatry inspired by the continental, phenomenological philosophic tradition.

1.2.1.3 Jaspers and Schneider – ego consciousness and ego disturbances

Jaspers confined the use of phenomenology to the study of "inner subjective experience". He is renowned as the founder of the phenomenological *method* in psychiatry. With this approach he aimed to establish an etiologically organized nosology of psychiatry, based on a differentiation of symptoms. With respect to symptoms, he focused more on the *forms* of awareness than the contents. Jaspers considered 'ego consciousness' (being conscious of his/her self) as characterized by four formal features: 1) ego demarcation in contrast to the external world and others, 2) a sense of activity, 3) a sense of identity over time, and 4) a sense of unity/of being the same person (Fuchs, 2015). The sense of activity ('activity consciousness') was considered by Jaspers to be particularly important for the normal sense of self, as this feature "personalized" perceptions, sensations, thoughts, feelings and actions (Burgy, 2011; Fuchs, 2012). In this way, these aspects of consciousness were experienced as "mine", as something saturated by the personal and the ego. If these aspects or acts of consciousness were bereaved of this quality of (automatic) "mineness", and instead were experienced as alien, this was termed 'depersonalization' (Burgy, 2011; Fuchs, 2012).

Schneider elaborated on these ideas from Jaspers in his investigations of schizophrenia (and Jaspers was for his part also later heavily influenced by Schneider (Burgy, 2011)). Disturbances in the sense of mineness, i.e. the *'ego disturbances'* ('Ichstörungen'), became paramount in Schneider's conceptualization of schizophrenia. These disturbances could only be diagnosed if they manifested as influence and passivity symptoms, in what he conceptualized as the 'first-rank symptoms' (e.g. forms of thought alienation and delusions about being influenced or controlled by some external force) (Burgy, 2011; Fuchs, 2012; Schneider, 1959). Schneider discarded the concept of depersonalization as a characteristic feature of schizophrenia, to differentiate between the ego disturbances and the alienation (depersonalization) experiences found in the neurotic disorders (which he considered to be

characterized by obscuration, remoteness and unreality) (Burgy, 2011). In this thesis, we found it interesting to discuss the validity of this distinction.

It should be noted that the Schneiderian ego disturbances concept had no link to the use of this term in the psychoanalytical literature, first introduced by Fenichel, who used the term to describe an immature ego with a fear of losing impulse control (Fenichel, 1938). The concept of ego disturbances was used in psychoanalytical theory to describe early "structural" personality disorders, influencing the work of Kernberg (O. Kernberg, 2017; O. F. Kernberg & Michels, 2009) among others.

1.2.1.4 From Schneider to the basic symptoms tradition

Subjective experiences in the early stages of schizophrenia have also been investigated in Anglo-American studies not situated in the continental phenomenological psychiatric tradition. Among these, we will mention two studies from the 1960s, based on interviews with patients in the early stages of schizophrenia (Chapman, 1966; McGhie & Chapman, 1961). As previously noted, Chapman proposed that certain specific disturbances in attention, particularly in the ability to filter out irrelevant stimuli, were the first and most fundamental signs of an incipient schizophrenia disorder. Early signs also included disturbances in visual perception (e.g. inability to perceive and interpret objects as a whole), blocking phenomena (not only of thoughts, but also in attention, perception, memory, speech and motility) and disturbances in speech production and motor function. In case reports from some of the interviews, we also find very vivid descriptions of severe self/identity disturbances, and disturbances in the sense of mineness, e.g.:

> Case 10: "When I look at somebody, my personality is in danger. I am undergoing a transformation and myself is beginning to disappear." (p. 232)(Chapman, 1966)
>
> Case 12: "I get shaky in my knees and my chest is like a mountain in front of me, and my body actions are different. The arms and legs are apart and away from me and they go on their own. That's when I feel I am the other person and copy their moments, or else stop and stand like a statue. I have to stop to find out whether my hand is in my pocket or not." (p. 232)(Chapman, 1966)

Gerd Huber, a student of Schneider, aimed to find the experiential (subjective) starting points of the ego disturbances in schizophrenia. This led to the basic symptoms approach, previously described. Huber considered subtle disturbances in thought processes as important early signs (Huber & Gross, 1989). Situated in this basic symptoms tradition, Klosterkötter investigated the transitional steps from the basic symptoms in the prodrome to the first-rank symptoms. A symptom like thought insertion would typically start with experiencing less control over

thought processes, involving basic symptoms like thought interference and disturbances of concentration. With increasing intensity, the person would experience her thoughts as increasingly strange and new, until reaching a point where they seemed to be carried out by someone else, as if they were alien. This intermediate stage between basic symptoms and psychotic symptoms involved so-called 'autopsychic depersonalization'. Finally these experiences would lose the "as if" character, and end in delusions of thought insertion (Klosterkotter, 1992).

Although the basic symptoms approach was and is phenomenologically oriented with respect to the focus on subtle, subjective disturbances, it still consisted to a large degree of making a compilation of single and unrelated symptoms (Fuchs, 2012). This changed with the phenomenological approach by Josef Parnas and Louis Sass, who reintroduced a phenomenological model of self-disorders in schizophrenia (L. Sass, 2003; L.A. Sass & Parnas, 2003). Within this model, anomalous subjective experiences, including many of the symptoms described by the basic symptoms approach, were connected in their assumed common rootedness in a core disturbance of basic self-awareness. This phenomenological approach and model heavily inspired and influenced the current thesis.

1.2.2 Sass and Parnas' self-disorder model of schizophrenia

Sass and Parnas integrated insights from classic European psychopathological descriptions, phenomenological philosophy, phenomenologically oriented psychiatry and the basic symptoms approach in their self-disorder model of schizophrenia (Parnas & Handest, 2003; L. Sass, 2003; L.A. Sass & Parnas, 2003). According to Sass and Parnas, schizophrenia is first and foremost a self-disorder characterized by an *ipseity disturbance* (ipse is Latin for 'self' or 'itself'), involving a decline in the *first-person quality* (subjectivity) of experience. This self-disorder/ipseity disturbance is also termed *basic self-disturbance* (BSD) in recent literature (Nelson & Raballo, 2015), and may phenomenologically manifest as a range of *anomalous self-experiences* (ASEs) (Parnas & Handest, 2003; Parnas, Moller, et al., 2005). We will use the terms self-disorder, BSD and the associated term ASEs interchangeably in this thesis to denote these particular kinds of distortions in self-experience.

1.2.2.1 Basic sense of self in normal conditions

This subjective first-personal quality is "basic" or "minimal" in the sense of being an implicit aspect of, and precondition for, all acts of awareness. It is not dependent on any conscious attributions to myself as the owner of my experiences and agent of my actions (L.A. Sass &

Parnas, 2003). As illuminated in phenomenological philosophy, e.g. in the pioneering works of Edmund Husserl (Husserl, 1931), consciousness is always characterized by *intentionality*. Intentionality refers to the *directedness* of consciousness, implying that I am always conscious *of* something. This intentionality may be "focal", focusing on "objects" in my field of consciousness (e.g. turning my attention to the feeling that my hands are cold), or it may be "tacit", i.e. the pre-reflective awareness of my body as a subject through which I experience and encounter the world (and my cold hands) (L. A. Sass, 2003b). Normally, this "tacit" subjectivity saturates all aspects of myself, i.e. sensations and perceptions of my body and the world, feelings, motivations, thoughts and actions with a continuing sense of *"my-ness"* and *"alive-ness"* (vitality), and of being *present* and *immersed* in the surrounding world (Parnas, 2003; L.A. Sass & Parnas, 2003). When I am walking in the woods, smelling the scent of pine trees and moss (possibly bringing back some childhood memories), and feeling the breeze in my face, I am pre-reflectively aware that it is *I* who feel, smell, hear, see, remember and move. This self-awareness is simultaneously a feeling of presence and of feeling alive in a world animated by my subjective experience of it. The French philosopher Merleau-Ponty pointed out that in the everyday transactions with the world, the sense of my bodily self and the sense of immersion in the world are inseparable, constituting a system:

> "Our own body is in the world as the heart is in the organism: it keeps the visible spectacle constantly alive, it breaths life into it and sustains it inwardly, and with it forms a system" (Merleau-Ponty, 2002)(p. 28)

The "my-ness" or "I-quality" of all experience is also a prerequisite for the experience of *coherence*, *continuity* and *real-ness*. Although the acts of my consciousness shift from moment to moment as I move in time and space, neither I nor the world feel fragmented or unreal because all these experiences, thoughts and actions self-evidently, automatically *belong to me*. This pre-reflective subjective quality saturates consciousness with a sense of *temporal flow* (the stream of consciousness), binding experiences together (Parnas & Handest, 2003). This basic self-awareness is also a precondition for the *explicit* recognition of myself as an invariant and enduring "I" who experience and encounter the world, and who is endowed with personal characteristics, history and a social identity (the 'narrative' or 'social' self) (Nelson & Raballo, 2015; Parnas, 2003; Parnas & Henriksen, 2014; L.A. Sass & Parnas, 2003).

1.2.2.2 Basic self-disturbance in schizophrenia and the schizophrenia prodrome

In schizophrenia, the basic sense of self no longer saturates every experience automatically, thus diminishing the sense of mineness (first-person givenness) and unity of experiences and agency. Aspects of mental life, e.g. perceptions, are decoupled from normally constitutive features of consciousness, and are thus no longer "intended" by the subject as meaningful experiences *for me*. The natural sense of being unquestionably present, aware, alive and temporally persistent is also concomitantly disturbed (Parnas & Henriksen, 2014; L.A. Sass & Parnas, 2003).

This decline of the sense of *subjectivity* (first-person perspective) is referred to as *'diminished self-affection'* or *'diminished self-presence'*(L. Sass, Borda, Madeira, Pienkos, & Nelson, 2018; L.A. Sass & Parnas, 2003). Another main aspect is *'hyperreflexivity'*. This refers to an *exaggerated self-consciousness* typically directed towards normally tacit and pre-reflective aspects of the self, e.g. proprioceptive sensations (as also described by Blankenburg (L. A. Sass, 2001)). An example of this could be that I become very aware of my own breathing, and begin to "observe" and analyze it as a kind of external object. My breathing, normally present as a subjective "ground" of experience, becomes objectified as a "figure" for explicit reflections. Although this may be considered as a form of *compensation* for the diminished self-affection, it is not necessarily characterized by *volitional*, self-controlled reflections. It may rather be *"operational"* and *"reflexive"* in the sense that this observational, analytical mode just "operates" as an altered way of structuring the acts of consciousness (but more deliberate hyperreflections may also be present).

Diminished self-affection and hyperreflexivity are the two main aspects of the ipseity disturbance/self-disorder in the first version of Sass and Parnas' model (Parnas, 2003; L. Sass, 2003; L.A. Sass & Parnas, 2003). Sass and Parnas also add that these aspects necessarily are accompanied by distortions in the *"grip"* or *"hold" of the field of awareness*, which refer to disturbances in the structuring of the perceptual and conceptual world (e.g. abnormal discrimination between familiar and strange stimuli). The disturbed grip or hold typically manifest as *perplexity* in the encounters with the world and '*common sense disturbances'*, as these phenomena are described by Blankenburg (Blankenburg & Mishara, 2001) and Stanghellini (Stanghellini, 2000; Stanghellini & Ballerini, 2011a). In more recent versions of the self-disorder model, the disturbed grip or hold of the field of awareness is described as a main aspect of the BSD, on par with the two other aspects (diminished self-affection/self-presence and hyperreflexivity) (L. Sass et al., 2018; L. A. Sass, 2014).

These central dimensions of BSD may surface as a range of intimately connected ASEs, which have been grouped in five domains: disturbed stream of consciousness (e.g. spatialization of thoughts), sense of presence and self-awareness (e.g. sense of inner void), corporeality (e.g. parts of body feel alien), self-demarcation (weakening of self-other/self-world boundaries) and existential reorientation (e.g. solipsism) (Parnas, 2003; Parnas & Handest, 2003; Parnas, Moller, et al., 2005).

BSD is considered as the primary 'trouble gènèrateur' in the prodrome of schizophrenia, driving symptom development and articulation (Parnas & Handest, 2003; L.A. Sass & Parnas, 2003). Closely parallel dimensions of experience were also suggested as core prodromal phenomena in a forerunning explorative in-depth investigation; namely 'disturbance of perception of self' and 'extreme preoccupation by and withdrawal to overvalued ideas' , (Moller & Husby, 2000). Early in the prodrome, the person may feel that something about him-/herself and the surrounding world is changing, "strange", "alien" and/or "wrong", but regularly find it hard to pinpoint exactly what these changes are, and to verbalize them (Moller & Husby, 2000). Even though he/she sees the same person as always in the mirror, and the appearance of people and the world is not hallucinatory transformed, something or everything feels strange. The whole *atmosphere* surrounding existence may feel *"uncanny"* (Fuchs, 2019), like if you are in the midst of a scary movie and sense that something evil is going to happen, but you don't know what it is. What is going on may seem arranged and artificial, as if it all was some kind of surreal play controlled by some unknown puppet master. The way people and things in the world appear and behave feels wrong, mysterious and even incomprehensible. This uncanny feeling has been described as a 'delusional mood' (Conrad, 1958; Jaspers et al., 1997a).

Conrad, in his stage model of schizophrenia, called this first prodromal stage (which may last for months and years) the 'trema' (stage fright) (Conrad, 1958; A. L. Mishara, 2010). According to Conrad, a tense feeling of *frightful expectation* characterize this period. What normally comprise the self-evident, pre-reflective background of acts of consciousness suddenly attracts attention, and acquires a strange, new sense of meaningfulness (e.g. how the sky looks or the feeling of the bodily sensations). This delusional mood infuse the experience of single objects and living beings, detaching them from their normal encompassing context, and transforming them into something enigmatic and threatening (e.g. the interior of a living room, the chairs, tables and so on, become prominent, as if the way they look and are arranged signify some hidden, important, meaning, directed at the observer) (Fuchs, 2005b).

These anomalies in self- and world-experience are leading to a search for (a compensatory) *transcendent meaning*, and the affected person may become engulfed in metaphysical, philosophical, religious or supernatural ponderings during the prodrome (existential reorientations) (Moller & Husby, 2000). The uncanniness and feeling of unpleasant expectation typically give rise to delusional-like, often solipsistic ideas, e.g. that the world and other people may not be real, that they may be creations of my imagination.

In the self-disorder model by Sass and Parnas such experiential changes are assumed to be intimately related to the primary dimensions of BSD, i.e. diminished self-affection and hyperreflexivity, with the accompanying disturbances in the field of awareness. With the diminished self-affection or self-presence, the person becomes *detached* from her own experiencing, thus becoming a *spectator* to herself, to her own thoughts, feelings, body, movements and actions, and even perceptions. Common descriptions of the latter could be phrases like: "I just see things – see them without experiencing them" or "my ears are like audio recorders, just registering the sounds". This observational stance implies and sustains the exaggerated self-consciousness, i.e. the *hyperreflexivity*, which transforms what is normally experienced as aspects of the self and of subjective mental life into external objects, i.e. a process of *alienation*. It should be mentioned that patients quite often report that they have experienced disturbances in self- and world-experience since childhood or early adolescence (Parnas & Henriksen, 2014). Accordingly, they may not remember and be aware of a marked *change* in experiental mode, as these disturbances have been there for such a long time that they have become quite "habitual", "ego-syntonic" aspects of how they experience themselves and the world (Parnas & Henriksen, 2014). In such cases, the distinction between prodromal and premorbid phases becomes blurry.

These phenomenological descriptions of anomalous self- and world-experiences during the prodromal phase of schizophrenia are mainly derived from individuals in the early stages of schizophrenia or other SSDs, e.g. (Moller & Husby, 2000; Parnas & Handest, 2003). The profound impact self-disorders were revealed to have in these subjects during the prodromal phase was a major motivation for the present thesis, exploring these phenomena in CHR subjects, some of which could be on the verge of psychosis and SSD development.

1.2.2.3 Basic self-disturbance as a driver of symptom development

In the prodrome, ASEs still have an "as-if" quality, e.g. "it is *as if* my arm doesn't belong to me", "thoughts feel alien, *as if* they don't belong to me", "I feel *as if* I am a robot". As can be

seen, taking away the "as if"-reservation turn these statements into Schneiderian first-rank symptoms. This is what is assumed to happen in Sass and Parnas self-disorder model. The hyperreflexivity and progressive diminishment of self-affection erode the feeling of being the owner of experiences and agent of actions. Fuchs describes the transition from self-disturbances to Scheiderian first-rank symptoms as a process progressing in four stages: 1. *Alienation of operative intentionality*, resulting from a lack of mineness or ipseity (e.g. feeling that my body moves like a machine, beginning to think about and observe my own thoughts), 2. *Disintegration of the intentional arc* (fragmented thoughts suddenly intruding, motor impulses, automatisms or thought/motor blockades), 3. *Externalization* (attribution of experiences to an external force), *experienced in an 'as if' mode*, and 4. *Breakdown of the 'as if' and transition to delusion* (Fuchs, 2015).

According to Conrad, *delusions* may arise as sudden "a-ha"-experiences, a revelation ('apophany') making sense of the strangeness and uncanniness characterizing the delusional mood (trema) stage (Conrad, 1958; A. L. Mishara, 2010). Commonly, the afflicted person attributes these experiences to the doings of some external, alien force or being, e.g. "An enemy power is controlling my thoughts and my behavior. It is all an experiment - the enemy power is testing me" or "People around me are not real people, but aliens who are watching and testing me". This revelation typically brings some relief to the person (Conrad, 1958; A. L. Mishara, 2010), as it identifies the "enemy" responsible for the very distressing and frightening experiences.

According to Sass and Parnas, *thought echo, thought broadcasting* and *auditory-verbal hallucinations* also manifest as consequences of the turning of attention to the processes of consciousness, in this case the "inner speech" which normally characterize the stream of consciousness (L.A. Sass & Parnas, 2003). This exaggerated self-consciousness brings into awareness normally transparent, implicit aspects of subjective consciousness. This may generate an increasing feeling of alienation, so that the "inner speech" is experienced as "voices", thought echo or thought broadcasting, produced by and controlled from an external source (L. Sass, 2003; L.A. Sass & Parnas, 2003).

In Sass and Parnas' model (Parnas et al., 2002; L. A. Sass, 2003a; L.A. Sass & Parnas, 2003), the so-called *negative symptoms* in the schizophrenia spectrum conditions, e.g. affective flattening, avolition and social withdrawal, may be accounted for by the *"loss of natural self-evidence"*, as described by Blankenburg (Blankenburg & Mishara, 2001). Experiences of the self, world and interpersonal situations are no longer automatically and intuitively

"assimilated" as self-evident aspects of myself or of outer reality. This hinders the normally spontaneous "attunement" and "common sense" orientation to the world, and engenders a profound sense of distance and detachment. Emotions may be experienced as alien, object-like sensations in the body, and the way people behave seems strange and even incomprehensible. This detachment and lack of attunement may then show itself as 'negative symptoms', e.g. withdrawal or diminished expression of affect.

The concept of *'disembodiment'* is also of relevance for the understanding of these disturbances of subjectivity (Fuchs, 2005a; Fuchs & Schlimme, 2009; Vittorio Gallese & Ferri, 2015; Stanghellini, 2009). While normally receding in the background of experience (as a pre-reflective awareness), the body is experienced as "detached" from the experiencing self, as if the person does not "inhabit" the body any more (i.e. disembodiment). This involves a pathologic *explication* and *reification* of the body and motor processes, e.g. experiencing the body as "robot-like". This disrupts the normal functioning of the body as a *transparent, subjective medium for experience, action, social understanding and empathy*, and comes in the way for a normal, spontaneous grasping of situations and other people, as well as the intuitive comprehension and mastering of activities (Fuchs, 2005a, 2017). The way people behave and look may then seem strange and unfamiliar, as if governed by some secret rules. Acts like reading, riding a bike, or even walking or talking, which is normally conducted in an automatic, integrated, habitual way, become reduced into single elements, thus disintegrating the "flow", naturalness, self-evident meaningfulness, coherence and familiarity of the actions. The person may feel awkward when walking, as if her legs are not fully under her control, and may compensate by putting a conscious effort into the act of moving one leg after the other, in turn making movements in fact awkward.

Not surprisingly, this disembodiment may manifest as *disorganization symptoms* (but also delusions and negative symptoms), due to the distortions in the embodied "compass" or "frame of reference" (the pre-reflective self-awareness) normally structuring, organizing and directing attention and other acts of consciousness. The meaning and significance of situations become difficult to grasp, the person loses grip of what she needs or wants, may feel overwhelmed by details, may have marked difficulties in directing her thoughts, and becomes disoriented and ambivalent. Her focus may be drawn to certain elements of the situations (e.g. focusing on the features of a face or the sound of a word), while losing grip of what normally matters, i.e. the interpersonally constituted common-sense meaning of the situation (e.g. the act of paying for goods to the cashier). Single thought fragments, e.g. a word crossing the

mind, may suddenly feel important and attract attention, while other aspects of consciousness recede in the background, resulting in a lack of cohesion, coherence and "natural flow" of thoughts and speech. It is not completely an "orchestra without a conductor", but suddenly the conductor (the embodied basic sense of self) becomes extremely aware of the notes the oboist is playing, while neglecting the other musicians and losing grip of the orchestral score.

As can be seen, BSD in the schizophrenia prodrome (and also in later SSD stages) is assumed to drive development of all the symptoms considered prototypical for SSDs. Hence, we wanted in this thesis to investigate in a CHR sample the relationships between BSD and a broad specter of symptoms considered as attenuated or clinically subthreshold versions of positive, negative and disorganization symptoms.

1.2.3 Basic self-disturbance – empirical findings and assessment

1.2.3.1 Pre-EASE studies of basic self-disturbance

As mentioned in the introduction, two qualitative, phenomenologically oriented studies in Norway and Denmark in the late 1990s both found self-disorders to be characteristic and very frequent features of the prodromal phase of schizophrenia spectrum disorders (Moller & Husby, 2000; Parnas et al., 1998). Based on their findings from in-depth interviews with 19 patients, Møller and Husby suggested the previously noted tentative core dimensions of prodromal experience: "disturbances in the perception of self", and "extreme pre-occupation with and withdrawal to overvalued ideas" (often of a metaphysical, supernatural or philosophical character). In the Parnas et al study, self-experience was phenomenologically explored in 18 cases, revealing self-disorders in 70%. These self-disorders were characterized by the central dimensions of basic self-disturbance, i.e. diminished self-affection/self-presence/disturbed ipseity, hyperreflexivity and disturbed hold of the field of perception and awareness. Patients often experienced these disturbances as more distressing than the frank psychotic symptoms (Parnas et al., 1998).

Following these two studies, a range of phenomenologically oriented studies have investigated self-disorders/self-disturbances in the schizophrenia spectrum and other conditions. In the earliest of these studies, these phenomena were explored with the BSABS (Gross et al., 1987) (or with a forerunner of BSABS) and later expanded with, and reanalyzed in the light of, items specifically targeting anomalous self-experiences. These studies were conducted by a Danish research group, affiliated with Josef Parnas. A general finding was that self-disorders were significantly more prevalent in ICD-10 schizophrenia spectrum disorders

than in other mental disorders. Levels of self-disorders did not differ significantly between schizophrenia and schizotypal disorders (Handest & Parnas, 2005; Parnas, Handest, et al., 2005; Parnas et al., 2003). One study found that self-disorders aggregated in residual/remitted schizophrenia spectrum conditions compared to remitted psychotic bipolar conditions (Parnas et al., 2003). Other studies investigated genetic linkage data from the Copenhagen Schizophrenia Linkage Study. These studies found that the levels of self-disorders were higher in subjects with SSDs than in subjects with other mental disorders or with no mental disorders (Parnas, Carter, & Nordgaard, 2016; Raballo et al., 2009), and higher in family members of subjects with schizophrenia, if they exhibited one or more schizotypal traits (Raballo & Parnas, 2010). The first prospective study of self-disorders was a five-year follow-up of 155 first-admission patients with 1) schizophrenia or other non-affective, non-organic psychotic disorders, 2) schizotypal disorder, and 3) other mental disorders outside of the schizophrenia spectrum. In this study, high levels of perplexity and self-disorders at baseline predicted development of schizophrenia spectrum disorders in patients with non-psychotic disorders (Parnas et al., 2011).

A meta-analysis from 2014 of 25 studies (published between 1990 and 2013) found marked disturbances in the sense of body ownership and agency in schizophrenia patients compared to healthy controls. Most of these studies were not associated with the phenomenological approach to self-disorder, and had an experimental design (e.g. investigating body ownership with the rubber hand delusion, and the sense of agency with action attribution or action monitoring tasks) or were based on self-report (Hur, Kwon, Lee, & Park, 2014)

1.2.3.2 The Examination of Anomalous Self-Experience (EASE) scale

In 2005, a symptom checklist for a semi-structured qualitative exploration and quantitative assessment of anomalous self-experiences was published, the Examination of Anomalous Self-Experience (EASE). The EASE contains 57 items (many of the items also include several sub-types) categorized in five domains: 1. Cognition and stream of consciousness, 2. Self-awareness and presence, 3. Bodily experiences, 4. Demarcation/transitivism and 5. Existential reorientation. The authors of the EASE were phenomenologically oriented psychiatrists and researchers from Denmark, Norway and Germany. The selection of items was based on a combination of clinical experience with incipient schizophrenia spectrum patients and empirical findings from the pre-EASE studies. The EASE have several overlaps with items in the BSABS, although definitions are not completely identical. The development of the instrument was also inspired and influenced by classical continental European

psychopathological descriptions, particularly by authors situated in the phenomenological tradition, continental phenomenological philosophy, and the basic symptoms approach (Parnas, Moller, et al., 2005). In line with the assumed Gestalt-character of BSD (i.e. a prototypical, psychopathological "whole"), the EASE has been demonstrated to have a mono-factorial structure (Nordgaard & Parnas, 2014; Raballo & Parnas, 2012), and to possess good to excellent internal consistency (Moller, Haug, Raballo, Parnas, & Melle, 2011; Nordgaard & Parnas, 2014; Raballo & Parnas, 2012). Interrater reliability for the scoring of EASE has also been demonstrated to be in the good to excellent range among trained and experienced clinicians and researchers (Moller et al., 2011; Nelson et al., 2012; Norgaard & Parnas, 2012). In all the studies presented in this thesis, EASE was the main instrument to investigate manifestations of BSD.

1.2.3.3 EASE studies on the diagnostic specificity of basic self-disturbance

Several studies using the EASE have replicated the general finding from pre-EASE studies of a selective aggregation of self-disorders in schizophrenia spectrum disorders, e.g. (Haug, Lien, et al., 2012; Nordgaard & Parnas, 2014; Raballo & Parnas, 2012). Among these, a study by Haug and colleagues found that total EASE scores significantly discriminated patients with schizophrenia from patients with either bipolar psychotic disorders or other psychotic disorders in a sample of 91 first-episode psychosis patients (Haug, Lien, et al., 2012). These EASE studies have been summarized in two reviews (Parnas & Henriksen, 2014; Raballo, Poletti, Preti, & Parnas, 2021).

A few studies indicate that anomalous self-experiences may be quite prevalent also in certain conditions outside of the schizophrenia spectrum. These include analyses of literature reports on depersonalized conditions (L. Sass, Pienkos, Nelson, & Medford, 2013) and from "introspectionist" experiments (L. Sass, Pienkos, & Nelson, 2013), as well as a study on a sample of patients with panic disorder (Madeira et al., 2017). The overlap between ASEs and depersonalization phenomena in conditions outside of the schizophrenia spectrum is of interest to investigate further, as it challenges the assumption that BSD is specific to SSDs only, and possibly connects at least some aspects of BSD to reactive phenomena typically seen in subjects experiencing severe stress and anxiety.

1.2.3.4 EASE studies on associations with conventional psychopathology measures

In this thesis, we were interested in investigating cross-sectional and prospective associations between BSD and a range of other psychopathology measures. Findings of associations

between BSD and such measures have been published from several studies, mainly after the launch of our investigation. Nordgaard et al. found that EASE total scores correlated weakly with positive symptoms, and moderately with negative symptoms, formal thought disorder and perceptual disturbances in a diagnostically heterogeneous first admission sample of 100 patients (46 with non-affective psychosis, 22 with schizotypal disorder and 32 with other mental disorders) (Nordgaard & Parnas, 2014). In a five-year follow-up of this sample, only including schizophrenia spectrum patients (n = 48), a significant correlation between the EASE total score and positive symptoms at follow-up was found, but no other significant associations between baseline or follow-up EASE with baseline or follow-up positive or negative symptoms. EASE total at baseline also predicted global symptomatic, but not functional outcome. The authors suggested that the weaker correlations in this follow-up study compared to the original baseline study were due to the more homogeneous and smaller sample in the follow-up study (Nordgaard, Nilsson, Saebye, & Parnas, 2017). In a seven-year follow-up study of 56 first treatment psychosis patients (35 schizophrenia and 21 non-schizophrenia), Svendsen and colleagues found that recovery was predicted by low levels of BSD at baseline and reduction in these levels from baseline to follow-up, and absence of a schizophrenia diagnosis. There were no diagnostic changes in SSD from baseline to follow-up (Svendsen et al., 2019).

Elevated total EASE levels have also been demonstrated to be significantly associated with suicidality measures in first-episode schizophrenia (Haug, Melle, et al., 2012; Skodlar & Parnas, 2010), poorer social functioning in both schizophrenia and bipolar patients (Haug et al., 2014) and childhood trauma in females with first-episode schizophrenia (Haug et al., 2015). EASE levels have not been found to correlate with duration of illness and untreated psychosis (Nordgaard & Parnas, 2014), and not with IQ (Nordgaard & Parnas, 2014; Nordgaard, Revsbech, & Henriksen, 2015) or neurocognitive measures (Haug et al., 2011; Nordgaard et al., 2015), except for a significant association between higher EASE levels and poorer verbal memory (Haug et al., 2011).

1.2.3.5 Investigations of the stability of basic self-disturbance

The question of whether BSD has a trait-like or state-like character has been investigated in prospective studies in Denmark (Nordgaard, Handest, et al., 2017; Nordgaard, Nilsson, et al., 2017) and in Norway (Svendsen et al., 2018), with some discrepancies in their findings. In the Danish studies (a 5-year follow-up of schizophrenia spectrum patients), a high temporal

persistence of BSD was found. In the Norwegian study (a 7-year follow-up of first episode psychosis patients), patients with schizophrenia disorders had a significant decline in total EASE scores. While the main effect was a decrease of BSDs at the group level, some patients had stable levels, some experienced increases, while others experienced decreases from baseline to follow-up. In patients with other psychotic disorders, the total EASE levels were stable (this latter group had stable *low* levels). In light of the lack of studies on the stability of BSD in CHR samples, we planned to investigate this in this research project.

1.2.3.6 Basic self-disturbance in CHR, other help-seeking youth and non-clinical samples

In a study investigating ASEs with the BSABS, Szily and Kery found that perplexity, self-disorders (e.g. depersonalization phenomena) and diminished affectivity predicted psychosis risk in a sample of 68 subjects with major depressive disorder, including 26 UHR subjects, (Szily & Keri, 2009). Davidsen conducted the first investigation using the EASE in a CHR sample (n =11, all UHR). ASEs were present in all participants, but levels and kind of phenomena varied considerably (Davidsen, 2009). Nelson, Thompson and Yung found that levels of BSD (measured with the EASE) were significantly higher in an UHR sample of 49 patients compared to the levels in 52 healthy controls ($p < .001$). The UHR participants were followed for a mean of 569 days, and during this period, 13 (26.5%) patients transitioned to psychosis. The total EASE score significantly predicted time to transition ($p < .05$), even when other significant predictors were controlled for (duration of symptoms prior to treatment and functioning levels). The study additionally found that self-disorders were most prevalent in subjects with schizophrenia spectrum disorders, irrespective of transition to psychosis (Nelson et al., 2012).

Two studies have replicated the findings in the Nelson et al. study, i.e. finding an aggregation of BSD (total EASE levels) in CHR subjects compared to the levels in non-CHR subjects (non-CHR subjects were in both these two studies comprised of help-seeking adolescents/young adults) (Comparelli et al., 2016; Raballo et al., 2016). In both these studies, higher EASE levels were associated with lower level of global functioning. Raballo and colleagues also found that EASE levels correlated with attenuated (SOPS) positive symptoms, cognitive (COGDIS) and cognitive-perceptual (COPER) basic symptoms (Raballo et al., 2016). Comparelli and colleagues did not find significant associations between EASE levels and prodromal symptoms (SOPS subscales) or neurocognitive measures (Comparelli et al., 2016). As can be seen, these findings regarding associations between ASEs and other symptoms were not congruent, pointing to the need for further investigations in CHR of

associations between BSD and other psychopathology measures, as we aimed to do in this thesis.

In a sample of 82 help-seeking non-psychotic adolescents, it was found that anomalous self-experiences were prevalent, but at a considerably lower level than prodromal symptoms (Koren et al., 2013). EASE correlated moderately with positive and negative symptoms scales in the Prodromal Questionnaire (Loewy, Pearson, Vinogradov, Bearden, & Cannon, 2011). Thirty-nine subjects from this sample were investigated seven years later for the presence of SSDs. High baseline EASE levels predicted SSD diagnoses (n = 9) seven years later (Koren et al., 2019). Torbet and colleagues found a significant association between anomalous self-experiences and schizotypal traits in a non-clinical sample (Torbet, Schulze, Fiedler, & Reuter, 2015). In three studies of non-clinical samples, Gaweda and colleagues found that ASEs (assessed with a self-report inventory based on the EASE: Inventory of Psychotic-like Anomalous Self-Experiences (IPASE)) were associated with psychotic-like experiences and psychosis proneness (Gaweda, Goritz, & Moritz, 2018; Gaweda, Pionke, et al., 2018; Gaweda, Prochwicz, et al., 2018).

When we planned this thesis, no studies to our knowledge had explicitly investigated associations between childhood adversities and later self-disorders. Hence, we wanted in our studies also to investigate such associations. In a suggested revision of the self-disorder model of schizophrenia, ASEs are proposed to partly be of a reactive, secondary nature, and partly of an endogenous, primary nature (Borda & Sass, 2015; L. Sass et al., 2018; L. A. Sass & Borda, 2015). If at least some BSD phenomena have a reactive character, related to adverse life circumstances and exacerbations of stress and anxiety, childhood trauma could constitute a possible vulnerability factor (L. Sass et al., 2018). It is of interest to describe this model revision in some detail, as it has been of significant relevance for particularly one of the studies in this thesis.

1.2.4 A suggested revision of the basic self-disturbance model

In our interactions with the world, we are continuously influenced by multisensory external and internal input. The organization and integration of this input is considered a prerequisite for the normal, continuous constitution of an embodied, basic or core sense of self, which is demarcated from the environment (Blanke, 2012; Borda & Sass, 2015; A. Damasio, 2010; Gallagher, 2005; V. Gallese & Sinigaglia, 2010; Panksepp & Biven, 2012; Postmes et al.,

2014; Stern, 1985). Early neurodevelopmental disturbances in multisensory integration and organization of information from different sensory modalities have been proposed as necessary, but not sufficient, conditions for the development of a complete psychotic syndrome in the schizophrenia spectrum (Borda & Sass, 2015; Postmes et al., 2014; L. Sass et al., 2018; L. A. Sass & Borda, 2015). Disturbances in multisensory integration also include alterations in *time* processing of sensory information, experienced as a decline in the moment-to-moment temporal flow of consciousness (Fuchs, 2007; Martin et al., 2014; Northoff & Stanghellini, 2016).

Particularly important may be disturbances in *somatosensory, sensory-motoric* and *interoceptive* feedback, which compromise the fundamental role of our "lived", "subjective" body in anchoring all experience and knowing (the "embodied consciousness") (Borda & Sass, 2015; A. Damasio, 2010; Fuchs, 2005a; Postmes et al., 2014; Tschacher, Giersch, & Friston, 2017). Interoceptive signals signify homeostatic needs for physical corrections, e.g. in the forms of hunger and thirst, and participate in the generation of *primordial feelings*, telling the organism about the bodily needs (A. Damasio, 2010). According to Damasio, these deep sub-cortical feelings also "tell" us that we (our body) *exist*, that we are *alive*, and that we are *present* in the world. In addition, the monitoring and mapping in the brain of the entire body and its movements, and of externally directed sensory portals, provide us with a *felt perspective* of the mind, relative to the world. The integration of information from this mappings, is the evolutionary most ancient essence of the self (protoself), providing a sense of "…relative coherence of functional state within a surround of dynamic processes…"(p. 212) (A. Damasio, 2010).

A range of studies have found disturbances in multisensory organization and integration in SSDs (Postmes et al., 2014; Silverstein & Keane, 2011; Uhlhaas & Silverstein, 2005). Disturbed integration of perceptual and motoric functions has also been found in children later developing schizophrenia (Gamma et al., 2014). These early disturbances are hypothesized in the revised self-disorder model to underlie trait-like *primary* forms of self-disorders in the schizophrenia spectrum, which are automatic or passively experienced ("operative" forms of diminished self-presence, hyperreflexivity and disturbed grip or hold of the field of awareness) (Borda & Sass, 2015; L. Sass et al., 2018). Examples could be kinestethic sensations or thought fragments, which suddenly "stand out" as salient, attracting attention (disembodied and loosened from a background context), driving operative hyperreflexivity and disturbed grip or hold. Operative diminished self-presence is considered as a

complementary aspect of this hyperreflexivity, in which the body, normally tacit and functioning as a transparent medium for experience and taken-for-granted self-hood, becomes detached, objectified and reified (Borda & Sass, 2015).

In the suggested revision of the self-disorder model it is further proposed that BSD is also characterized by *secondary* forms of hyperreflexivity, diminished self-presence and disturbed grip or hold of the field of awareness. It is assumed that these forms emerge as *reactions* to the primary disturbances in early neurodevelopment, but also as (defensive) reactions to environmental stressors and trauma. These secondary forms of BSD may overlap to a considerable degree with depersonalization and derealization phenomena outside of the schizophrenia spectrum (L. Sass et al., 2018; L. A. Sass & Borda, 2015). This is in accordance with the diathesis-stress model, and with accumulating evidence for the pathogenic role of environmental stress and childhood trauma in the development of psychosis (Mayo et al., 2017; Misiak et al., 2017; Popovic et al., 2019; Read, Fosse, Moskowitz, & Perry, 2014; Selten, van der Ven, Rutten, & Cantor-Graae, 2013; Stilo & Murray, 2019; Varese et al., 2012). These secondary forms may also partly overlap with more *volitionally* induced anomalous self-experiences, which has been described to result from certain introspective techniques in early 20th century psychological experiments (e.g. (Titchener, 1909)), Eastern meditation and modernist art and literature (L. Sass, Pienkos, & Nelson, 2013; Louis A. Sass, 1992; L. A. Sass & Borda, 2015).

According to the revised self-disorder model, SSDs are characterized by a *combination* of primary and secondary forms of BSD. Still, some individuals may be more characterized by primary BSD (typically emerging during childhood development), while others more of secondary BSD (typically emerging in adolescence or early adulthood). Secondary forms of BSD are suggested to constitute a necessary *second hit* for the development of a complete psychotic syndrome. This updated BSD model thus considers secondary forms of BSD as *transdiagnostic* phenomena, occurring both within and outside of the schizophrenia spectrum. In conditions outside the schizophrenia spectrum, secondary BSD will rarely progress and manifest as psychotic symptoms because these conditions (e.g. depersonalization disorder) are not characterized by the encompassing neurodevelopmental disturbances and vulnerabilities frequently found in schizophrenia spectrum conditions (Borda & Sass, 2015; Parnas & Henriksen, 2014; L. Sass et al., 2018; L. A. Sass & Borda, 2015). If this updated self-disorder model holds promise, it may also open up a larger window for early intervention in CHR

conditions, targeting secondary, reactive BSD phenomena and factors that contribute to the development of these phenomena.

As CHR subjects often experience depersonalization and derealization (Büetiger et al., 2020), and as some CHR conditions include prodromal schizophrenia or schizotypal conditions while others may never develop a schizophrenia spectrum disorder, it was of interest to us in this thesis also to explore and analyze depersonalization phenomena/ASEs across such diagnostic boundaries.

1.2.5 Neurocognitive and neurobiological correlates to BSD

Phenomenologically oriented research and theories should be complemented by research in other fields and traditions in order to address findings and hypotheses at other levels of enquiry, and gain a more integrated understanding of the investigated phenomena and processes (Nelson, Whitford, Lavoie, & Sass, 2014b). A range of neurocognitive or neurobiologically oriented studies have investigated disturbances in self-experience in the schizophrenia spectrum and in CHR. We will here briefly describe some models developed along with these studies (not in more detail as we did not analyze neurocognitive or neurobiological data in this thesis).

Several authors have proposed *'prediction error'* models, which describe how disturbances in agency, sense of ownership to experiences and, consequently, psychotic symptoms may arise (Corlett, Taylor, Wang, Fletcher, & Krystal, 2010; Feinberg, 1978; Fletcher & Frith, 2009; Frith, 1992; Gray, 1998; Hemsley, 1994). In these models, it is proposed that self-generated stimuli are not attenuated as they normally would. This may result in the perception of these stimuli as something externally produced (Feinberg, 1978; Frith, 1992). These prediction errors may then constitute an experiential basis for the development of a *belief* that own movements are affected and controlled by some external force, i.e. delusions typical in first-rank symptoms.

Prediction errors have been proposed to be (at least partly) related to a dysregulation in dopaminergic transmission in sub-cortical striatal neural circuits (Howes & Kapur, 2009; Nelson, Whitford, Lavoie, & Sass, 2014a). An excessive and dysregulated dopamine transmission may "mark" stimuli and internal representations which are normally not attended to (e.g. kinesthetic sensations or a passing thought fragment), as something "worthy" of conscious attention (Heinz et al., 2019; Howes & Kapur, 2009; Kapur, 2003). These disturbances in the *attribution of salience* to stimuli and events have been suggested as one of

the neurocognitive mechanisms associated with BSD, particularly hyperreflexivity and disturbed grip or hold on perceptual/conceptual fields (Nelson, Whitford, et al., 2014a). In addition to this 'hypersalience' (banal stimuli experienced as strange), it has also been suggested that 'hyposalience' (experiencing the strange as if it was banal, an "anything goes" orientation) may underlie aspects of BSD, particularly diminished presence or diminished vitality, as well as delusion formation (L. Sass & Byrom, 2015)

This hyposalience has been proposed to be related to *default mode network* (DMN) activity (L. Sass & Byrom, 2015). Disturbances in the activation of the DMN may play one of the roles in the psychopathology of self-disorders in schizophrenia (Robinson, Wagner, & Northoff, 2016) and in UHR conditions (Bang et al., 2018). The DMN is normally activated when a person withdraws from an orientation towards practical activities in the world, in favor of mind-wandering introspective activities (Broyd et al., 2009). DMN disturbances may be particularly associated with secondary BSD phenomena (L. Sass & Byrom, 2015; L. A. Sass & Borda, 2015). These disturbances imply that the DMN is not deactivated when attending to external stimuli, resulting in disturbances in external orientation and engagement, and an excessive awareness of internal processes, thus constituting neurobiological correlates to hyperreflexivity (Nelson, Whitford, et al., 2014b), and the confusion regarding whether stimuli (e.g. inner speech) are internally or externally "produced" (Northoff & Qin, 2011). The simultaneous activation of the DMN and the Task Positive Network (TPN) possibly also infuse experiences of the world with a dream-like quality (L. Sass & Byrom, 2015).

The neural circuits of DMN include cortical midline structures (CMS) (as well as inferior parietal and lateral temporal areas), which have been found to be activated during tasks involving judgements about the self-relevance of stimuli (Northoff et al., 2006). CMN abnormalities have been found both in schizophrenia spectrum disorders (Ebisch & Aleman, 2016) and in CHR conditions (Bonoldi et al., 2019). In the study by Bonoldi and colleagues, higher severity of BSD (measured with the EASE) was correlated with smaller anterior cingulate volumes (part of CMS) in UHR subjects (Bonoldi et al., 2019).

1.3 Unanswered questions

When planning this thesis, only one report had been published from a study investigating ASEs in a CHR (UHR) sample cross-sectionally (Davidsen, 2009), and there was a lack of prospective CHR studies investigating BSD/ASEs. In light of the preponderance of self-disorder phenomena found in retrospective studies of the schizophrenia prodrome (Moller & Husby, 2000; Parnas et al., 1998), cross-sectional and prospective studies of CHR samples and other non-psychotic conditions are needed. Such studies may illuminate several aspects of BSD, which previous studies have not been designed to investigate. First, investigations of the presence, quality and severity of BSD phenomena (ASEs) in CHR may reveal whether these are characteristic features of these conditions, and whether there are differences between CHR subjects who are more versus less affected by these experiences. Second, cross-sectional and prospective studies investigating associations between ASEs and positive, negative and disorganization symptoms, as well as psychosocial functioning, may cast a light on the hypotheses of the BSD model suggested by Sass and Parnas (L.A. Sass & Parnas, 2003), implying an intimate relationship between BSD and the development of symptoms and functional deficits during the prodrome. This is of course of interest regarding the question of whether ASEs could be used as markers of adverse clinical and functional future outcomes in CHR. Third, the understanding and evidence base regarding vulnerability factors and precursors for the development of BSD is still quite restricted. Hence, there is a need to investigate whether certain background factors, including childhood trauma and childhood functioning, are associated with the risk of BSD development. Fourth, investigating BSD in CHR, along with associations with clinical diagnoses, may expand and nuance previous findings as to whether BSD is specific to SSDs or if BSD may also characterize other disorders and conditions (given the considerable psychopathological and diagnostic heterogeneity of CHR conditions (van Os & Guloksuz, 2017)). In light of the high frequency of depersonalization and derealization symptoms in CHR conditions (Büetiger et al., 2020; Madeira et al., 2016), it is also of interest to increase our understanding of these phenomena, including differential-diagnostic considerations. Finally, prospective studies of BSD are necessary to investigate in more detail whether anomalous self-experiences are trait-like phenomena or state-like, reactive/defensive phenomena, or both.

2. AIMS

The overall aim of this thesis was to investigate the presence, quality and severity of BSD phenomena/ASEs (measured with the EASE) in subjects at putative increased risk for psychosis, and the cross-sectional and prospective relationships between these phenomena, other clinical symptoms and functioning, and background factors.

The first aim was to investigate the total level and single item occurrence of ASEs in a CHR sample, and the associations between ASEs, clinical characteristics (SOPS positive, negative, disorganization and general symptoms, as well as global functioning) and background factors (childhood trauma and childhood psychosocial functioning). This investigation was cross-sectional, based on baseline data.

The second aim of the study was to explore and compare in detail the presence and quality of depersonalization phenomena and ASEs in two selected CHR cases, characterized respectively by DSM-IV depersonalization disorder and DSM-IV schizotypal personality disorder. We were interested in the specificity of ASEs, and also in the differences and similarities in other clinical characteristics and psychopathological pathways between the two cases.

The third aim was to prospectively investigate in a CHR sample whether the severity of ASEs at baseline were associated with, and predicted, clinical (symptoms and clinical diagnoses) and functional outcome after one year, including symptomatic and functional remission.

The fourth aim was to explore trajectories of ASEs in CHR subjects from baseline to the one-year follow-up, and associations between ASEs at follow-up and other baseline and follow-up clinical characteristics (symptoms, global functioning, clinical diagnoses).

3. METHODS

3.1 Setting

The present research project is a part of the Norwegian Thematically Organized Psychosis (TOP) study, which is affiliated with the University of Oslo and the Oslo University Hospital. The TOP study is a large, ongoing translational research study investigating biological and clinical characteristics of psychotic disorders, aiming to enhance knowledge and understanding of pathophysiological mechanisms. Clinical and neurocognitive data, structural and functional MRI data, and genetic information are collected. The main diagnostic categories included in the TOP study are schizophrenia and bipolar spectrum disorders. The present research project is the first to include CHR subjects in the TOP study. The participants were recruited from public adult and child/adolescent outpatient psychiatric units (as well as one team including both adolescents and adults in the 14-30 years age range) in Oslo and adjacent catchment areas (units affiliated with the Oslo University Hospital, Diakonhjemmet Hospital, Akershus University Hospital and Vestre Viken Hospital Trust) from June 2012 to December 2015. The treatment facilities were either teams dedicated to early intervention in psychosis or units offering specialized health care for psychotic disorders or for a range of mental disorders through a regular referral system. None of the early intervention teams were "pure" CHR teams, but assessed and treated both CHR and first episode psychosis patients. In contrast with the units based on a traditional referral system, these teams accepted self-referrals. They also had outreach activities, mainly targeting other mental health professionals and services, and counsellors at schools, in order to improve the detection of CHR or first-episode psychosis subjects.

3.2 Design

This research project encompassed four studies, which differed in their designs. The first study had a cross-sectional descriptive-correlational design, which involved analyses of the total sample and sub-group comparisons. The second study was a phenomenologically oriented investigation of two cases, comparing these two with respect to symptomatology, psychopathological dimensions and pathways, background factors and other patient characteristics. The third study had a prospective design, and the fourth study had a combination of a cross-sectional descriptive-correlational and a prospective design. As in the first study, cross-sectional analyses in study IV were either descriptive (e.g. describing the severity of ASEs at baseline or at follow-up in the total sample or in sub-groups) or they were

correlational, analyzing relationships between variables at baseline or follow-up. The prospective analyses compared clinical and other patient characteristics at baseline with clinical and other outcome variables at the one-year follow-up. The prospective studies did not involve any interventions between baseline and follow-up.

3.3 Procedure

Written and verbal information about the research project, including descriptions of inclusion/exclusion criteria, was distributed to clinicians working at psychiatric units offering specialized care and treatment to adolescents and young adults. If the treating clinicians suspected that one of their patients could be at risk of developing psychosis, they contacted project manager TGV, and verbally referred the patients. Patients received written and verbal information about the research project, and a preliminary clinical screening was conducted by TGV (based on communication with the clinicians and the patients). If the patients consented to be assessed for inclusion, they were interviewed with the SIPS, to formally decide at-risk status, and eligibility for inclusion in the study. The patients participated in the studies on the condition of an informed written consent. For patients below 18 years, parents consented as well. The participants consented to take part both in baseline assessments and in one-year follow-up assessments.

After inclusion, the participants underwent extensive clinical baseline assessments during the next 2-4 weeks. The TOP study protocol involves a range of measurements covering demographic, clinical and neuropsychological assessments. In this thesis, only assessments of relevance for the present studies are presented.

The presented demographic and clinical assessments were conducted by TGV, an experienced clinical psychologist. He had been trained by Norwegian experts in the field in the main clinical interviews used in this research project, i.e. the SIPS and the EASE, and had attended a TOP study reliability and training program for assessments with the Structured Clinical Interview for DSM-IV-Axis I disorders (SCID-I). Regarding EASE, TGV was supervised and trained by one of the authors and certified instructors of the EASE, PM. The findings and conclusions from the assessments were regularly discussed with PM and JIR, both experienced researchers and psychiatrists.

Between baseline and follow-up, the participants received treatment as usual at their local health service units. This included psychosocial interventions, psychotherapy and standard medication. If any of the participants transitioned to psychosis between baseline and follow-

up, this was reported to TGV, who evaluated whether the condition met criteria in the SIPS for a psychotic syndrome (Miller et al., 2003). One year after the first baseline interviews, the participants were contacted by TGV, who then carried out the follow-up assessments.

3.4 Participants

At baseline, 53 patients were interviewed for eligibility for inclusion. Among these, 15 were excluded due to meeting exclusion criteria (n = 7) or not meeting inclusion criteria (n = 2), or because they declined to participate in or complete all assessments (n = 6). Hence, 38 participants were included at baseline. The main target group for the research project was subjects at psychiatric outpatient units meeting CHR criteria. The inclusion criteria were age 15-29 years and meeting criteria for one or more of three prodromal syndromes (Criteria of Prodromal Syndromes (COPS), as specified in the SIPS (Miller et al., 2002). These three syndromes constitute UHR criteria (Fusar-Poli, Borgwardt, et al., 2013; Schultze-Lutter et al., 2015), and include the Attenuated Psychotic Symptoms (APS) syndrome, the Brief Intermittent Psychotic (BIPS) syndrome, or the Genetic Risk and Deterioration (GRD) syndrome (Miller et al., 2003). A description of these syndromes is presented in Table 1.

In addition, we did not exclude subjects in the same age range with longstanding, non-progressive, attenuated psychotic symptoms, not meeting formal APS criteria with respect to onset or progression of symptoms. This subgroup, which we in this thesis have termed the 'non-progressive symptoms group', is also more precisely defined in Table 1. Like the included subjects meeting formal CHR criteria, subjects in this subgroup were suspected to be at increased risk of psychosis by their treating clinicians. Although the risk may not be as high as in subjects with recent symptoms of escalating severity, subjects with persistent attenuated psychotic symptoms may still be at increased risk of psychosis (Fusar-Poli et al., 2012; Yung et al., 2003), and may also be at high risk of other clinical disorders and deficits in functioning (J. Addington et al., 2011; Beck, Andreou, et al., 2019; Lin et al., 2015; Michel, Ruhrmann, Schimmelmann, Klosterkotter, & Schultze-Lutter, 2018) (Fusar-Poli et al., 2012; Yung et al., 2003). It is possible that the non-progressive symptoms group would have met criteria for an APS syndrome with the 'current status specifier' 'persistence', as defined in a classification system for longitudinal outcomes in CHR states suggested by Woods and colleagues (S. W. Woods et al., 2014) (included in the SIPS version 5.5., March 2014). This classification system was however published two years after inclusion commenced to the current research project.

Following inclusion, all participants were also assessed according to cognitive basic symptoms high-risk criteria (COGDIS) (F. Schultze-Lutter et al., 2007), as part of the baseline assessments. The criteria are also described in table 1.

Table 1. Criteria for UHR/COPS, non-progressive attenuated psychotic symptoms, and the COGDIS

Prodromal syndromes	**Criteria of Prodromal Syndromes (COPS)**
Attenuated Positive Symptom syndrome Scale of Prodromal Symptoms (SOPS), positive subscale, include unusual thought content/delusional ideas, suspiciousness/persecutory ideas, grandiosity, perceptual abnormalities/hallucinations, disorganized communication	One or more of the 5 SOPS positive items scoring in the prodromal range (rating of 3-5) AND Symptoms beginning within the past year or increasing 1 or more points within the past year AND Symptoms occurring at least once per week for last month
Brief Intermittent Psychotic Symptom syndrome	One or more of the 5 SOPS positive items in the psychotic range (rating of 6) AND Symptoms beginning in the past 3 months AND Symptoms occurring currently at least several minutes per day at least once per month
Genetic Risk and Deterioration syndrome	First degree relative with history of any psychotic disorder OR Criteria for schizotypal personality disorder met in patient AND GAF drop of at least 30% over the last month vs 1 year ago
Non-progressive symptoms group	**Criteria for the non-progressive symptoms group**
	One or more of the 5 SOPS positive items scoring in the prodromal range (rating of 3-5) AND Symptoms occurring at least once per week for last month
COGDIS symptoms	**COGDIS criteria**
Inability to divide attention, thought interference, thought pressure, thought blockages, disturbance of receptive speech, disturbance of expressive speech, unstable ideas of reference, disturbances of abstract thinking, captivation of attention by details of the visual field	Presence of ≥ 2 of the 9 basic symptoms with a SPI-A score of ≥ 3 within the last 3 months

Exclusion criteria were the following: present or previous psychotic disorder as defined in the DSM-IV Axis I criteria, current antipsychotic treatment or for ≥ 4 weeks lifetime (dose equivalent to ≥ 5 mg Olanzapine per day), organic or clearly substance-induced CHR symptoms, current IQ below 70, and inability to speak/comprehend Norwegian.

Six of the participants who were included at baseline did not take part in the follow-up assessments (attrition rate was 15.8 %). This was either due to unwillingness to participate (*n* = 2) or because we were not able to reach them (*n* = 4). Hence, 32 participants took part in the follow-up assessments (study III and IV).

In the first study, the sample comprised all 38 participants included at baseline. Among these, 31 met CHR criteria and seven met criteria for the non-progressive symptoms group. In table 2, the CHR status of these participants is specified.

Table 2 CHR status of the participants in study I

CHR status	**Participants, *n***
CHR positive, including:	31
APS only	17
APS + COGDIS	10
APS + COGDIS + GRD	1
COGDIS only	3*
Non-progressive sympt. grp.	7

*The COGDIS only subjects were originally included due to meeting criteria for the non-progressive symptoms group, but later categorized as CHR positive due to meeting COGDIS criteria.

In the second study, we purposely selected two of the CHR participants from study I (after the baseline assessments were completed) to compare ASEs in a patient diagnosed with DSM-IV schizotypal personality disorder and in a patient diagnosed with DSM-IV depersonalization disorder (diagnoses set in this research project). Both these cases met COGDIS criteria (i.e. CHR), but not UHR criteria.

The third and fourth study included the same sample, comprised of the 32 participants completing both the baseline and the one-year follow-up assessments. Among the six participants who did not take part in the follow-up assessments, four were from the APS only subgroup, one was from the COGDIS only subgroup, and one was from the non-progressive symptoms group. Hence, the third and fourth study included 26 participants who were CHR positive, and six participants with non-progressive symptoms, at baseline.

3.5 Clinical assessments

3.5.1 UHR criteria, severity of symptoms, and the psychosis syndrome

As previously described, the SIPS (Norwegian version 3.1, published 2005) was used to assess at baseline whether the participants met UHR criteria (termed Criteria of Prodromal Syndromes (COPS) in the SIPS (Miller et al., 2003)) or criteria for the non-progressive symptoms group. In addition, the SIPS was used to explore the presence and severity of a range of symptoms frequently occurring in CHR conditions, both at baseline (all four studies) and at the follow-up assessments (study III and IV). To this purpose, the SIPS include the SOPS (Scale of Prodromal Symptoms), which is a Likert scale used to assess the severity of five positive symptoms, six negative symptoms, four disorganization symptoms and four general symptoms. The scale ranges from 0 (= *absent*) to 6 (= *severe and psychotic* for the SOPS positive symptoms /= *extreme* for the other symptoms) for each symptom. These symptoms comprise four subscales, in this thesis termed SOPS positive, SOPS negative, SOPS disorganization and SOPS general. The item scores in each subscale reflected the severity of symptoms during the last month. The subscale level of severity was computed by summing up the item scores on each subscale.

The SIPS also include criteria for a psychotic syndrome (Presence of Psychotic Syndrome (POPS)) (Miller et al., 2003). These criteria require that one or more of the SOPS positive symptoms get a score of 6, and that the psychotic symptoms are present at least 4 days per week for a month, *or*, that the psychotic symptoms are seriously disorganizing or dangerous. The POPS criteria were used to evaluate whether the participants had transitioned to psychosis between baseline and follow-up (registered in study III and IV). SIPS interviews were video- or audiotaped (all participants consented to this).

As previously described, the SIPS has shown excellent reliability properties, with an overall inter-rater reliability (IRR) agreement of 0.95 for the total SOPS score and above 0.75 for all the four subscales (Miller et al., 2003). Transition risk for subjects identified with the SIPS has been demonstrated to be 28.1 % (95 CI from 25.1% to 31.3%) at 31 months (Fusar-Poli et al., 2012). The SIPS also shows excellent prognostic accuracy regarding the differentiation of subjects with high psychosis risk from subjects with low risk (P. Fusar-Poli, M. Cappucciati, et al., 2015). In the current research project, inter-rater reliability regarding the assessment of UHR/COPS criteria and SOPS positive symptoms was established by scoring nine case vignettes from the North American Prodrome Longitudinal Study (NAPLS) (J. Addington et

al., 2007), and comparing these scores to the final scores from NAPLS raters. The agreement between TGV and the NAPLS raters was 100 % regarding the assessment of UHR/COPS criteria. Also regarding SOPS positive item scores, excellent inter-rater reliability was found, with single measure intra-class correlation coefficient (ICC) of 0.95 (95% CI: 0.82-0.99) (two-way mixed effects model, absolute agreement, calculated with SPSS version 25).

3.5.2 Basic self-disturbance/anomalous self-experiences

We explored ASEs at baseline (all four studies) and at follow-up (study III-IV) with the EASE. The EASE interviews were also video- or audiotaped (all consented to this), to ensure that qualitative aspects (e.g. registration of verbatim statements) were appropriately attended to, and to strengthen the quality of the quantitative scoring. Each of the 57 main items and sub-items in the EASE was scored on a 0-4 Likert scale (0 = absent, 1 = questionably present, 2 = mild, 3 = moderate and 4 = severe). To compare with other studies in the field, e.g. (Haug, Lien, et al., 2012; Koren et al., 2019; Nordgaard, Nilsson, et al., 2017; Raballo et al., 2016), we transformed the scores on each item to binary 0-1 scores. A 0-score implied that the symptom was absent or questionably present, and a 1-score implied that the symptom was definitely present (covering the 2-4 scores on the Likert scale).

We assessed the severity of BSD by summing up the scores on all main EASE items (sub-items excluded), giving an EASE total score. This total score is in this thesis also referred to as the BSD level, EASE level or level of ASEs. At baseline, the timeframe for exploration of ASEs was lifetime. Hence, the baseline EASE total scores reported in study I-IV reflected this lifetime exploration. However, we did an additional scoring of the baseline EASE interviews, based on a retrospective investigation of the video-/audiotaped interviews and the written documentation of the participants' answers and descriptions. This scoring reflected ASEs as experienced during the previous year and/or currently, and is reported along with the lifetime scores in study IV. At follow-up (study III and IV), we assessed ASEs occurring during the last year (after the baseline assessments) and/or currently.

In study II, TGV thoroughly scrutinized videotaped baseline EASE interviews of the two selected cases, and discussed these with PM. Based on these interviews, descriptions of ASEs were first analyzed and categorized according to the EASE manual, and second, analyzed and categorized according to descriptions of the two core dimensions of BSD: diminished self-affection and hyperreflexivity. The second analysis was based on an ad hoc theoretical approach, comparing the verbatim statements of the two cases with paradigmatic descriptions

of the two core BSD dimensions (L. Sass, 2003; L.A. Sass & Parnas, 2003) as well as with descriptions of core symptoms characterizing depersonalization in disorders outside of the schizophrenia spectrum, primarily in depersonalization disorder (Sierra & David, 2011).

Among trained interviewers, the EASE possess good to excellent interrater reliability (Moller et al., 2011; Nelson et al., 2012). We examined inter-rater reliability by scoring nine video-taped EASE interviews from a study by Haug and colleagues (Haug, Lien, et al., 2012). TGV's EASE scores were compared with the scores from Haug and PM. The inter-rater reliability was in the moderate range, with an ICC of 0.62 (95% CI: 0.24 – 0.88) (two-way mixed effects model, absolute agreement). TGV was extensively supervised by PM through training and scoring of a considerable amount of full EASE-interviews prior to the study, and further; the video-recorded project interviews were consecutively discussed with PM, after the formal scoring was finished, during the first inclusion phase.

3.5.3 COGDIS criteria

The assessment at baseline of cognitive disturbances comprising the COGDIS criteria adhered to the descriptions of these criteria in the SPI-A (F. Schultze-Lutter et al., 2007). As previously noted in section 1.1.3, the SPI-A has been demonstrated to display good inter-rater reliability (Frauke Schultze-Lutter et al., 2007). Still, this assessment was based on information collected in the EASE and SIPS interviews. As descriptions of seven of the nine COGDIS symptoms overlap considerably with description of EASE items (EASE items 1.1, 1.3, 1.4, 1.12.1, 1.12.2, 1.17 and 5.1) (Parnas, Moller, et al., 2005; F. Schultze-Lutter et al., 2007), the most important source of information to assess the COGDIS symptoms was the EASE interviews.

3.5.4 Clinical diagnoses

Clinical diagnoses were set at baseline based on information from the Structured Clinical Interview for DSM-IV Axis I disorders (SCID-I), all modules (First, 1997). For those participants who transitioned to psychosis between baseline and follow-up (confirmed according to POPS criteria in the SIPS), a differential diagnostic assessment was carried out with the Structured Clinical Interview for DSM-IV Axis I Disorders, modules A-D (SCID-I), based on information from clinical records and interviews. Participants who did not transition to psychosis were not reassessed with the SCID-I at follow-up. However, we used a checklist for DSM-IV Schizotypal Personality Disorder, included in the SIPS, to assess criteria for this

disorder in all participants both at baseline (all four studies) and at follow-up (study III and IV).

3.5.5 Functioning

Global functioning was assessed at baseline and follow-up with the Global Assessment of Functioning (GAF) scale, split version (G. Pedersen, Hagtvet, & Karterud, 2007). This version assesses the global severity of symptoms with the GAF symptom (GAF-S) scale, and level of global functioning with the GAF functioning (GAF-F) scale. Each scale is scored from 0 to 100, where lower scores indicate more severe symptoms and lower level of functioning. The scores reflected overall symptom severity and level of global functioning during the last week preceding the assessment. In study I, we report the baseline GAF-S and GAF-F scores. In study III and IV we only report the GAF-F scores, both at baseline and follow-up. This was due to recommendations of using measures of functioning not conflated by symptomatic severity when addressing functional remission (T. Y. Lee et al., 2014).

3.5.6 Symptomatic and functional remission

In study III and IV, we assessed remission from attenuated psychotic symptoms and functioning. Measuring of remission from CHR states combining symptomatic and functional aspects of outcome has been recommended (T. Y. Lee et al., 2014; Polari et al., 2018). With respect to symptomatic remission, we focused on remission of SOPS positive symptoms, and defined this as a score of ≤ 2 on all SOPS positive symptoms (all included subjects had at least one SOPS positive symptom with a score of 3 or more at baseline). This criterion was in accordance with other studies defining symptomatic remission as no longer presenting with attenuated psychotic (positive) symptoms meeting threshold for an UHR state (T. Y. Lee et al., 2014; Polari et al., 2018; Schlosser et al., 2012; Simon et al., 2013). Functional remission was defined as a GAF-F ≥ 70 score, reflecting a good to very good level of functioning, *or* improved functioning, defined as a ≥ 10-point improvement on GAF-F at follow-up compared to the baseline GAF-F score. This functional remission criterion was inspired by, but not identical to, the functional remission criterion suggested in a consensus statement by experts in the field of CHR research (defined as a score of ≥ 70 on the Social and Occupational Functioning Assessment Scale (SOFAS) or a ≥ 5 point improvement on the SOFAS compared with baseline functioning) (Polari et al., 2018).

3.5.7 Childhood trauma and childhood psychosocial functioning

At baseline, we assessed childhood trauma with the Childhood Trauma Questionnaire, Short Form (CTQ-SF). CTQ-SF is a self-report inventory with 28 items, each scored on a 5-point Likert scale from 0 (= never true) to 5 (= very often true). It covers five subsets of childhood abuse or neglect (before the age of 18): physical abuse, sexual abuse, emotional abuse, emotional neglect and physical neglect (Bernstein, Ahluvalia, Pogge, & Handelsman, 1997; Bernstein et al., 2003). Childhood functioning and adjustment was assessed at baseline with the Premorbid Adjustment Scale (PAS), based on semi-structured interviews with the participants (Cannon-Spoor, Potkin, & Wyatt, 1982). The PAS rates level of functioning on a scale from 0 (best level of functioning) to 6 (worst level of functioning), covering four age periods. We only used scores from the childhood (0-11 years) and early adolescent period (12-15 years) in the analyses in thesis, covering four domains: sociability and withdrawal, peer relationships, scholastic performance, and adaption to school. The baseline scores from the CTQ-SF and PAS were used in analyses of data in study I, III and IV. Information collected with these instruments was also included in the investigation and description of background and history in the two cases in study II.

3.5.8 Demographics, medication, substance use, depressive symptoms and treatment

We collected information at baseline on demographic data, medical history and medication, from a detailed clinical interview and clinical records. In study I, III and IV, demographic data and data regarding medication were analyzed with descriptive and other statistical methods. In study II, we scrutinized and compared qualitative descriptions of life situation, background and medical history of the two cases, as revealed through all the clinical interviews at baseline and clinical records. Lifetime diagnoses of alcohol or drug disorder were established via the SCID-I interview (First, 1997). We also obtained information at baseline on alcohol and drug abuse during the last 12 months through the self-report inventories Alcohol Use Disorders Identification Test (AUDIT) (Bohn, Babor, & Kranzler, 1995; Cassidy, Schmitz, & Malla, 2008) and Drug Use Disorders Identification Test (DUDIT) (Hildebrand, 2015). Results from this mapping of substance abuse were not presented in the papers from the studies (I-IV), but were included in qualitative descriptions of the two cases in study II. These data were also used to analyze the effect of substance abuse as a possible confounder in study I, III and IV. Current depression at baseline was assessed with the Calgary Depression Scale for Schizophrenia (CDSS) (D. Addington, Addington, Maticka-

Tyndale, & Joyce, 1992). In the same vein as with AUDIT and DUDIT, results from this assessment were not presented in the papers from the studies, but analyzed to investigate whether current depression could be a confounder associated with the outcome measures. Information concerning amount and kinds of treatment between baseline and follow-up (individual psychotherapy sessions, medication, family work sessions, other psychosocial interventions, hospitalizations and discontinuation of treatment) was obtained via a questionnaire answered by treating clinicians or through interviews with the participants if they no longer were in treatment. This information supplemented the analyses in study III and IV.

3.6 Ethical considerations

The current research project is part of the TOP study (see section 3.1), approved by the Regional Committee for Medical Research Ethics and the Norwegian Data Inspectorate. The research project described in this thesis received an additional approval from the Regional Committee for Medical Research Ethics. All participants signed a written informed consent, and if they were below 18 years (n = 12) their parents signed the consent too. As previously noted, all the participants also consented (with their signature) to be videotaped or audiotaped during the EASE and SIPS interviews. The participants received thorough verbal and written information about the assessments (both at baseline and at follow-up) and the aims of the research project. The consent included an approval of letting the research team have access to clinical/medical records until the follow-up assessments were completed. The patients were told that it was voluntary to participate, possible to withdraw from the study at any time for no specified reason, and that it would have no negative consequences for them and their treatment if they refused to participate or if they later withdrew from the study. They were also informed about the security of data handling and confidentiality. The patients were offered NOK 500 to participate in the study, and were compensated for traveling expenses.

Although comprehensive and time consuming, the burden of taking part in the assessments was not considered to exceed a thorough clinical examination in ordinary clinical settings. The assessments were sensitive to the patients' present level of illness, discomfort and endurance, and were carried out over several appointments. One could raise concerns of relevance to this research project regarding the potential stigma of being defined as being at high risk of psychosis, and the fear this may instigate in the assessed person, e.g. (Moritz et al., 2019). However, the hold in this contention has been questioned. Regarding stigma, CHR

individuals may experience this *before* they are labeled as CHR, due to the symptoms themselves and the fear of being mentally ill (Corcoran, 2016; Yang et al., 2015). Yung and colleagues refer to studies in CHR (at-risk mental states) samples showing that getting the opportunity to talk about unusual experiences with a clinician is appreciated, reduces stress and anxiety, increases understanding, and even is experienced as beneficial for recovery. Even being asked questions from a structured interview and to be informed about their condition, was found to be reassuring (Yung et al., 2019). In a similar vein, it is conceivable that being asked questions about anomalous self-experiences may instigate unpleasant feelings, worries and fear of impending psychosis. However, many patients who have been interviewed with the EASE remark the relevance of the questions, express relief about being questioned and validated by a clinician who is familiar with these phenomena, and appreciate the help they are getting with getting a vocabulary to describe their experiences (Škodlar & Henriksen, 2019). Hence, we considered the benefits of being assessed with instruments like the SIPS and the EASE to be potentially higher than the disadvantages.

Following the assessments, all participants and their treating clinicians were thoroughly informed about the results from the assessments. In the dialogue with the participants, both in advance of and after the assessments, we emphasized a sensitive, careful communication. We conveyed that "risk" status is not a disorder in itself, that symptoms may improve, that opportunities for treatment improve by finding out more about their condition, and that recovery is possible. A written report from the assessments was shared with treating clinicians if the participants approved.

In study II, we purposely selected two illustrating cases. These patients were informed about this specific study, and asked if they were willing to participate in it. They both signed a written consent designed for this specific study, approving the publishing of the case descriptions in a peer-reviewed paper. We changed or removed descriptions of biographical details, background, life situation and medical history which could identify the two cases.

3.7 Statistical analyses

We performed all statistical analyses with the Statistical Package for Social Sciences (SPSS), version 25. Subgroup differences in clinical and sociodemographic characteristics were analyzed with a range of statistical methods. All tests were two-tailed, and the level of significance was set to 0.05, if not otherwise specified. For comparisons of continuous variables in two groups, we used independent samples t-tests for normally distributed

variables and the Mann-Whitney U tests for skewed variables. The Fisher's exact test was used to analyze subgroup differences in categorical variables (due to the relatively small samples). Analyses of differences in continuous variables between three subgroups (investigated in study IV) were carried out with the non-parametric Kruskal-Wallis test. Repeated measures comparisons of continuous variables (comparing baseline and one year follow-up scores) were carried out with paired samples t-tests for normally distributed variables and the Wilcoxon Signed Rank Test for analyses of data without normal distribution (study III and IV).

We investigated correlations between variables with the Pearson correlation coefficient or the Spearman rank order correlation analyses, depending on type of variables. As we conducted multiple comparisons, we adjusted the alpha level of significance according to Bonferroni corrections. Due to the exploratory nature of the studies (the studies did not explicitly state hypotheses to be tested), we also reported results significant according to nominal *p*-values ($p < .05$). In study I, we performed a standard multiple regression analysis to investigate the relative contribution on total explained variance in the dependent variable (mean EASE total score) of four independent variables (showing at least nominally significant correlations with the dependent variable). In study III, we used block-wise hierarchical multiple regression tests to investigate whether EASE total scores at baseline explained a significant amount of the variance in the follow-up outcome variables, after controlling for the influence of the baseline equivalents of the follow-up variables. As previously described, we did not perform any statistical analyses specific for the qualitative case investigations in study II. More detailed descriptions of statistical methods are presented in the papers covering study I, III and IV.

4. RESULTS/SUMMARY OF PAPERS

Paper I: Anomalous self-experiences are strongly associated with negative symptoms in a clinical high-risk for psychosis sample

Background: Anomalous self-experiences (ASEs) are considered as central features of the schizophrenia spectrum disorders and prodromal schizophrenia. There is a need for studies exploring ASEs in potentially prodromal conditions, i.e. in clinical high risk (CHR) for psychosis, and the relationships between ASEs, other clinical characteristics and background factors. We aimed to investigate total and single-item prevalence of ASEs in a CHR for psychosis sample, and associations with conventional psychosis-risk symptoms, present and childhood global/psychosocial functioning, and childhood trauma.
Methods: The sample (n = 38) included 31 CHR, according to ultra-high risk or cognitive basic symptoms (COGDIS) criteria, and seven with non-progressive attenuated positive symptoms. Psychopathological evaluations included Examination of Anomalous Self-Experience (EASE), Structured Clinical Interview for Prodromal Syndromes (SIPS), (including a checklist for DSM-IV schizotypal personality disorder)/Scale of Prodromal Symptoms (SOPS), Schizophrenia Proneness Instrument – Adult (SPI-A) (only the COGDIS-criteria), Structured Clinical Interview for DSM-IV Axis I disorders (SCID-I), Global Assessment of Functioning – Split version (S-GAF), Premorbid Adjustment Scale (PAS) and Childhood Trauma Questionnaire – Short form (CTQ-SF). Analyses examined whether differences in mean EASE total scores were associated with clinical and demographic characteristics (investigating sub-group differences), and correlations between EASE total, other psychopathological variables and background factors (PAS, CTQ-SF).
Results: The mean total EASE score was in line with reports from other CHR samples, and was particularly enhanced in schizotypal personality disorder and in subjects meeting COGDIS-criteria. The four most frequent EASE-items (ruminations/obsessions, distorted first-person perspective, diminished presence, derealization) were present in two-thirds or more of the participants. EASE total did not differ between subjects meeting CHR formal criteria and subjects with non-progressive attenuated positive symptoms, and was not associated with demographic and background factors. EASE total was significantly associated with negative and disorganization symptoms. A multiple regression analysis revealed that the severity of negative symptoms explained most of the variance in EASE total.

Conclusions: These results corroborate other findings that ASEs are frequent and important features in CHR conditions and in the schizophrenia spectrum. The co-presence of ASEs and COGDIS criteria may point to a sub-group particularly vulnerable to schizophrenia spectrum disorders. The strong relationship between ASEs and negative symptoms is in line with both early and recent phenomenologically oriented theories on self-disorders in schizophrenia, but may not necessarily imply the development of a schizophrenia spectrum disorder. The lack of a significant relationship between ASE and positive symptoms may partly be related to a restricted range of positive symptoms in the sample. The strong associations with negative symptoms and cognitive disturbances (COGDIS) should be investigated in longitudinal studies to address causality, psychopathological pathways and schizophrenia spectrum specificity.

Paper II: Anomalous self-experiences: markers of schizophrenia vulnerability or symptoms of depersonalization disorder: a phenomenological investigation of two cases

Background: Basic self-disturbance (BSD) is proposed to constitute the clinical core of schizophrenia spectrum disorders, including prodromal states and schizotypy. ASEs are suggested as phenotypic variants of BSD, representing markers of schizophrenia vulnerability. However, ASEs also include depersonalization and derealization symptoms, which are not restricted to the schizophrenia spectrum, but may also occur in non-psychotic conditions like depersonalization disorder (DPD). It is unclear to what extent the prevalence and nature of ASEs are differing between the two conditions. The main aim of this paper was to assess and compare ASEs in both conditions, based on literature and two prototypical cases. This might expand the understanding of these phenomena, and strengthen the basis for clinical differentiation.

Methods: One patient with schizotypal personality disorder (SPD) and one with DPD were selected from an ongoing clinical high-risk of psychosis study. ASEs were assessed with the EASE, and analyzed according to the two central dimensions of BSD: diminished self-affection and hyperreflexivity, as well as according to prototypical aspects of depersonalization. The cases were also analyzed and compared with respect to chronology, other symptomatology and psychopathological pathways.

Results: Both cases revealed ASEs reflecting the central dimensions of BSD as well as prototypical aspects of depersonalization. Only the SPD-case linked ASEs to psychotic-like ideas of external influence and control. The symptoms had an insidious early childhood onset

with no obvious triggers in the SPD-case, combined with distrust in others and disturbances in social functioning since childhood. In the DPD-case, ASEs had an abrupt adolescence onset, triggered by second-time cannabis use and panic anxiety. In contrast with the SPD-case, the DPD-case reported childhood emotional abuse and neglect, and had a first-degree relative with schizophrenia.

Conclusions: The similarities and differences in ASEs, symptomatology and developmental pathways of the two cases might be accounted for by an updated model of self-disorders. The model proposes that schizophrenia manifests as a result of a combination of early 'primary' onset of ASEs, reflecting disturbances in early neurodevelopment, and later occurring, 'secondary' ASEs of a more defensive-protective character. In line with this, the DPD-case may be characterized only by secondary ASEs (possibly related both to childhood and more recent adversities and stressors), and thus better protected against psychotic decompensation than the SPD-case, tentatively affected by a combination of primary and secondary ASEs. The striking similarities between the two cases on a phenomenological level may question the clear categorical separation of non-psychotic disorders like DPD from "mild" schizophrenia spectrum disorders (SPD). Closely considering psychopathological, social and medical history, in addition to a phenomenological investigation of ASEs, may enhance the specificity of ASEs as phenotypic markers of vulnerability for SSDs and psychosis.

Paper III: Basic self-disturbance in subjects at clinical high risk for psychosis: relationship with clinical and functional outcomes at one year follow-up

Background: BSD is assumed to drive symptom development in schizophrenia spectrum disorders and in CHR for psychosis. Most CHR subjects have enduring clinical needs and suffer from psychosocial impairments, both in transitioning to psychosis and non-transitioning cases. Exploration of BSD phenomena could help to identify CHR subjects with high likeliness of symptomatic and functional non-remission. We aimed to investigate in a one-year follow-up study whether the clinical and functional trajectories in CHR subjects were associated with, and predicted by, the severity of BSD at baseline.

Methods: We investigated the relationship between BSD at baseline, assessed with the EASE, and symptoms and functional outcome at a one-year follow-up in 32 patients, including 26 CHR (UHR and/or COGDIS) and six with non-progressive attenuated psychotic symptoms. The mean follow-up time was 13 months. At follow-up, symptoms were assessed with the SIPS/SOPS and global functioning with the GAF – split version. We defined full remission as a score of ≤ 2 on all SOPS positive symptoms, together with a good level of functioning

(GAF-F ≥70) or improved functioning (≥10-point improvement on GAF-F compared to baseline functioning).

Results: Correlations between baseline BSD levels and follow-up positive, negative and disorganization symptoms, and follow-up global functioning level, were significant. Hierarchical regression analyses revealed that higher levels of baseline BSD predicted more severe positive symptoms and lower global functioning at follow-up, after adjusting for baseline positive symptoms and functioning. Subjects who were not in symptomatic and functional remission after one year had higher levels of BSD and negative symptoms, and lower functioning level, at baseline. These results were not affected by removing the four subjects in the sample who had transitioned to psychosis from the analyses. Baseline BSD in participants with schizophrenia spectrum diagnoses at follow-up (9 of 12 were schizotypal personality disorder) were at the levels seen in schizotypal disorders in previous studies, but not significantly different from the other participants.

Conclusions: The co-presence of a high severity of BSD, negative symptoms and deficiencies in psychosocial functioning in CHR may constitute a particularly strong prognostic risk index for symptomatic and functional non-remission, even in non-transitioning cases. Early identification and assessment of BSD may constitute a useful prognostic tool and a signal for therapeutic targets in CHR conditions. Further CHR studies investigating these relationships with larger samples are recommended.

Paper IV: Basic self-disturbance trajectories in clinical high-risk for psychosis – a one year follow-up study

Background: BSD has been proposed as a driver of symptom development in schizophrenia spectrum conditions. Investigations of BSD trajectories in CHR may cast a light on the question of the stability of BSD, and analyses of associations with clinical and other patient characteristics may identify CHR individuals at highest risk of adverse clinical and functional outcomes.

Methods: In a one-year follow-up of 32 patients (15-29 years) at putative risk for psychosis, we investigated changes in BSD levels (assessed with the EASE) from baseline to follow-up. Associations between follow-up BSD levels and other clinical, functional and socio-demographic characteristics at baseline and follow-up were analyzed. BSD trajectories from baseline to follow-up were identified, and associations between these trajectories and other clinical and functional characteristics were also analyzed. Clinical high-risk (CHR) status and

symptom severity were assessed with the SIPS/SOPS scales and the cognitive basic symptoms high-risk criteria (COGDIS). DSM-IV diagnoses, functioning and other clinical characteristics were assessed with standard clinical instruments.
Results: Higher baseline severity of negative symptoms and meeting COGDIS criteria were associated with higher BSD levels at follow-up. At follow-up, higher BSD levels correlated with higher severity of positive, negative, disorganization and general symptoms, and with a lower level of global functioning. We found higher follow-up BSD levels in subjects with schizotypal personality disorder (SPD) at baseline (n = 5) and in schizophrenia spectrum cases at follow-up (n = 12), including SPD (n = 9). Mean BSD levels decreased significantly from baseline to follow-up, but individual trajectories varied considerably. Subjects with increased BSD levels (n = 7) had higher baseline BSD levels, as well as non-remission of SOPS positive symptoms and functional decline from baseline to follow-up.
Conclusions: The strong associations between BSD levels and other psychopathological measures at follow-up may point to a consolidation of a more severe psychopathological gestalt in certain particularly vulnerable CHR subjects. These CHR subjects may more often be characterized by negative symptoms and cognitive disturbances (COGDIS criteria) at initial assessments, and be more at risk of disorders in the schizophrenia spectrum. The heterogeneity in BSD trajectories may imply that the stability of BSD is more influenced by individual characteristics than previously thought. Overall, the current study indicates that subgroups in the CHR population with a higher risk of clinical non-remission or even a deteriorating course may be identified by supplementing CHR criteria (including COGDIS) with assessment of BSD and negative symptoms.

5. DISCUSSION

5.1 Main findings

Phenomenological approaches are indispensable to explore and describe subjective, first-person experience, and to elucidate the fundamental relationships between this experiential level and symptomatic expressions (Nelson, Yung, Bechdolf, & McGorry, 2008; Parnas & Handest, 2003). In this thesis, we combined a phenomenological approach, based on in-depth interviews with the EASE, with the use of other instruments focusing primarily on symptomatic expressions, e.g. the SIPS and SCID-I. The four studies included a range of research questions, but here we categorize and discuss the main findings according to three main topics (with some overlaps between these). The first topic concerned the *frequency, severity* and *stability* of BSD phenomena (ASEs) in CHR conditions. Second, we discuss findings of the cross-sectional and longitudinal *relationships* between BSD and other symptoms, aspects of functioning and background factors, focusing in particular on the *prognostic significance* of BSD for clinical and functional outcomes. Third, the findings were of interest regarding the *specificity* of BSD with respect to clinical (diagnostic) outcomes, with a particular focus on the assumed affinity (in the BSD model) with schizophrenia spectrum conditions (including prodromal states and schizotypy), and the possible overlap with depersonalization conditions outside the schizophrenia spectrum.

5.1.1 BSD in CHR for psychosis – frequency, severity and stability

In the first study, we found total levels of ASEs in line with reports from other UHR studies (Comparelli et al., 2016; Koren, Lacoua, Rothschild-Yakar, & Parnas, 2016; Nelson et al., 2020; Nelson et al., 2018; Nelson et al., 2012; Park et al., 2020; Raballo et al., 2016). These levels did not differ significantly between those meeting formal CHR criteria (UHR and/or COGDIS) and subjects in the non-progressive symptoms group. Levels of ASEs were significantly higher in subjects meeting COGDIS criteria than in UHR subjects not meeting these criteria, even when removing EASE items with considerable overlap with COGDIS items from the analyses. Considering the self-disorder model, this latter finding may not come as a surprise, as disturbances in the stream of consciousness (reflected in the COGDIS criteria) are considered as frequently occurring aspects of a more encompassing psychopathological 'Gestalt' characterized by self-disorders (Parnas, 2011; Parnas, Moller, et al., 2005; L.A. Sass & Parnas, 2003). With 'Gestalt' it is here referred to certain meaningful, clinically prototypical "wholes", jointly constituted by both "outer" (i.e. symptomatic

expressions) and "inner" aspects (e.g. subjective experiences and beliefs) (Parnas, 2011; Parnas & Jansson, 2015). After the preparation of our study, a meta-analysis has been published which compared the scores on BSD/self-disorder measures between different diagnostic groups. This meta-analysis found that CHR subjects scored significantly higher than healthy controls and non-CHR subjects with other mental illness (a category comprising a heterogeneous specter of clinical diagnoses), but significantly lower than patients diagnosed with SSDs (Raballo et al., 2021). Combined, the results from the first study in this thesis and these other CHR studies point to BSD as a frequent, often prominent feature of CHR conditions.

This prominence was underlined by the results from the analyses in study I regarding the frequency and distribution of single ASEs (EASE-items). Each of the eleven most frequent EASE items (19% of the 57 main EASE items) were present in 45% or more of the participants. Among these, were items reflecting the prototypical core BSD dimensions/processes of diminished self-affection/self-presence and hyperreflexivity, e.g. EASE items 2.1 *Diminished sense of basic self* (present in 50% of the participants), 2.2 *Distorted first-person perspective* (present in 68%), 2.4 *Diminished presence* (present in 66%) and 2.6 *Hyperreflectivity* (present in 47%). As discussed in the paper from study I, there were considerable overlaps with the findings in two other studies investigating single EASE-item frequency, one in a UHR sample (Davidsen, 2009), and one in a SSD sample (Nordgaard, Nilsson, et al., 2017). These findings indicated a *phenomenological continuity* between ASEs in CHR and ASEs in schizophrenia or other SSDs. However, the question of this phenomenological continuity is still quite open, as no studies to our knowledge have yet compared the occurrence of item-specific ASEs between CHR and diagnostic groups. In addition, we can neither preclude that overlaps nor discrepancies between different studies could be affected by differences between the raters in how they score the EASE, i.e. inter-rater reliability issues.

5.1.1.1 The stability of BSD in CHR for psychosis

BSD in the schizophrenia spectrum and the schizophrenia prodrome is considered to have a mainly *trait-like* character (Nordgaard, Handest, et al., 2017; Parnas & Henriksen, 2014) or to be characterized by a *combination of trait-like and state-like BSD features*, as proposed in the suggested revision of the self-disorder model (Borda & Sass, 2015; L. Sass et al., 2018; L. A. Sass & Borda, 2015). In study IV, we found a significant decline in EASE total scores in the full sample from baseline (*Md* = 12, scores based on last year experiences) to the one-year

follow-up (*Md* = 8.5). However, individual BSD trajectories varied considerably. In subjects with declining BSD levels, the magnitude of the decline varied, and seven of the 32 participants (22%) in study IV had increasing BSD levels. Increasing EASE levels were significantly associated with increases in SOPS positive symptoms and a decline in functioning level between baseline and follow-up. The majority (5 of the 7) in this group was diagnosed with SSDs at follow-up.

If ASEs at least partly reflect secondary, reactive, "defensive" forms of hyperreflexivity, diminished self-presence and disturbed "grip" of the cognitive/perceptual field of awareness, as assumed in the revised self-disorder model (L. Sass et al., 2018), certain temporal changes in BSD levels may be expected. In line with the affective pathway to psychosis hypothesis (Myin-Germeys & van Os, 2007; Trotman et al., 2014), these secondary ASEs could be amenable to fluctuations in concordance with changes in environmental and social stressors, and in interaction with neurobiological and psychological factors like stress vulnerability, stress sensitization and the ability to adapt to stressful life-events. CHR conditions are clinically very heterogeneous (Fusar-Poli, Yung, et al., 2014; van Os & Linscott, 2012), possibly including more subjects with state-like ASEs than in samples restricted to more homogeneous SSDs. However, it is conceivable that a person is still affected by trait-like BSD even though EASE total scores decline, as several of the subjects in the sample with declining EASE levels still presented with EASE levels at follow-up above what is generally found in UHR samples (Raballo et al., 2021). Possibly, the more reactive ASEs tend to remit while more primary, trait-like ASEs do not, in the same person.

It should be mentioned that the majority of subjects in our sample with stable EASE levels or a small decline in these levels, had low EASE levels, both at baseline and follow-up. In subjects with low baseline levels, we cannot expect a significant decline due to a floor effect of the EASE measure. Hence, we should be careful not to suggest that this relative stability in EASE levels was due to primary, trait-like BSD. It was more likely an artefact of the floor effect, reflecting that the subjects in this group were affected by ASEs in a low degree or not at all. At least, such assumptions would have to be investigated in detail, in each case.

Follow-up SSD subjects (n = 12) had stable EASE levels as a group, although the individual BSD trajectories varied, and the EASE total score was significantly higher at follow-up in this group than in the other subjects in the sample. These findings support that self-disorders are more severe in the schizophrenia spectrum (Raballo et al., 2021). Variations in the individual BSD trajectories for the SSD subjects are in line with the updated BSD model, and may point

to individual variations with respect to the predominance of primary versus secondary forms of BSD (and the interplay of these forms) (Borda & Sass, 2015; L. Sass et al., 2018; L. A. Sass & Borda, 2015).

As demonstrated in study IV, longitudinal assessments of BSD with the EASE may reveal state or trait characteristics of significant prognostic relevance. In the next section we will more closely inspect the relationships between BSD and other psychopathology measures, and discuss the prognostic implications of identifying (high levels of) BSD in CHR for psychosis.

5.1.2 Cross-sectional and prospective relationships between BSD and other psychopathology measures

5.1.2.1 Cross-sectional associations at baseline and at follow-up

The strong, positive correlation at baseline in study I between EASE total and negative symptoms, as well as the significantly higher EASE total scores in subjects meeting COGDIS criteria compared to the other participants (also significant when removing items from the analyses overlapping the most between the EASE, SIPS and SPI-A measures), were in accordance with the self-disorder/BSD model (Nelson & Raballo, 2015; L. A. Sass, 2003a; L.A. Sass & Parnas, 2003). However, we did not find a significant relationship between EASE total and SOPS positive symptoms at baseline in study I, and this negative finding seemed at first sight to contradict the assumptions of the BSD model (L.A. Sass & Parnas, 2003). This could be due to a restricted range of positive symptoms in the baseline sample, reflecting the inclusion criteria in the current research project. Prediction studies are quite often facing this problem (Wiberg & Sundstrom, 2009). This finding was in line with another study which only included UHR subjects (Comparelli et al., 2016), and we may speculate that this study faced this problem too. In two other studies including CHR subjects, significant associations were found between EASE total and measures of positive symptoms, but both these studies included a broader help-seeking sample, with inclusion criteria not restricted with respect to positive symptoms (Koren et al., 2013; Raballo et al., 2016).

Still, the methodological problem of restricted range may not be the only explanation for the non-significant relationship. In a study by Madeira and colleagues, CHR individuals affected by so-called “Truman symptoms” did not have higher CAARMS scores than CHR individuals without these symptoms (Madeira et al., 2016). As these symptoms are described, they seem to be variants of ASEs (“…the ordinary is changed or different, and leading to a “Truman

explanation. ” (p. 270), referring to the 1998 Peter Weir’s movie), and to be related to core BSD aspects (“… profound change of the subjectivity and self-awareness, resulting in an unstable first-person perspective…”, p. 271) (Madeira et al., 2016). Possibly, the non-significant association between Truman symptoms and CAARMS scores in this study, and between ASEs and positive symptoms at baseline in our study, also reflected the heterogeneous nature of CHR conditions. In some of these conditions, attenuated positive symptoms may be non-prodromal trans-diagnostic phenomena, triggered or worsened by adverse environmental circumstances and increased psychological stress. Hence, they are also likely to fluctuate and remit if the stress is relieved, and less likely to progress to a frank psychotic state (van Os & Guloksuz, 2017). We may speculate that such transient CHR conditions are also less likely to be associated with BSD.

In contrast with the non-significant association at baseline, we found in study IV significant and strong cross-sectional correlations between EASE total and SOPS positive symptoms at the one-year follow-up. EASE total was also significantly correlated at follow-up with all the other SOPS subscales (negative, disorganization and general symptoms), as well as with global functioning (GAF-F), at follow-up. Hence, a *consolidation of a clinical Gestalt* seemed to have taken place for those CHR subjects with the most adverse outcomes. Possibly, this contrast between the baseline versus the one-year follow-up findings reflected differences in state- versus trait-characteristics of clinical conditions. Symptomatic expressions, although seemingly “similar”, may reflect varying psychopathological processes and clinical Gestalts (Parnas & Jansson, 2015). In one person, perceptual disturbances may reflect a transient stress-induced state in a person with an otherwise quite stable experience of the self and the world. In another person, such perceptual disturbances may constitute one of several manifestations of a fundamental, trait-like transformation of subjective experience of the world and the self (i.e. reflections of a more severe, all-encompassing psychopathological Gestalt). Hence, an exploration of subjective experiences in CHR states may be crucially important for an adequate interpretation and *understanding* of the condition and psychopathological processes, as noted by Parnas and Handest:

> “A faithful description of experience is the first step in any taxonomic project or in any effort to correlate pathological experience to its biological substrate” (Parnas & Handest, 2003)(p.131).

5.1.2.2 Prospective investigations of associations between baseline and follow-up measures

SOPS subscale scores did also decline in the total sample from baseline to follow-up (study III), but only 11 (34.4%) participants reached full symptomatic (from attenuated positive symptoms) and functional remission. Higher baseline EASE levels were significantly associated with adverse clinical and functional outcomes at the one-year follow-up in study III and IV. More precisely, non-remission of positive symptoms (SOPS) and global functioning (GAF-F) was predicted by higher baseline EASE levels (controlling for the effect of the baseline SOPS positive variable and the baseline GAF-F variable). Higher baseline EASE levels were also significantly associated with higher SOPS negative and disorganization symptoms scores at follow-up. Removing the four subjects who transitioned to psychosis between the baseline and follow-up assessments from the analyses had no significant impact on these findings. Svendsen and colleagues found a comparable kind of pattern in a seven-year follow-up study of first-treatment patients with psychotic disorders. In this study, patients with lower baseline BSD levels were significantly more likely to have recovered (full remission and regained functioning) after seven years than patients with higher baseline BSD levels (Svendsen et al., 2019). Both the findings in this thesis and in the study by Svendsen and colleagues pointed to the prognostic significance of assessing BSD. Possibly, as previously suggested, symptoms and functional deficits were more intimately interconnected with, and driven by, trait-like BSD, and thus less likely to remit (or more likely to reoccur) in CHR subjects with the most adverse outcomes at follow-up.

Other clinical factors associated with adverse symptomatic and functional outcomes at the one-year follow-up were more severe baseline negative symptoms and a lower level of global functioning (study III). Interestingly, these clinical features, but not baseline positive symptoms, were significantly associated with future severity of positive symptoms, maybe again pointing to the more state-like character of positive symptoms in many CHR subjects (van Os & Guloksuz, 2017). More severe negative symptoms and meeting COGDIS criteria at baseline, was also associated with high follow-up BSD levels, and subjects with increasing EASE levels had significantly higher baseline SOPS negative scores than subjects with declining EASE levels.

Negative symptoms and/or deficits in global functioning have repeatedly been demonstrated to constitute risk factors for adverse clinical outcomes in CHR for psychosis (and in the general youth population (Dominguez, Saka, Lieb, Wittchen, & van, 2010)). This includes an increased risk for psychosis (Jean Addington et al., 2017; Paolo Fusar-Poli et al., 2015;

Healey et al., 2017; Oliver et al., 2020; Valmaggia et al., 2013; Zhang et al., 2020), and also clinical and functional non-remission in non-transitioning conditions (Beck, Studerus, et al., 2019; Carrion et al., 2016; Koutsouleris et al., 2018; Schlosser et al., 2015; Schlosser et al., 2012). Persistent negative symptoms may constitute a particularly strong risk factor for poor outcome in CHR, particularly psychosocial functioning, even in the absence of transition to psychosis (Carrion et al., 2016; Yung, Nelson, McGorry, Wood, & Lin, 2018). Deficits in global functioning are marked in CHR for psychosis, almost as severe as in subjects with psychotic disorders (Paolo Fusar-Poli et al., 2015). Negative symptoms are also highly prevalent in CHR for psychosis (Piskulic et al., 2012b), and along with deficiencies in global functioning, a major reason for individuals to seek help at CHR services (Falkenberg et al., 2015).

In line with an empiricist-behavioral approach, assessment of negative symptoms have in general focused on observable aspects, while ignoring the subjective dimension of these symptoms (L. A. Sass, 2003a). Observable symptoms, e.g. diminished affective expressions, have been equated with diminished affective *experience*, which may not be the case (L. A. Sass, 2003a; L.A. Sass & Parnas, 2003). Reliance on this positivistic approach to assessment, may have seriously limited the understanding of negative symptoms. The limited understanding of factors underlying the development and maintenance of these symptoms have been highlighted as a central cause for the dearth of successful effects of pharmacological and psychological interventions (P. Fusar-Poli, E. Papanastasiou, et al., 2015; Kirkpatrick, Fenton, Carpenter, & Marder, 2006).

As described in the introduction section, disturbances in the basic sense of self may constitute a central driving force for the development and maintenance or recurrence of both negative and other symptoms during the prodrome (Blankenburg & Mishara, 2001; Parnas, 2011; L.A. Sass & Parnas, 2003). These disturbances obviously may even underlie psychosocial impairments (Haug et al., 2014; Stanghellini & Ballerini, 2011b), as measured with GAF or other functioning measures. Hence, the strong cross-sectional and prospective associations between BSD, negative symptoms and global functioning may be due to BSD constituting the core of the overall clinical condition, which is intimately linked to its symptomatic and functional manifestations.

Still, negative symptoms, as defined and operationalized in Anglo-American psychiatry, are not restricted to the schizophrenia spectrum and prodromal states. Symptoms like blunted affect, anhedonia or avolition occur quite frequently in several disorders outside the

schizophrenia spectrum, e.g. in depressive disorders (G. P. Strauss & Cohen, 2017). Depressive disorders were the most common DSM-IV diagnoses in the sample in this thesis (in line with other CHR studies (Fusar-Poli, Nelson, et al., 2014)), and we cannot preclude that high SOPS negative symptom ratings in some subjects reflected a psychopathological Gestalt characterized by depression. However, these symptoms may be more state-like than negative symptoms in the SSDs (G. P. Strauss & Cohen, 2017), and not as strongly associated with BSD as in the SSDs. The consolidation of an encompassing psychopathological Gestalt at follow-up, in subjects with high levels of BSD and more severe negative symptoms both at baseline and follow-up (study III and IV), may point to a subgroup with more stable negative symptoms and associated deficits in functioning, which may also be more likely to belong to the schizophrenia spectrum. Hence, we conclude that there is a high need for researchers and clinicians alike to be more attentive to the subjective dimension of negative symptoms and deficits in functioning.

The significant associations between BSD levels (both at baseline and follow-up) and follow-up SOPS disorganization symptoms, as well as the strong relationship between meeting COGDIS criteria at baseline and high BSD levels at baseline and follow-up, were also in line with the BSD model. These associations highlight the need to be attentive to the experiential aspects of disorganization symptoms and cognitive disturbances in CHR conditions as well. The importance of exploring the subjective dimensions of cognitive disturbances in CHR, is underlined by the stronger affinity between meeting COGDIS criteria and future schizophrenia, compared to meeting the UHR criteria (Fusar-Poli, Bechdolf, et al., 2013).

In summary, the findings regarding associations between BSD and other psychopathology measures support the *prognostic significance* of BSD in CHR conditions. An important finding was that a combination of high baseline BSD levels, negative symptoms and low levels of functioning may identify CHR individuals at high risk of symptomatic and functional non-remission. Although not related to remission in our sample (study III), the presence of cognitive disturbances may also add to this prognostic significance, given the association with future BSD levels (study IV). Finally, following BSD trajectories in time is of importance, as subjects with high EASE levels at both baseline and follow-up, and in particular subjects with increasing EASE levels, had more adverse clinical and functional outcomes at follow-up (study IV).

5.1.2.3 Cross-sectional and prospective associations between BSD and background factors

In order to further understand the pathogenesis of BSD, empirical investigations are needed exploring putative childhood and adolescence vulnerability or risk factors for the development of BSD. Such investigations are still sparse in this research field (Parnas & Henriksen, 2014). In light of the updated BSD model, vulnerability factors may be found in 1) early neurodevelopmental disturbances, and symptomatic and functional manifestations of these disturbances (suggested to be associated with "primary" BSD), and in 2) adverse environmental circumstances (suggested to be associated with "secondary" BSD) (L. Sass et al., 2018). In this research project, we assessed at baseline (premorbid) childhood/adolescent psychosocial functioning and adjustment with the PAS, and childhood trauma with the CTQ-SF, to address possible early vulnerability factors.

No significant associations were found between PAS at baseline and BSD levels at baseline (study II) or follow-up (in study IV, the association between PAS Early adolescence subscale correlated with EASE total at follow-up at a significance level of $p < .05$, but this correlation was not significant after Bonferroni-correction). The results may reflect that BSD in CHR is not necessarily overall related to disturbances in childhood functioning. If it is the case that BSD is primarily related to secondary factors in a considerable proportion of CHR subjects, we may not expect to find significant associations with childhood functioning in the sample as a whole. In samples restricted to the schizophrenia spectrum however, we might expect to find more childhood clinical and functional manifestations of self-disorders (Nordgaard & Parnas, 2014). Indeed, analyses of PAS scores revealed that individuals with SSD diagnoses at follow-up ($n = 12$) had significantly higher scores ($p < .05$) than non-SSD individuals ($n = 20$). However, PAS scores were not significantly correlated with EASE total in neither of these two groups (these analyses are not included in the analyses presented in the papers from studies 1-IV). This should be considered in the light of the small sample size (increasing the risk of Type I errors), and the diagnostically more homogeneous SSD group with generally higher BSD scores.

We did neither find any significant (Bonferroni-corrected) correlations between scores on the CTQ-SF (total scale and subscales) and EASE total scores at baseline or follow-up (higher scores on the CTQ-SF subscale Emotional Neglect correlated with higher EASE total scores at baseline at a significance level of $p < .05$, but this correlation was not significant after Bonferroni correction). As with the results regarding associations between PAS and EASE total scores, this could be due to the small sample size. It should also be mentioned that the

instrument CTQ per se has been criticized for not capturing childhood traumas good enough, omitting exposure to peer victimization (bullying) and being witness to domestic violence, and not providing any information about changes in exposure levels during development (Teicher & Parigger, 2015).

One study has found a significant correlation between CTQ-SF total scores and EASE total in females with first-episode schizophrenia (Haug et al., 2015), and in another study a significant association was found between school bullying victimization and EASE scores, in a combined UHR and first-episode psychosis sample (Rasmussen et al., 2020). In a study of a non-clinical sample, ASEs were linked to childhood trauma (measured with the CTQ-SF), and functioned as a mediator between childhood trauma and psychotic-like experiences (Gaweda, Goritz, et al., 2018). It could also be noted that persistent negative symptoms in CHR subjects, which we found to be strongly linked to higher BSD levels at baseline and follow-up, have also been found to be associated with childhood trauma (Yung et al., 2018). Hence, although evidence is still sparse and we did not find significant associations, findings from these other studies suggest that there may be some links between childhood trauma and later BSD, which should be explored in future studies, also with other instruments than the CTQ, to capture all important aspects of childhood trauma.

Concerning socio-demographic factors (age, gender, country of birth, years of education, current work/school status, civil status), we did not find any links with BSD, except for a gender difference in the stability of EASE. In contrast to the significant decrease in EASE total from baseline to follow-up in females, there was no such significant decrease in males. The EASE total scores in males were nominally higher than in females, at both time points, but these differences did not reach a statistically significant level. We found a similar pattern regarding SOPS negative and disorganization symptoms, with nominally higher scores in males, and a significant decrease from baseline to follow-up in females, but not in males. The more severe follow-up outcome in men is in line with studies finding more severe symptoms and functional deficits in men than women in CHR samples, particularly with respect to negative symptoms, social functioning and longer duration of untreated illness (Barajas, Ochoa, Obiols, & Lalucat-Jo, 2015; Rietschel et al., 2017)

5.1.3 The specificity of BSD for clinical (diagnostic) outcomes

We found that participants who were diagnosed with SSDs at baseline (n = 5, all schizotypal personality disorder; SPD) had significantly higher EASE total scores than the other participants at baseline (study I) and follow-up (study IV). As previously noted, subjects diagnosed with SSDs at follow-up (n = 12, nine with SPD, two with schizophrenia, one with schizophreniform disorder) also had significantly higher EASE total scores at follow-up (study IV). The EASE levels at baseline in the twelve follow-up SSD subjects were in line with other studies on schizotypal disorders/schizotypal personality disorders (Nordgaard & Parnas, 2014; Raballo & Parnas, 2012), but not significantly higher than the levels in the other participants in our study (study III). However, we must keep in mind that we compared this group to other CHR subjects, which also, in general, score higher on BSD measures than subjects with other mental disorders (Raballo et al., 2021), and who may be at increased risk of a psychotic disorder in the schizophrenia spectrum (Fusar-Poli, Bechdolf, et al., 2013). In addition, the small sample size at follow-up (n = 32) may have increased the risk of not detecting a "true" difference between the sub-groups (increased risk of Type II error).

Our findings were partly in line with the meta-analysis by Raballo and colleagues, and with previous reviews and summaries of research in the field (Hur et al., 2014; Nelson & Raballo, 2015; Parnas & Henriksen, 2014), concluding that self-disorders selectively aggregate in the SSDs (including schizotypy), compared to other mental illness and healthy controls (Raballo et al., 2021). However, there may still be some specific conditions and disorders outside the SSDs characterized by ASEs, and maybe in particular conditions characterized by depersonalization and derealization (L. A. Sass, 2014).

5.1.3.1 BSD – a blend of transdiagnostic and specific diagnostic features?

As illuminated in study II in this thesis, high levels of ASEs were present in a depersonalization disorder (DPD) case, corresponding with descriptions of items in the EASE manual and with descriptions of diminished self-presence and hyperreflexivity, i.e. core dimensions of the BSD model. These findings also included examples of disturbances in the sense of mineness of experiences (e.g. reflected in quotes like "I feel sometimes that it's not me who see the things I see in a way… as if I'm not experiencing the things I see."). This was not surprising as such disturbances are also considered as central features of the depersonalization syndrome (Ciaunica, Charlton, & Farmer, 2020; Sierra & Berrios, 2000; Sierra & David, 2011). Still, this challenges the assumption that disturbances in the sense of mineness of experience distinguishes schizophrenia spectrum disorders from

depersonalization conditions outside of this spectrum (Burgy, 2011). The results from this study were in line with a quasi-empirical study, which found that published descriptions of DPD overlapped considerably with the descriptions of EASE items (L. Sass, Pienkos, Nelson, et al., 2013).

Severe, chronic and debilitating depersonalization syndromes, as afflicting the DPD case in study II, are quite rare, although more common than generally believed, with a prevalence of about 1-2% (Hunter, Sierra, & David, 2004; W. E. Lee, Kwok, Hunter, Richards, & David, 2012). However, more transient depersonalization and derealization experiences may constitute the third most common psychiatric symptoms after anxiety and depression (Simeon et al., 1997). In addition to the quite common presence of fleeting depersonalization experiences in the general population (lifetime prevalence between 26 % and 74 %), these symptoms are frequently occurring in several mental disorders (in clinical samples present in 30-82 % (Hunter et al., 2004)), including depression, anxiety and personality disorders, and posttraumatic stress-disorder (American Psychiatric Association, 2013; Baker et al., 2003; Hunter et al., 2004; Korzekwa, Dell, Links, Thabane, & Fougere, 2009; van Huijstee & Vermetten, 2018).

Studies indicate that depersonalization and derealization symptoms are particularly frequent in adolescence, and the onset (including onset of DPD) is often in adolescence or young adulthood (Baker et al., 2003; Michal et al., 2015; Simeon, Knutelska, Nelson, & Guralnik, 2003). As comorbid mental disorders are common in CHR (Albert, Tomassi, Maina, & Tosato, 2018; Boldrini et al., 2019; Lim et al., 2015), and CHR subjects usually are identified in adolescence or young adulthood (Schultze-Lutter et al., 2015; Woodberry et al., 2016), we may expect depersonalization and derealization symptoms to be quite frequent in CHR conditions. This has indeed been confirmed in a recent study, which found such symptoms in 50.5 % of a CHR sample (n = 97), compared to 16.5 % in a clinical control sample (n = 91) (Büetiger et al., 2020). Possibly, the high frequency of these symptoms in CHR subjects compared to clinical controls may be due to higher BSD levels in CHR for psychosis. In these CHR subjects, depersonalization and derealization may constitute aspects of a more comprehensive BSD gestalt more likely to be associated with a schizophrenia prodrome or with a “mild” SSD configuration, i.e. schizotypal conditions. Still, considering the frequency of these symptoms in clinical populations, and particularly in youth, it is likely that in a considerable proportion of CHR subjects, depersonalization experiences have a transient

character and do not constitute signs of (trait-like) BSD gestalts associated with incipient SSDs.

The findings in our study II, and in the studies by Sass and colleagues on published descriptions of depersonalization (L. Sass, Pienkos, Nelson, et al., 2013) and intense introspection cases (L. Sass, Pienkos, & Nelson, 2013), and in a panic disorder sample (Madeira et al., 2017), all point to a phenomenological continuity between depersonalization phenomena not related to schizophrenia spectrum conditions and certain ASEs occurring as aspects of the SSDs and the schizophrenia prodrome. As noted in the study by Madeira and colleagues, 13 EASE items were almost identical to items in the Cambridge Depersonalization Scale (Madeira et al., 2017; Sierra & Berrios, 2000). These findings seem at first sight to question the specificity of ASEs as markers of risk for SSDs in CHR conditions. However, there are probably also several nuances and differences at the detailed experiential/phenomenological level, and in the approximation to and development of delusional-like or delusional ideas, between schizophrenia spectrum conditions (including prodromal states) and depersonalized conditions outside of the schizophrenia spectrum. It seems that EASE items reflecting the most severe distortions of normal selfhood, e.g. a sense of being profoundly, ontologically different from others, and confusion of self-other boundaries, are rare in depersonalized conditions outside of the schizophrenia spectrum (L. Sass, Pienkos, Nelson, et al., 2013). These kind of differences were also found in study II. In contrast with the DPD case, the SPD case wondered if he had been alive forever, and was inclined to attribute experiences to the doings of some external force.

We also need to keep in mind that depersonalization and derealization in disorders outside of the schizophrenia spectrum are generally more *state-like* than trait-like, related to exacerbations of psychological stress, panic episodes, fatigue, drug use or physiological/somatic conditions (e.g. migraine or vertigo symptoms) (Hurlimann, Kupferschmid, & Simon, 2012; Michal et al., 2015). We suspect this also to be the case for many CHR subjects who endorse depersonalization and derealization experiences. In this respect, the chronic depersonalized condition of the DPD case we investigated in study II may only represent a small minority of CHR subjects with such experiences (DPD or other dissociative disorders are not listed among comorbid mental disorders in studies of CHR samples (Catalan et al., 2021; Lim et al., 2015; S.W. Woods et al., 2009)).

It should also be noted that patients diagnosed with DPD may be schizotypal (Parnas & Handest, 2003). DPD patients have been demonstrated to score higher on schizotypy

measures than healthy controls (Simeon, Guralnik, Knutelska, & Nelson, 2004), and possibly there may be overlaps between these conditions. The categorical separation of DPD from SSDs in the diagnostic manuals, and in most of the research literature, may not necessarily map discrete psychopathological and phenomenological entities in the "real world". As discussed in the paper from study II, a dimensional view may be more appropriate, in line with the more dimensionally oriented approaches to psychopathology research and diagnostic practice in recent years (American Psychiatric Association, 2013; Lilienfeld & Treadway, 2016; Linscott & van Os, 2013; Waszczuk et al., 2020). From a dimensional point of view, we may place ASEs on a continuum from transient phenomena in the general population, via more clinically significant symptoms in mental disorders outside the schizophrenia spectrum (probably affecting a considerable amount of CHR subjects), via more severe manifestations in DPD, prodromal schizophrenia and schizotypal conditions, and, at the endpoint, trait-like, severe ASEs in schizophrenia (L. Sass, Pienkos, Nelson, et al., 2013; Scharfetter, 2008).

5.1.3.2 Understanding overlaps and discrepancies between BSD and depersonalization

If there is a phenomenological continuity between BSD in SSDs (including the schizophrenia prodrome) and depersonalization outside the schizophrena spectrum, how are we to understand this? Possibly, a common denominator may be *disruptions in emotional processing*, related to diminished or abnormal processing of bodily signals, e.g. interoceptive, proprioceptive and vestibular signals and feedback (Postmes et al., 2014; Salami, Andreu-Perez, & Gillmeister, 2020; Sierra & David, 2011). These signals, also termed bodily "resonance" (Fuchs & Koch, 2014), are considered indispensable for the normal experience and feeling of emotions, and for the *embodiment* of acts of consciousness (A. Damasio, 2010; A. R. Damasio, 1994; Fuchs & Koch, 2014; Postmes et al., 2014; Seth & Friston, 2016).

In depersonalization conditions outside of the schizophrenia spectrum, disruptions in emotional processing are assumed to particularly take the form of enduring *emotional numbing* (Medford et al., 2016; Phillips & Sierra, 2003; Sierra & Berrios, 1998). This emotional numbing is suggested to result from an evolutionally developed functional response, which protects the person from overwhelming anxiety and stress (Stein & Simeon, 2009). In these conditions, disruptions in emotional processing are considered related to prefrontal hyperactivity and *inhibition* of autonomic responses and emotional-related activity in brain areas, e.g. the insula (Medford et al., 2016; Phillips & Sierra, 2003; Tanaka, 2018). This protection may come at the cost of profound changes in the experience of the self, including unreality feelings, detachment and disturbances in the sense of agency or mineness

of experience (Sierra & David, 2011). In most cases however, e.g. in panic disorders, emotional numbing is probably a transient phenomenon, but in DPD, it seems to prevail as a chronic condition (Baker et al., 2003; Medford et al., 2016; Sierra & Berrios, 1998). Possibly, manifestations of this numbing may also present as some of the negative symptoms, as they are measured with the standard clinical instruments, including SIPS/SOPS.

In the SSDs, disruptions in emotional processing may also partly be related to defensive-reactive responses to overwhelming stress and anxiety, i.e. secondary ASEs in the revised self-disorder model (L. A. Sass & Borda, 2015). However, in contrast with depersonalized conditions outside of the schizophrenia spectrum, SSD subjects may additionally be affected by marked *disruptions in neurodevelopment* (Friston, Brown, Siemerkus, & Stephan, 2016; Kraguljac & Lahti, 2021; Nath, Wong, & Srivastava, 2021), including aberrant maturation and connectivity of prefrontal regions (Gao, Yang, Mack, & Chamberlin, 2021). These involve early disruptions in perceptual integration, including the processing of bodily signals considered central for the processing of emotions and for establishing a stable sense of self (Borda & Sass, 2015; Postmes et al., 2014).

These neurodevelopmental disturbances, which are assumed to underlie "primary BSD" in the updated self-disorder model, render the person more vulnerable for the most severe distortions of normal selfhood, and for a psychotic decompensation, during adolescence and young adulthood (in contrast with depersonalization cases outside of the schizophrenia spectrum). These psychopathological processes may involve long-term and short-term responses to the primary BSD aspects, but also responses to challenging life circumstances and trauma (Borda & Sass, 2015; L. Sass et al., 2018; L. A. Sass & Borda, 2015). Even in schizotypal conditions, we find more severe cognitive disturbances and deficiencies than in depersonalized conditions (DPD-subjects display some deficits in attention and short-term memory, but not more severe disruptions) (Ettinger et al., 2015; Flückiger et al., 2019; Guralnik, Schmeidler, & Simeon, 2000; Shepherd, Laurens, Matheson, Carr, & Green, 2012; Simeon & Hamilton, 2008)

5.1.3.3 Conclusive remarks regarding diagnostic specificity

In conclusion, the specificity of ASEs as markers of vulnerability for the SSDs may be enhanced by carefully considering both the overall, encompassing psychopathological gestalt and the specific configuration of ASEs (e.g. presence of ASEs reflecting more severe erosion of self-other boundaries), in the context of social and medical history, childhood cognitive and psychosocial functioning, and earlier and present life circumstances and stressors. In light of

the revised self-disorder model, subjects vulnerable for SSDs may be more affected by (primary) trait-like self-disturbances likely to impinge on childhood functioning. In non-SSD conditions, ASEs may have a solely reactive (secondary) character. With the exception of DPD, these ASEs may be of a more transient nature, e.g. manifesting as an abrupt onset of depersonalization and derealization in the context of a stressful life situation or during, and in the aftermath, of an episode of drug-induced anxiety and panic (the latter pattern is quite common for DPD (Medford et al., 2003; Sierra, Medford, Wyatt, & David, 2012; Simeon, Kozin, Segal, & Lerch, 2009), but rarely described in the SSDs).

5.2 Methodological issues

5.2.1 Sample issues: representability and generalizability

5.2.1.1 Setting

Participants were consecutively recruited from naturalistic, public health care settings in Oslo and adjacent areas, both in urban and more rural communities. Mental health care in Norway is organized in catchment areas, where all inhabitants in a defined area are offered public health care, as long as they meet certain criteria with respect to the severity of the condition and the expected benefit of treatment (entitled/right to treatment). This health care system diminishes the socio-demographical biases associated with health care systems in countries more divided into either private or public treatment facilities. The participants were either patients discovered by early intervention in psychosis teams or units offering specialized health care for psychotic disorders or for a range of mental disorders through a regular referral system. TGV, who did the first screening and later clinical assessments, were in regular contact with clinical units to discuss potential cases. However, due to limited capacity, early intervention teams were prioritized, along with a few other specialized outpatient units for psychosis treatment. In general, treating clinicians in the early intervention teams were better trained in detecting risk of psychosis. It is likely that these factors affected and biased the recruitment to the study, with more participants recruited from these teams than from the other units. Still, we suspect that the differences in the referral systems and organization of the clinical units resulted in a more heterogeneous sample than CHR samples with participants recruited exclusively through early intervention measures. We also suspect that the recruitment of patients to this research project to a considerable degree reflected the naturalistic way patients at risk of psychosis are detected in this region of Norway.

5.2.1.2 Factors affecting recruitment

Inclusion of patients to this research project was dependent on the ability of the treating clinicians to detect risk of psychosis, and the motivation of both the clinicians and the patients regarding study participation. The extensive assessment resulted in two assessment reports (one clinical report and one regarding neurocognitive assessment), which were shared with both the patients and clinicians (if the patients consented to this). This was possibly the most central factor regarding motivation for participation (maybe in particular for the clinicians). Referrals to the research project were based on the information given about the study in advance to the clinical units. In this information, it was described that we were interested in investigating disturbances in self-experience in subjects suspected to be at increased risk of psychosis. Although it was not an inclusion criterion to be affected by ASEs, it cannot be precluded that the referring clinicians may have become somewhat biased by this information, thus referring more patients with ASEs than what characterizes the CHR population in general. However, as previously noted (see section 5.1.1) the total levels of ASEs were in line with levels found in other studies.

It is possible that some patients were reluctant to participate and to be assessed in such a research project due to factors like suspiciousness, more severe symptoms and psychosocial impairments. However, comparing the baseline sample with CHR samples from other studies, the participants did not seem to be less affected regarding symptom severity, level of global functioning and the presence of comorbid mental disorders (J. Addington et al., 2015; Hengartner et al., 2017; T. Y. Lee et al., 2014; Lim et al., 2015; Ruhrmann et al., 2010; Velthorst et al., 2009). The included subjects were compensated with NOK 500 for their participation in the study. We believe this did not significantly affect and biased motivation to participate. One reason for this is that the information about this economic compensation was given after they already had consented to meet TGV for a first screening (this information was included in the informed consent to participate in the study).

5.2.1.3 Inclusion criteria

Adding to the heterogeneity of the sample were the inclusion criteria, which were not restricted to formal UHR criteria, as defined in the SIPS (Norwegian version 3.1). Subjects with longstanding, non-progressive attenuated psychotic symptoms were also included. As mentioned in the paper from study IV, these subjects could possibly have met criteria in a current CHR classification system for an APS syndrome with the current status specifier "persistence" (S. W. Woods et al., 2014), included in a recent version of the SIPS

(McGlashan, Walsh & Woods, version 5.5). We controlled for the inclusion of the non-progressive group by doing all statistical analyses both with and without the non-progressive symptoms group. The results were not significantly affected by including this group.

Following inclusion, all subjects were also assessed with respect to the COGDIS criteria. Three of the subjects initially included as belonging to the non-progressive symptoms group were redefined as CHR, based on meeting COGDIS criteria (one of these did not participate in study III and IV), and ten simultaneously met COGDIS and UHR criteria. Hence, being defined as CHR in this research project was based on two quite different criteria sets, which may have increased the heterogeneity of the included sample. We compared subjects meeting the COGDIS criteria with subjects not meeting these criteria in the statistical analyses in all studies, except study II (the qualitatively oriented study). As described in the papers from study I and IV, meeting COGDIS criteria were associated with some of the outcome measures. Although the sample at baseline and in the follow-up studies was quite heterogeneous with respect to CHR measures, all the included subjects scored 3 or more on at least one SOPS positive symptoms (thus meeting either APS or non-progressive symptoms criteria).

5.2.1.4 Attrition of patients between baseline and follow-up

Between the baseline and follow-up investigations, six of the 38 participants at baseline dropped out. Hence, the sample in study III and IV comprised the remaining 32 subjects, and statistical analyses comparing baseline and follow-up variables in these two studies only included these 32 subjects. This attrition could potentially have biased the sample due to factors like differences in functioning and symptomatology. However, there were no significant differences between these six and the remaining participants regarding clinical or demographic characteristics (see supplementary material S2 in paper IV for details). Hence, we considered the sample in study III and IV to be representative for subjects included at baseline. However, the small sample size (in all studies, but particularly in study III and IV) may have increased the risk of reduced external validity, and may have diminished the reliability of the findings (Hackshaw, 2008).

5.2.1.5 Possible confounders

Due to the naturalistic setting, it was difficult to control for all potentially confounding variables. As previously described, when doing analyzes of the total sample (e.g. binary correlation analyses), we always controlled for 1) the effect of dropping out from the follow-

up assessments or 2) the effect of belonging to the non-progressive symptoms group. We also controlled for the effect of demographic variables. As noted in paper IV, this revealed a gender difference in the stability of BSD.

We partly controlled for the effect of medication in the exclusion criteria, but between baseline and follow-up the patients received treatment as usual, without any restrictions regarding medication use. As described in paper III and IV, medication use were not associated with any of the outcome measures. This should be considered in light of the fact that most of the subjects who used antipsychotics were prescribed daily doses considerably below what is considered a recommended antipsychotic dose, and some had discontinued treatment several months before the follow-up. We also controlled for the effect of other treatment variables between baseline and follow-up, including whether the participants had discontinued treatment or not, but none of these potential confounders had any effect on the outcome measures in study III and IV.

As described in the exclusion criteria, subjects were not excluded due to substance abuse, except in circumstances where the risk symptoms were considered as directly induced by the substances. None of the outcome measures in study I, III and IV were significantly associated with alcohol or substance abuse during the last 12 months (assessed with the AUDIT (Bohn et al., 1995) and the DUDIT (Berman, Bergman, Palmstierna, & Schlyter, 2005; Hildebrand, 2015)). To our knowledge, no studies have investigated associations between BSD and substance abuse in particular. Such studies are of interest, as drug use (particularly cannabis, hallucinogens, ketamine and MDMA) is a frequent trigger of both short-lasting and chronic depersonalization and dereralization (DPD) (Medford et al., 2003; Reutens, Nielsen, & Sachdev, 2010; Simeon et al., 2009). Cannabis was also the trigger of these symptoms in the DPD case in study II. Further, drug and alcohol abuse has been linked to anhedonia, which is also a common symptom in schizophrenia, and hypothesized to be a manifestation of BSD (Juckel, Sass, & Heinz, 2003)

We also investigated whether current depression at baseline (assessed with the CDSS (D. Addington et al., 1992)) affected the outcome measures, and found no significant associations. Other studies have demonstrated significant associations between BSD and depression. In these studies, BSD has been considered to be a risk factor for depressive symptoms and suicidal ideation rather than the other way around (Haug, Melle, et al., 2012; Haug et al., 2016; Koren et al., 2017; Skodlar & Parnas, 2010). However, Fuchs also discusses how melancholic depression may lead to a self-disorder due to the

"corporealization" of the body, which has lost its capacity for emotional resonance. Still, this melancholic self-disorder is contrasted to the disembodiment of the self in schizophrenia, involving a loss of the sense of mineness of the body (Fuchs, 2005a).

5.2.2 Design issues - correlation or cause and effect

The designs varied somewhat between the studies. Study I had a cross-sectional design, set up to investigate correlations between variables as well as sub-group differences in dependent variables. A cross-sectional design implies a reduced knowledge of the sequence of phenomena. Hence, we could not know whether ASEs *caused* SOPS negative symptoms and cognitive disturbances or if it could be the other way around. Possibly, it is somewhat misleading to use the concepts cause and effect in this context. Rather than cause-effect relationships, significant associations may reflect that some symptoms constitute interrelated expressions of an encompassing psychopathological Gestalt, (as discussed in the study I paper) (Parnas et al., 2002; L.A. Sass & Parnas, 2003).

Study III and IV were prospective cohort studies, thus making it possible to investigate the trajectories of symptoms and functioning levels from baseline to the one-year follow-up. The design in study IV was also cross-sectional, as we were interested in investigating relationships between the follow-up variables, e.g. correlations between EASE total scores and SOPS subscale scores. With the prospective designs, we were interested in investigating how the variance in the scores of the follow-up (dependent) variables was related to differences in baseline (independent) variables, e.g. how EASE total scores at baseline was associated with psychosocial functioning (GAF-F scores) at follow-up (study III). This could indicate possible causal relationships between the baseline and follow-up variables. In study III, we also investigated the predictive value of baseline EASE total on SOPS positive symptoms and functioning at follow-up in hierarchical regression analyses, which could indicate causal relationships somewhat stronger. Although we did find that EASE total predicted scores on these variables, it should be noted that several possible confounders were not controlled for in these analyses, including the effect of several other baseline variables.

Study III and IV had some shortcomings in their design, which limited the possibility of drawing conclusions about causal relationships. First, as discussed earlier, the sample was rather small, thus increasing the risk of reduced external validity of the findings. This risk was even higher when comparing small subgroups in the sample (e.g. those who met COGDIS criteria at baseline vs. those who did not). Second, if we had included a control group

consisting of help-seeking patients not characterized by CHR criteria and attenuated psychotic symptoms, we could have conducted analyses comparing the trajectories of the clinical variables between these two groups. Findings of significant relationships between baseline and follow-up variables in the CHR group, but not in the control group, could have strengthened hypotheses about BSD as a prominent (core) feature of many CHR conditions, driving the development and expression of prodromal symptoms.

5.2.3 Measurement issues: validity and reliability

5.2.3.1 General clinical assessment

To ensure reliable clinical assessments, TGV attended courses by experts in the field and underwent training for the main clinical interviews used in the presented studies (SIPS, EASE, SCID-I). As previously described, interrater reliability regarding SIPS and EASE was also measured, revealing excellent (SIPS) and moderate (EASE) reliability. In addition, EASE scores and the results of the other clinical assessments were discussed on a regular basis with PM (one of the main authors and instructors of the EASE) and JIR, both experienced psychiatrists and researchers. We believe these regular meetings diminished the negative effect of the limitations regarding interrater reliability.

There were some overlaps between some of the instruments used in this research project with respect to item descriptions. In particular, the descriptions of COGDIS criteria in the SPI-A overlapped with certain item descriptions in the EASE. This is not surprising in light of the fact that several EASE items belonging to the cognitive domain were slightly modified versions of items in the BSABS, and the BSABS constitute the basis for the SPI-A (Parnas, Moller, et al., 2005; F. Schultze-Lutter et al., 2007). This could obviously have increased the risk of spurious associations between the variables. However, even when removing items from the EASE directly overlapping with COGDIS items from the statistical analyses, subjects meeting COGDIS criteria at baseline had significantly higher EASE scores at baseline (see study I) and at follow-up (see study IV). There were also some partly overlaps between symptom descriptions of SOPS items and EASE items, which could possibly explain the strong correlations between total EASE scores and SOPS negative subscale scores. However, these correlations also remained strong and significant when removing EASE items overlapping with certain SOPS items from the analyses (see paper from study I). Hence, we assume that the demonstrated associations were not due to spurious relationships.

The time period covered by the assessment instruments differed considerably (e.g. SOPS: last month, GAF: last week, EASE: lifetime (all studies) or last year (study III and IV)). This could imply that ASEs were present before other symptoms, and possibly constituted a causal or triggering factor. However, this remained a quite open question as we (and the instruments) did not rigorously focus on the *onset* of symptoms, with the exception of SOPS positive symptoms (in order to assess APS criteria), and we did not control for all possible confounders. Hence, we cannot preclude that some other symptoms had been present at least as long as ASEs in some of the included subjects. However, considering that ASEs in self-disorders reflect disturbances of structural aspects of subjectivity, often dating back to childhood or early adolescence (Parnas & Henriksen, 2014), we suspect that ASEs in CHR often may predate other symptomatic manifestations. Secondly, we could not be sure whether significant cross-sectional associations reflected current symptoms only or whether they reflected an association between previous symptoms (e.g. ASEs 1-2 years ago) and current symptoms (e.g. negative symptoms last month). If we had assessed ASEs, other symptoms and aspects of functioning during the same time window, e.g. last month, we could have been more confident in concluding that associations reflected a concurrence of symptoms and BSD phenomena in time. Adding information about when ASEs and other symptoms started and how they developed would also have been useful regarding the possibility of suggesting causal relationships, but such data would be vulnerable to recollection biases, and very challenging to collect precisely.

The validity and the reliability of the assessments at the one-year follow-up in study III and IV may be questioned due to the fact that TGV also did these assessments. Hence, he was not blind with respect to the results of the baseline assessments, although he countered this limitation by not looking at the previous scores from the baseline assessments when scoring the follow-up instruments. In line with the procedure regarding the baseline assessments, also the results of the follow-up assessments were discussed with PM and JIR, in order to diminish the risk of clinician-rating biases.

5.2.3.2 Assessments with the SIPS/SOPS

In all studies, we used the SIPS instrument, including the SOPS, to assess UHR criteria, criteria for a psychotic syndrome, and the presence and severity of psychosis-risk symptoms. The SIPS/SOPS is widely used and accepted for these purposes, and has been considered to possess sound psychometric properties (Fusar-Poli, Cappucciati, Rutigliano, et al., 2016; P. Fusar-Poli, M. Cappucciati, et al., 2015; Miller et al., 2003). Still, it should be noted that we

used a Norwegian translation of an early version of the SIPS/SOPS, which had not been validated and tested regarding reliability in a Norwegian clinical sample. As described previously, the validity of the two UHR syndromes BLIPS/BIPS and GRD has been questioned (Fusar-Poli, 2017; Schultze-Lutter et al., 2015). However, none of the subjects in the sample met BIPS criteria, and only one met GRD criteria (in combination with APS and COGDIS criteria). The remaining UHR subjects met APS criteria (either exclusively or in combination with COGDIS criteria).

Scores on the SOPS positive symptoms were also used to define whether the subjects met criteria for the non-progressive symptoms group and remission criteria. As previously noted in the introduction section, and according to clinical experience and the literature, subjects with longstanding attenuated positive symptoms seem to have a high risk for several clinical comorbidities and psychosocial impairments (J. Addington et al., 2011; Beck, Andreou, et al., 2019; Lin et al., 2015; Schlosser et al., 2012). Still, in light of the ad hoc definition of criteria for the non-progressive symptoms group, these criteria may be questioned. It is however relevant that this group did not differ from the rest of the individuals on several core measures. As demonstrated in study III, levels of BSD, negative symptoms and psychosocial functioning had a significant impact on non-remission, while attenuated positive symptoms had not. These characteristics did not differ significantly between the non-progressive symptoms group and the group meeting full, formal CHR criteria. We suspect that this lack of clinical differences may be due to pre-selection of patients, i.e. which patients were evaluated by their treating clinicians and referred to this research project. All participants, also in the non-progressive symptoms group, were help-seeking and distressed, and referred from clinicians who were worried that the patients were at high risk of psychosis. Hence, in the same vein as discussed regarding CHR criteria (Fusar-Poli, Schultze-Lutter, et al., 2016; van Os & Guloksuz, 2017), we should be careful not to put too much weight on attenuated positive symptoms as primary markers of risk for adverse outcomes.

The validity of the remission criteria may also be questioned, as these differed somewhat from other proposed remission criteria in the CHR research field, e.g. (T. Y. Lee et al., 2014; Polari et al., 2018; Simon et al., 2013; S. W. Woods et al., 2014). However, these criteria overlapped with other proposed remission criteria regarding the positive symptoms criterion, and was in line with recommendations to include remission of functioning criteria in addition to symptomatic remission criteria (T. Y. Lee et al., 2014; Polari et al., 2018).

We used the sum scores of the four SOPS subscales as measures of the severity of positive, negative, disorganization and general symptoms. An exploratory analysis of the factorial structure of the SOPS found symptom structures overlapping considerably with manifest schizophrenia. All negative symptoms loaded on one factor, four of five positive symptoms loaded on another factor, and the general symptoms loaded on a third factor (Hawkins et al., 2004). Still, there have been few studies analyzing SOPS subscale sum scores, and the construct validity of the symptoms and subscales may not be satisfactory. A recent review (published after the present studies were conducted) have questioned the validity of the SOPS negative symptoms subscale in particular (in addition to criticisms of negative symptoms ratings with the CAARMS and SPI-A) (Gregory P. Strauss, Pelletier-Baldelli, Visser, Walker, & Mittal, 2020). The SIPS is criticized for defining items based on outdated conceptualizations of negative symptoms, and including items not considered as belonging to the negative symptoms construct (particularly the items *ideational richness* and *occupational functioning*). It is also criticized for a lack of construct validity regarding each of the included items (e.g. conflating asociality, social anxiety and social skill under the item term *social anhedonia*) (Gregory P. Strauss et al., 2020). The SIPS/SOPS is also criticized for a variety of other methodological reasons, e.g. scale development by an individual research group based on small, not sufficiently representative samples, and failure to derive scales based on iterative, data-driven processes. Although these criticisms are directed in particular towards the assessment of negative symptoms with the SIPS, these points of criticisms probably have relevance for the other SOPS subscales too. A new, next-generation assessment scale for negative symptoms in CHR youth, the Negative Symptom Inventory-Psychosis Risk (NSIPR), has been developed by Strauss, Mittal and Walker, and a multi-site psychometric study is currently taking place to validate this scale (Gregory P. Strauss et al., 2020).

5.2.3.3 Assessment of BSD and COGDIS criteria

Aspects or manifestations of BSD (ASEs) were assessed with the EASE. This instrument requires a considerable amount of training, psychopathological competence and acquaintance with phenomenological descriptions of consciousness (Parnas, Moller, et al., 2005). As previously noted, the EASE has demonstrated sound psychometric properties, including good to excellent internal consistency and inter-reliability of EASE scores among trained raters. It possesses a mono-factorial structure, in line with the proposed gestalt-like quality of BSD (Moller et al., 2011; Nelson et al., 2012; Norgaard & Parnas, 2012; Raballo & Parnas, 2012). However, the results of two of these studies were based on small samples (Moller et al., 2011;

Raballo & Parnas, 2012), and studies investigating the factorial structure of EASE items in larger samples are warranted. The inter-rater reliability regarding EASE scores in the current research project was in the moderate range (ICC = 0.62, 95% CI: 0.24-0.88), when TGV compared his EASE total scores of nine videotaped EASE interviews from a study by Haug and colleagues (Haug, Lien, et al., 2012) with the scores of two other raters: PM and Haug. The numerous running EASE-rating supervisions throughout this project most probably enhanced the reliability further, but the results of the presented studies should be interpreted with some caution in light of this limitation.

The assessment of COGDIS criteria was based on an ad hoc procedure, comparing qualitative symptom descriptions from the EASE interviews, supplemented with information from the SIPS interviews and symptom descriptions in the SPI-A. Information regarding the severity, current presence and frequency of the symptoms (necessary to score the presence or absence of COGDIS criteria) was also gathered in these interviews. TGV was not specifically trained in the assessment with the SPI-A. Although the reliability of this ad hoc procedure may be vulnerable, we believe this procedure was sufficient to assess these criteria in a proper way. This assumption is based on the emphasis on a phenomenological exploration of subjectively experienced disturbances in both these instruments, and the considerable overlaps with the EASE. Still, two of the COGDIS items did not directly overlap with EASE items (COGDIS items C4 *Disturbance of receptive speech* and O3 *Disturbance of abstract thinking*) (Parnas, Moller, et al., 2005; F. Schultze-Lutter et al., 2007), and it cannot be precluded that the exploration of these COGDIS items may have been compromised to some degree.

5.2.3.4 Diagnostic assessments

A full version of the SCID-I was used for differential diagnostic assessments at baseline, and for those who, according to criteria in the SIPS, transitioned to psychosis between baseline and follow-up, we did a reassessment with the SCID-I at follow-up (modules A-D). To meet criteria for a psychotic syndrome in the SIPS require a longer duration of symptoms (present for more than one hour, four times a week, for a month) than DSM-IV criteria for brief psychotic disorder (duration from one day to one month) (First, 2004), unless the symptoms are seriously disorganizing or dangerous (Miller et al., 2003). This implies that the time threshold for getting a psychotic disorder diagnosis may be higher in the SIPS than in the DSM-IV. However, there is reason to assume that this discrepancy had no implications for the present individuals, as no other subjects than the four who transitioned to psychosis scored at a psychotic level (= 6) on any of the SOPS positive items at follow-up.

We did not conduct a full differential diagnostic assessment of DSM-IV Axis II personality disorders, but only assessed the DSM-IV SPD diagnosis with the checklist for this disorder in the SIPS. The reason for this decision was the young age of several of the participants. In adolescents, it may be difficult to differentiate between characteristic aspects of common Axis I disorders and personality dysfunction, e.g. regarding trait or trait-like features like impulsivity, affective instability or aggression. However, personality disorders typically starts in adolescence, and there is strong scientific evidence for the validity of a personality disorder diagnosis during this life period (K. Thompson & Chanen, 2019). Hence, in retrospect we consider this a limitation of the studies.

5.2.3.5 GAF and other measures

We investigated global functioning at baseline and at follow-up with the split version of the GAF (S-GAF, divided in a symptom and a functioning score) (G. Pedersen et al., 2007). The S-GAF was used to avoid the risk of conflating symptom severity and functional impairments, and in the analyses in study III and IV we only included the functioning score. With the single measure GAF scale included in the DSM-IV, it has been shown that clinical diagnoses and symptoms were (erroneously) stronger predictors of GAF ratings than social or occupational functioning (Moos, Nichol, & Moos, 2002). The reliability of the GAF has been questioned, but has been shown to be acceptable among trained and experienced raters (both the single measure GAF and the split version) (Hilsenroth et al., 2000; G. Pedersen et al., 2007). The validity of S-GAF has been confirmed by finding discriminant and concurrent associations to other clinical measures (Geir Pedersen & Karterud, 2012). TGV, who did the GAF assessments, had extensive clinical experience with using the S-GAF, but it cannot be precluded that there could have been a risk of clinician-rating biases affecting the GAF-scores.

Through semi-structured interviews with the PAS, we assessed childhood (0-11 yrs) and early adolescent functioning (12-15 yrs). This instrument was developed for the use in patients with schizophrenia to assess premorbid adjustment (Cannon-Spoor et al., 1982), but has been used in a range of CHR studies. Premorbid functioning has been demonstrated to be lower in CHR individuals than in healthy controls (Dannevang et al., 2018; Lyngberg et al., 2015; Tikka et al., 2013), and to be on par with premorbid functioning in subjects with psychosis (J. Addington, Penn, Woods, Addington, & Perkins, 2007). The assessment with the PAS is vulnerable to recollection biases, e.g. recall could be obscured by current symptoms (Lyngberg et al., 2015). However, it should be noted that patients with schizophrenia have

been shown to be as reliable as subjects with no psychiatric symptoms in recalling earlier functioning (Brill, Reichenberg, Weiser, & Rabinowitz, 2008). Assessment of childhood trauma with the CTQ-SF or other self-report measures may also be vulnerable for recollection biases. However, such self-reports have been demonstrated to be reasonably reliable, to not be affected by current psychotic symptoms, and to show good concurrent and convergent validity when comparing with other measures and clinical notes (Fisher et al., 2011).

5.2.4 Design and data analysis in study II

In study II, we selected two cases from the CHR sample in the overarching research project as examples of a schizophrenia spectrum patient (the SPD case), and a case with depersonalization and derealization as primary symptoms (the DPD case). We thoroughly scrutinized and analyzed the qualitative descriptions of subjective experiences and the overall clinical picture (mainly obtained through the comprehensive video/audio-taped EASE and SIPS interviews), and the background and medical history. Further, we did an ad hoc theoretically based categorization and selection of descriptions of ASEs from the two subjects. This categorization and selection was based on 1) comparisons with the two central dimensions of BSD: diminished self-affection and hyperreflexivity, as described by the founders of the self-disorder model (L.A. Sass & Parnas, 2003), and 2) comparison with descriptions of the four symptom groups suggested to constitute the depersonalization syndrome (Sierra & David, 2011). Similarities and differences in the descriptions of ASEs between the two subjects were also highlighted, along with similarities and differences in background and medical history.

We cannot claim that the selected cases were representative for SPD and DPD cases in general. Some may question the selection of a DPD case with a genetic/familial vulnerability for SSDs (who also met COGDIS criteria), assuming that this case in fact displayed a mild configuration of schizophrenia spectrum psychopathology (see also criticism of the validity of the DPD diagnosis (Parnas & Handest, 2003)). However, this case did not meet sufficient criteria for any of the SSDs, and the clinical picture was more typical for DPD. We did not deliberately seek and select a patient with this genetic vulnerability. However, in light of a dimensional perspective of mental disorders, we found it interesting to investigate a case meeting formal DPD criteria (but not SPD or other SSD criteria), who also displayed genetic and symptomatic risk factors for schizophrenia.

In this study, as in qualitative research in general (Crowe, Inder, & Porter, 2015), subjective experiences and qualitative in-depth descriptions of these experiences were emphasized as the main sources of data, collected through semi-structured interviews. However, the ad-hoc procedure of study II did not fully meet the standards of qualitative research methodology, including qualitative case studies (Simons, 2009), with respect to design, data collection and analysis (e.g. thematic analysis or content analysis) (Creswell & Poth, 2018; Crowe et al., 2015; Denzin & Lincoln, 2013). It could be said that we did a form of thematic analysis, but unlike the thematic categorizations in study II (based on the EASE and the BSD model), themes in qualitative research using thematic analyses as a method are not pre-defined and theory-driven (Crowe et al., 2015).

Although not meeting the full requirements of a qualitative case study, the design and phenomenological methodology opened up the possibility of gaining more concrete, in-depth insights into the subjectively experienced aspects of symptoms and phenomena, and their relationships, in the context of background, life events and medical history. Through qualitative studies, theories may be developed and hypotheses generated. These can be further investigated through empirical research, possibly leading to findings expanding on or challenging current theories and models. An example from study II are the descriptions of disturbed ipseity (mineness of experience) in the DPD case, which may challenge the assumption that such disturbances are specific to the schizophrenia spectrum (Burgy, 2011; Nelson & Raballo, 2015; Parnas & Henriksen, 2014). Although we should be careful not to generalize this finding to other DPD cases, it is in line with findings from another study of reports of depersonalization experiences (L. Sass, Pienkos, Nelson, et al., 2013), and may thus point to a future empirical research target (e.g. comparing ASEs in a larger sample of DPD patients and SSD patients).

5.3 Strengths, limitations and future research

Strengths and limitations have already been discussed in this thesis, but some main points should be pointed out and highlighted.

5.3.1 Strengths

First prospective CHR project assessing with the EASE at two time points. The assessment of BSD in CHR samples is still an underexplored area of research, and even more regarding prospective studies. This is to our knowledge the first prospective CHR research project assessing BSD with the EASE at two time points, along with assessments of other symptoms (SOPS) and functioning (S-GAF) at the same time points. This is a strength of this project, opening up the possibility for investigations of longitudinal relationships between the assessed variables, and the stability of BSD, other symptoms and functioning. The comprehensive clinical assessments, particularly at baseline, is also a strength, resulting in a thoroughly described sample. The additional scoring of EASE at baseline, reflecting "last year" ASEs, is another strength of the study. This made it possible to investigate the development of ASEs from one year to the next year (in study IV), which to our knowledge, has not been investigated in other prospective studies of BSD.

A naturalistically representative CHR sample. Another strength is the recruitment of participants from the public health care system in Norway, and from a large catchment area. This may have resulted in a more naturalistically representative CHR sample than samples recruited via private clinics with more selected populations. We will also highlight as a strength of this research project the combination of thorough, phenomenological, in-depth, qualitatively oriented investigations (even though not fully meeting the standards of qualitative research methods) and empirical, quantitative research methods.

5.3.2 Limitations

Limited sample size. One of the main limitations in this research project is the small sample size, which ended up as smaller than originally planned due to problems with recruiting enough participants (the plan was to recruit 50 CHR patients). This diminished the statistical power of the analyses, increased the risk of Type 2 errors, and limited the external validity of the study. More participants could probably have been recruited during a shorter period of time if there had been an assessment team affiliated with this research project, which could have been more often and regularly in contact with the clinical units, and contributed to clinical assessments.

Lack of a control group. When planning this research project, we intended to include 40 healthy controls. However, we ended up with not including a control sample due to unforeseen practical and logistic difficulties. This limited the possibility of doing comparative analyses, and may have compromised the internal validity of the findings. Possibly, including a control group consisting of other help-seeking patients not meeting CHR criteria rather than healthy controls in a matched design, would have been even more appropriate. In this way, we could have been more confident in conclusions regarding the specificity of the findings for the CHR population.

Inclusion of the non-progressive symptoms group. As previously discussed, another limitation may have been the inclusion of the non-progressive symptoms group, which increased the heterogeneity of the sample and resulted in a sample less representative for the CHR population. Still, as previously described, the patients in this group did not differ on other clinical or demographic variables, except for being older. It could also be mentioned as a limitation the positive symptom inclusion criterion (see APS criteria and non-progressive symptoms group criteria), which resulted in a restricted sample with respect to the range in positive symptoms scores. This may have affected some of the analyses, e.g. possibly resulting in weaker correlations between positive symptoms and other variables.

Not blinded at follow-up assessments. With respect to measurement, a main limitation was the fact that TGV did all the clinical assessments at baseline and at follow-up. Hence, he was not completely blind to the results from the baseline assessments when conducting the follow-up assessments, although he scored the follow-up instruments without considering (looking up) the scores at baseline.

Limitations related to the use of some of the instruments. First, this included the moderate inter-rater reliability regarding the rating of EASE (rating of video-taped interviews from another study (Haug, Lien, et al., 2012)). However, this limitation was countered to some degree by having regular meetings with PM and JIR to discuss these ratings and other measurement results. The ad hoc assessment procedure regarding the COGDIS criteria, and the lack of training and calibration regarding the use of SPI-A, was another limitation, along with the lack of formal training and calibration with respect to the assessment of global functioning with the S-GAF. As previously noted, not assessing other Axis II disorders than SPD may also be considered as a limitation. The differences in the time periods covered by the assessment instruments also limited conclusions regarding the relationships between the

variables, e.g. with respect to which symptoms and phenomena occurred first (and thus possibly could have acted as a causal factor).

Other limitations. With respect to data analysis, we have previously pointed to the lack of control of some possible confounders as a limitation, although we did control for several confounders in many of the analyses. Finally, as discussed in the previous section (5.2.4), the conclusions in study II were limited due to the ad hoc qualitatively oriented approach to the study of the two cases, which did not meet the full requirements of qualitative research methods.

5.3.3 Future research

The findings from this thesis suggest a range of interesting research topics to pursue further in cross-sectional and prospective studies with larger CHR samples, also including clinical or healthy control groups. Prospective studies should investigate whether levels of BSD may have an effect on future clinical and functional outcomes, as we found in study III and IV. These investigations should not restrict clinical outcomes to transition to psychosis and SSD diagnoses, but also other outcomes like non-remission from CHR states. Associations between BSD and positive, negative and disorganization symptoms (including cognitive disturbances as described in the SPI-A), and the predictive value of BSD, should also be investigated further in prospective studies with control groups and controlling for confounders. The strong link between ASEs and negative symptoms found in this thesis may be of particular interest. However, other assessment instruments than the SIPS/SOPS should be considered in assessing negative symptoms, given recent criticisms of the use of the SOPS negative subscale (Gregory P. Strauss et al., 2020). Researchers should carefully considerate the appropriate time periods covered by the assessment instruments, particularly the EASE. Additionally, it is recommended to register (approximately) when and how symptoms started (e.g. slowly or more abrubtly, possible triggers), as well as the concurrence in time of ASEs and other symptoms (e.g. with Experience Sampling methods (Wright et al., 2021)). This is of importance to further investigate BSD as a trait or state factor, and whether BSD indeed is a driver of other prototypical SSD symptom development, as assumed in the BSD model (L.A. Sass & Parnas, 2003).

Vulnerability factors possibly associated with the development of BSD should also be investigated further in larger samples, including the factors investigated in this thesis: childhood trauma and premorbid social and role functioning. We would also recommend that

future cross-sectional and prospective studies continue to investigate and compare ASEs across diagnostic groups in larger samples. Of special interest would be comparisons of patients with dissociative disorders (or only subjects with DPD) with SSD subjects and/or CHR subjects. This could expand on or challenge previous findings regarding the specificity of ASEs/BSD for the SSDs, and would also be of interest to see whether levels of BSD in dissociative disorders may have an effect on future outcomes in this clinical group (e.g. whether subjects with high BSD levels would "drift" toward a SSD diagnosis or other clinical and functional outcomes).

5.4 Implications

Although the limitations of the presented studies diminish the possibility of drawing firm conclusions, the findings point to certain implications. First, this concerns the importance of assessing the presence and severity of BSD in CHR. This may not only be of importance with respect to identifying risk factors for transition to psychosis (Nelson et al., 2012), but also in closing-in on CHR subjects who may be at higher risk of other adverse clinical and functional outcomes in non-transitioning cases. Given findings that the majority of non-transitioning CHR subjects continue to be troubled with clinical symptoms, psychosocial impairments and mental disorders in the years following the initial CHR assessment (Beck, Andreou, et al., 2019; Schlosser et al., 2012), there is a need to identify prospectively these subjects in order to target and tailor interventions.

Most importantly, identification of BSD is uniquely important both for the clinical understanding of the patient and his/hers symptoms, and for psychotherapy and other therapeutic interventions (Irarrazaval, 2013; Nischk, Dölker, Rusch, & Merz, 2015; Pérez-Álvarez, García-Montes, Vallina-Fernández, Perona-Garcelán, & Cuevas-Yust, 2011; Škodlar & Henriksen, 2019). BSD phenomena are regularly difficult to verbally communicate (Moller & Husby, 2000), and are either not or only to a minor degree asked for in standard clinical instruments like the SCID or SIPS/SOPS (and if they are, they are generally subjected to 3rd person operationalizations). Hence, phenomenological explorations of these phenomena (with the EASE) may be necessary to get close to the experiential substrate of the more overt symptoms. Identifying pronounced ASEs may point to BSD as an underlying psychopathological organizer and common ground for the seemingly disparate symptomatic manifestations (Parnas, 2011). These explorations enables a tuning-in to these often profoundly disturbing experiences, which may be crucial in getting a better grip on the

patients' inner world and in generating a more genuine contact, therapeutic relation and understanding of their condition.

For patients with schizophrenia, a general goal in therapy may be the diminishment of feelings of self-alienation and estrangement in the relationships with other people and the world (Škodlar & Henriksen, 2019). We believe this should constitute an important, general goal in CHR subjects suffering from marked BSD too. Through phenomenological explorations of self-experience and experience of others, clinicians aid the patient with establishing and co-constructing a verbal language and personal narrative for these experiences. This may constitute a common ground for further phenomenological explorations in a psychotherapeutic context, leading the patient towards dialogue, co-creation of meaning, and embodied self-experience and understanding. Skodlar and Henriksen portrays the role as psychotherapist as follows:

> "The psychotherapist's role is like that of an anchor, of a dialogue partner, and, at the same time, of a translator or bridge to the minds of others, to commonsensical knowledge, expectations and reactions." (p.6) (Škodlar & Henriksen, 2019)

Through this inter-subjective dialogue and relationship, a sense of subjectivity and first-person perspective may be recovered (Irarrazaval, 2013; Stanghellini & Lysaker, 2007). In addition to alleviating feelings of anxiety, despair and isolation, this strengthening of the sense of self and presence in the world may hopefully also diminish the risk in CHR subjects for developing a frank, psychotic condition and for psychosocial deterioration.

It should be noted that other interventions than individual psychotherapy may also be helpful in pursuing the general goal of diminishing alienation experiences and promoting a stronger sense of unity of the self. Immersion and absorption in physical or creative activities may diminish hyperreflexivity and increase the sense of being present, not only in the activities, but also in the body, the world and in relationships with others (Škodlar & Henriksen, 2019).

We will add one last implication of the findings. In study IV, we found that BSD levels may not be stable in many CHR subjects, and that increases of BSD levels was accompanied by non-remission or worsening of positive symptoms and functioning. In some, ASEs may fluctuate in accordance with experienced stress and adversities (L. Sass et al., 2018), and may thus constitute markers of general distress. Hence, increasing levels of ASEs over time may also be of use to the patient and therapist as signs of a worsening of the general, clinical condition.

6. CONCLUSION

This thesis investigated BSD with the EASE in CHR subjects at two time points: baseline and one-year follow-up. ASEs (manifestations or variants of BSD) were assessed along with a range of other clinical, functional, background and demographic variables at baseline and follow-up. High levels of ASE were strongly associated with more severe negative symptoms at baseline. Higher ASE levels at baseline, along with more severe negative symptoms and lower levels of global functioning at baseline, were also significantly related to symptomatic and functional non-remission at follow-up. In general, *a consolidation of a clinical gestalt took place from baseline to follow-up in subjects with the highest baseline levels of ASEs*. This gestalt was characterized by *strong prospective and cross-sectional relationships between BSD at baseline or follow-up and SOPS positive, negative and disorganization symptoms, and global functioning, all at follow-up*. This clinical picture typically characterized SSD subjects in the sample, in line with the BSD model for schizophrenia. However, the sample was relatively small, and the follow-up period quite short, so these studies could not fully address to which extent high baseline ASE levels predicted psychosis and a drifting towards future SSD diagnoses.

In light of these findings, high baseline levels of ASEs may indeed constitute an important clinical, prognostic marker of adverse clinical and functional outcomes. Identification of such prognostic markers are of interest as many CHR subjects continue to struggle with clinical symptoms and psychosocial impairments even if no transition to psychosis is taking place (Beck, Andreou, et al., 2019). An even stronger prognostic marker of an unfavorable course may be the combination of high baseline levels of ASEs and negative symptoms and impairments in psychosocial functioning (basic symptoms cognitive disturbances [COGDIS] may also constitute such markers, but are to a large degree incorporated in the EASE).

Measuring ASEs during the last year both at baseline and follow-up, also revealed considerable variations in the individual trajectories of ASEs. This is in line with the suggested revision of the BSD model, suggesting that such variations and combinations of trait-like and state-like features may indeed be characteristic, particularly in diagnostically heterogeneous groups (L. Sass et al., 2018), as typical for CHR samples. As described in study IV, following ASE trajectories over some time may add even more to the prognostic significance of ASEs, given the more severe symptoms and functional non-remission, or even functional decline, in subjects with high or increasing ASE levels. Even though we cannot

firmly conclude that BSD *caused* these outcomes, the findings from study III of the predictive value of BSD for future outcomes indicated a possible causal role.

As discussed in study II, ASEs overlapped considerably with depersonalization and derealization symptoms in a severe depersonalization condition, and transient variants of depersonalization and derealization are not uncommon in CHR (Büetiger et al., 2020). Hence, we should be careful not to jump to the conclusion that ASEs in CHR necessarily imply a SSD vulnerability. Careful considerations of ASEs in the context of life situation, other clinical symptoms, personal and medical history are recommended, both for understanding the patient and the possible underlying psychopathological processes, and for differential diagnostic considerations. As non-SSD depersonalization and derealization symptoms in general may be of a more reactive nature than more trait-like ASEs in SSDs, with the exception of the chronic symptoms in the more rare DPD condition, assessing ASE trajectories over time may also be of use in these considerations.

The findings of this thesis were based on assessments in a small, clinically quite heterogeneous sample, which did not include a control group. However, we believe these findings are of importance in generating new and updated hypotheses to pursue in future CHR studies with larger samples and clinical or healthy control groups. The preponderance of BSD phenomena in the sample in this thesis and in other CHR studies, the profound impact these phenomena may have on the person's wellbeing, life quality and functioning, and the prognostic significance of these phenomena, all point to the importance of thoroughly assessing and therapeutically addressing these phenomena over time in CHR individuals.

7. REFERENCES

Addington, D., Addington, J., Maticka-Tyndale, E., & Joyce, J. (1992). Reliability and validity of a depression rating scale for schizophrenics. *Schizophr Res, 6*(3), 201-208. doi:10.1016/0920-9964(92)90003-n

Addington, J., Addington, D., Abidi, S., Raedler, T., & Remington, G. (2017). Canadian Treatment Guidelines for Individuals at Clinical High Risk of Psychosis. *Canadian Journal of Psychiatry. Revue Canadienne de Psychiatrie, 62*(9), 656-661. doi:10.1177/0706743717719895

Addington, J., Cadenhead, K. S., Cannon, T. D., Cornblatt, B., McGlashan, T. H., Perkins, D. O., . . . Heinssen, R. (2007). North American Prodrome Longitudinal Study: a collaborative multisite approach to prodromal schizophrenia research. *Schizophr.Bull., 33*(3), 665-672. doi:sbl075 [pii];10.1093/schbul/sbl075 [doi]

Addington, J., Cornblatt, B. A., Cadenhead, K. S., Cannon, T. D., McGlashan, T. H., Perkins, D. O., . . . Heinssen, R. (2011). At clinical high risk for psychosis: outcome for nonconverters. *The American Journal of Psychiatry, 168*(8), 800-805. doi:10.1176/appi.ajp.2011.10081191

Addington, J., Liu, L., Buchy, L., Cadenhead, K. S., Cannon, T. D., Cornblatt, B. A., . . . McGlashan, T. H. (2015). North American Prodrome Longitudinal Study (NAPLS 2): The Prodromal Symptoms. *Journal of Nervous and Mental Disease, 203*(5), 328-335. doi:10.1097/nmd.0000000000000290

Addington, J., Liu, L., Perkins, D. O., Carrion, R. E., Keefe, R. S. E., & Woods, S. W. (2017). The Role of Cognition and Social Functioning as Predictors in the Transition to Psychosis for Youth With Attenuated Psychotic Symptoms. *Schizophrenia bulletin, 43*(1), 57-63. doi:10.1093/schbul/sbw152

Addington, J., Penn, D., Woods, S. W., Addington, D., & Perkins, D. O. (2007). Social functioning in individuals at clinical high risk for psychosis. *Schizophr Res, 99*(1), 119-124. doi:10.1016/j.schres.2007.10.001

Albert, U., Tomassi, S., Maina, G., & Tosato, S. (2018). Prevalence of non-psychotic disorders in ultra-high risk individuals and transition to psychosis: A systematic review. *Psychiatry Res, 270*, 1-12. doi:10.1016/j.psychres.2018.09.028

American Psychiatric Association. (1987). *Diagnostic and statistical manual of mental disorders (DSM-III-R)* (3rd ed., rev. ed.). Washington, D.C: American Psychiatric Association.

American Psychiatric Association. (2013). *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5®)*. Washington, D.C.: American Psychiatric Publishing.

Andreasen, N. C. (2007). DSM and the death of phenomenology in america: an example of unintended consequences. *Schizophr.Bull., 33*(1), 108-112. doi:sbl054 [pii];10.1093/schbul/sbl054 [doi]

Baker, D., Hunter, E., Lawrence, E., Medford, N., Patel, M., Senior, C., . . . David, A. S. (2003). Depersonalisation disorder: clinical features of 204 cases. *Br J Psychiatry, 182*, 428-433.

Bang, M., Park, H. J., Pae, C., Park, K., Lee, E., Lee, S. K., & An, S. K. (2018). Aberrant cerebro-cerebellar functional connectivity and minimal self-disturbance in individuals at ultra-high risk for psychosis and with first-episode schizophrenia. *Schizophr Res, 202*, 138-140. doi:10.1016/j.schres.2018.06.031

Barajas, A., Ochoa, S., Obiols, J. E., & Lalucat-Jo, L. (2015). Gender differences in individuals at high-risk of psychosis: a comprehensive literature review. *ScientificWorldJournal, 2015*, 430735. doi:10.1155/2015/430735

Beck, K., Andreou, C., Studerus, E., Heitz, U., Ittig, S., Leanza, L., & Riecher-Rossler, A. (2019). Clinical and functional long-term outcome of patients at clinical high risk (CHR) for psychosis without transition to psychosis: A systematic review. *Schizophr Res*. doi:10.1016/j.schres.2018.12.047

Beck, K., Studerus, E., Andreou, C., Egloff, L., Leanza, L., Simon, A. E., . . . Riecher-Rössler, A. (2019). Clinical and functional ultra-long-term outcome of patients with a clinical high risk (CHR) for psychosis. *European Psychiatry, 62*, 30-37. doi:10.1016/j.eurpsy.2019.08.005

Beiser, M., Erickson, D., Fleming, J. A., & Iacono, W. G. (1993). Establishing the onset of psychotic illness. *Am J Psychiatry, 150*(9), 1349-1354. doi:10.1176/ajp.150.9.1349

Berman, A. H., Bergman, H., Palmstierna, T., & Schlyter, F. (2005). Evaluation of the Drug Use Disorders Identification Test (DUDIT) in criminal justice and detoxification settings and in a Swedish population sample. *Eur.Addict.Res., 11*(1), 22-31. doi:EAR2005011001022 [pii];10.1159/000081413 [doi]

Bernstein, D. P., Ahluvalia, T., Pogge, D., & Handelsman, L. (1997). Validity of the Childhood Trauma Questionnaire in an adolescent psychiatric population. *Journal of the American Academy of Child & Adolescent Psychiatry, 36*(3), 340-348.

Bernstein, D. P., Stein, J. A., Newcomb, M. D., Walker, E., Pogge, D., Ahluvalia, T., . . . Zule, W. (2003). Development and validation of a brief screening version of the Childhood Trauma Questionnaire. *Child Abuse and Neglect, 27*(2), 169-190. doi:https://doi.org/10.1016/S0145-2134(02)00541-0

Blanke, O. (2012). Multisensory brain mechanisms of bodily self-consciousness. *Nature Reviews: Neuroscience, 13*(8), 556-571. doi:10.1038/nrn3292

Blankenburg, W., & Mishara, A. T. (2001). First steps toward a psychopathology of "common sense". *Philosophy, Psychiatry, & Psychology, 8*(4), 303-315. doi:http://dx.doi.org/10.1353/ppp.2002.0014

Bleuler, E. (1950). *Dementia praecox or the group of schizophrenias*. Oxford, England: International Universities Press.

Bohn, M. J., Babor, T. F., & Kranzler, H. R. (1995). The Alcohol Use Disorders Identification Test (AUDIT): validation of a screening instrument for use in medical settings. *Journal of Studies on Alcohol, 56*(4), 423-432. doi:10.15288/jsa.1995.56.423

Boldrini, T., Tanzilli, A., Pontillo, M., Chirumbolo, A., Vicari, S., & Lingiardi, V. (2019). Comorbid Personality Disorders in Individuals With an At-Risk Mental State for Psychosis: A Meta-Analytic Review. *Front Psychiatry, 10*, 429. doi:10.3389/fpsyt.2019.00429

Bolt, L. K., Amminger, G. P., Farhall, J., McGorry, P. D., Nelson, B., Markulev, C., . . . Allott, K. A. (2019). Neurocognition as a predictor of transition to psychotic disorder and functional outcomes in ultra-high risk participants: Findings from the NEURAPRO randomized clinical trial. *Schizophr Res, 206*, 67-74. doi:10.1016/j.schres.2018.12.013

Bonoldi, I., Allen, P., Madeira, L., Tognin, S., Bossong, M. G., Azis, M., . . . McGuire, P. (2019). Basic Self-Disturbances Related to Reduced Anterior Cingulate Volume in Subjects at Ultra-High Risk for Psychosis. *Front Psychiatry, 10*, 254. doi:10.3389/fpsyt.2019.00254

Borda, J. P., & Sass, L. A. (2015). Phenomenology and neurobiology of self disorder in schizophrenia: Primary factors. *Schizophr Res, 169*(1-3), 464-473. doi:10.1016/j.schres.2015.09.024

Bosnjak Kuharic, D., Kekin, I., Hew, J., Rojnic Kuzman, M., & Puljak, L. (2019). Interventions for prodromal stage of psychosis. *Cochrane Database of Systematic Reviews*(11). doi:10.1002/14651858.CD012236.pub2

Brill, N., Reichenberg, A., Weiser, M., & Rabinowitz, J. (2008). Validity of the Premorbid Adjustment Scale. *Schizophr Bull, 34*(5), 981-983. doi:10.1093/schbul/sbm128

Broyd, S. J., Demanuele, C., Debener, S., Helps, S. K., James, C. J., & Sonuga-Barke, E. J. (2009). Default-mode brain dysfunction in mental disorders: a systematic review. *Neuroscience and Biobehavioral Reviews, 33*(3), 279-296. doi:10.1016/j.neubiorev.2008.09.002

Burgy, M. (2011). Ego disturbances in the sense of Kurt Schneider: historical and phenomenological aspects. *Psychopathology, 44*(5), 320-328. doi:10.1159/000325059

Büetiger, J. R., Hubl, D., Kupferschmid, S., Schultze-Lutter, F., Schimmelmann, B. G., Federspiel, A., . . . Kindler, J. (2020). Trapped in a Glass Bell Jar: Neural Correlates of Depersonalization and Derealization in Subjects at Clinical High-Risk of Psychosis and Depersonalization-Derealization Disorder. *Front Psychiatry, 11*, 535652. doi:10.3389/fpsyt.2020.535652

Cannon-Spoor, H. E., Potkin, S. G., & Wyatt, R. J. (1982). Measurement of premorbid adjustment in chronic schizophrenia. *Schizophr Bull, 8*(3), 470-484.

Cannon, T. D., & Mednick, S. A. (1993). The schizophrenia high-risk project in Copenhagen: three decades of progress. *Acta Psychiatrica Scandinavica. Supplementum, 370*, 33-47. doi:10.1111/j.1600-0447.1993.tb05359.x

Carrion, R. E., Demmin, D., Auther, A. M., McLaughlin, D., Olsen, R., Lencz, T., . . . Cornblatt, B. A. (2016). Duration of attenuated positive and negative symptoms in individuals at clinical high risk: Associations with risk of conversion to psychosis and functional outcome. *Journal of Psychiatric Research, 81*, 95-101. doi:10.1016/j.jpsychires.2016.06.021

Cassidy, C. M., Schmitz, N., & Malla, A. (2008). Validation of the alcohol use disorders identification test and the drug abuse screening test in first episode psychosis. *Can.J.Psychiatry, 53*(1), 26-33.

Catalan, A., Salazar de Pablo, G., Vaquerizo Serrano, J., Mosillo, P., Baldwin, H., Fernández-Rivas, A., . . . Fusar-Poli, P. (2021). Annual Research Review: Prevention of psychosis in adolescents - systematic review and meta-analysis of advances in detection, prognosis and intervention. *Journal of Child Psychology and Psychiatry and Allied Disciplines, 62*(5), 657-673. doi:10.1111/jcpp.13322

Chapman, J. (1966). The early symptoms of schizophrenia. *Br J Psychiatry, 112*(484), 225-251. doi:10.1192/bjp.112.484.225

Ciaunica, A., Charlton, J., & Farmer, H. (2020). When the Window Cracks: Transparency and the Fractured Self in Depersonalisation. *Phenomenology and the cognitive sciences, 20*(1), 1. doi:10.1007/s11097-020-09677-z

Cicero, D. C., Neis, A. M., Klaunig, M. J., & Trask, C. L. (2017). The Inventory of Psychotic-Like Anomalous Self-Experiences (IPASE): Development and validation. *Psychological Assessment, 29*(1), 13-25. doi:10.1037/pas0000304

Comparelli, A., Corigliano, V., De Carolis, A., Pucci, D., Angelone, M., Di Pietro, S., . . . Girardi, P. (2016). Anomalous self-experiences and their relationship with symptoms, neuro-cognition, and functioning in at-risk adolescents and young adults. *Comprehensive Psychiatry, 65*, 44-49. doi:10.1016/j.comppsych.2015.09.011

Conrad, K. (1958). *Die beginnende Schizophrenie : Versuch einer Gestaltanalyse des Wahns*. Stuttgart: Thieme.

Corcoran, C. M. (2016). Ethical and Epidemiological Dimensions of Labeling Psychosis Risk. *AMA J Ethics, 18*(6), 633-642. doi:10.1001/journalofethics.2016.18.6.msoc2-1606

Corlett, P. R., Taylor, J. R., Wang, X. J., Fletcher, P. C., & Krystal, J. H. (2010). Toward a neurobiology of delusions. *Progress in Neurobiology, 92*(3), 345-369. doi:10.1016/j.pneurobio.2010.06.007

Cornblatt, B. A., & Carrión, R. E. (2016). Deconstructing the Psychosis Risk Syndrome: Moving the Field of Prevention Forward. *JAMA Psychiatry, 73*(2), 105-106. doi:10.1001/jamapsychiatry.2015.2454

Creswell, J. W., & Poth, C. N. (2018). *Qualitative inquiry & research design : choosing among five approaches* (4th ed., international student ed. ed.). Thousand Oaks, Calif: Sage.

Crowe, M., Inder, M., & Porter, R. (2015). Conducting qualitative research in mental health: Thematic and content analyses. *Aust N Z J Psychiatry, 49*(7), 616-623. doi:10.1177/0004867415582053

Damasio, A. (2010). *Self comes to mind: Constructing the conscious brain*. New York, NY: Pantheon/Random House; US.

Damasio, A. R. (1994). *Descartes' error: emotion, reason, and the human brain*. New York: Grosset/Putnam.

Dannevang, A. L., Randers, L., Gondan, M., Krakauer, K., Nordholm, D., & Nordentoft, M. (2018). Premorbid adjustment in individuals at ultra-high risk for developing psychosis: a case–control study. *Early Interv Psychiatry, 12*(5), 839-847. doi:10.1111/eip.12375

Davidsen, K. A. (2009). Anomalous self-experience in adolescents at risk of psychosis. Clinical and conceptual elucidation. *Psychopathology, 42*(6), 361-369. doi:000236907 [pii];10.1159/000236907 [doi]

De Herdt, A., Wampers, M., Vancampfort, D., De Hert, M., Vanhees, L., Demunter, H., . . . Probst, M. (2013). Neurocognition in clinical high risk young adults who did or did not convert to a first schizophrenic psychosis: a meta-analysis. *Schizophr Res, 149*(1-3), 48-55. doi:10.1016/j.schres.2013.06.017

Demjaha, A., Valmaggia, L., Stahl, D., Byrne, M., & McGuire, P. (2012). Disorganization/cognitive and negative symptom dimensions in the at-risk mental state predict subsequent transition to psychosis. *Schizophr Bull, 38*(2), 351-359. doi:10.1093/schbul/sbq088

Denzin, N. K., & Lincoln, Y. S. (2013). *Collecting and interpreting qualitative materials* (4th ed. ed.). Los Angeles: SAGE.

Dominguez, M. D., Saka, M. C., Lieb, R., Wittchen, H. U., & van, O. J. (2010). Early expression of negative/disorganized symptoms predicting psychotic experiences and subsequent clinical psychosis: a 10-year study. *Am.J.Psychiatry, 167*(9), 1075-1082. doi:appi.ajp.2010.09060883 [pii];10.1176/appi.ajp.2010.09060883 [doi]

Ebisch, S. J. H., & Aleman, A. (2016). The fragmented self: imbalance between intrinsic and extrinsic self-networks in psychotic disorders. *Lancet Psychiatry, 3*(8), 784-790. doi:10.1016/s2215-0366(16)00045-6

Ettinger, U., Mohr, C., Gooding, D. C., Cohen, A. S., Rapp, A., Haenschel, C., & Park, S. (2015). Cognition and brain function in schizotypy: a selective review. *Schizophr Bull, 41 Suppl 2*, S417-426. doi:10.1093/schbul/sbu190

Falkenberg, I., Valmaggia, L., Byrnes, M., Frascarelli, M., Jones, C., Rocchetti, M., . . . Fusar-Poli, P. (2015). Why are help-seeking subjects at ultra-high risk for psychosis help-seeking? *Psychiatry Res, 228*(3), 808-815. doi:10.1016/j.psychres.2015.05.018

Feinberg, I. (1978). Efference copy and corollary discharge: implications for thinking and its disorders. *Schizophr Bull, 4*(4), 636-640. doi:10.1093/schbul/4.4.636

Fenichel, O. (1938). Ego disturbances and their treatment. *The International Journal of Psychoanalysis, 19*, 416-438.

First, M. B. (1997). *Structured clinical interview for DSM-IV Axis I disorders (SCID-I) : clinician version : User's guide for the Structured clinical interview for DSM-IV Axis I disorders*. Washington, D.C: American Psychiatric Press.

First, M. B. (2004). *DSM-IV-TR guidebook* (H. A. Pincus & A. Frances Eds.). Washington, DC: American Psychiatric Pub.
Fisher, H. L., Craig, T. K., Fearon, P., Morgan, K., Dazzan, P., Lappin, J., . . . Morgan, C. (2011). Reliability and comparability of psychosis patients' retrospective reports of childhood abuse. *Schizophr Bull, 37*(3), 546-553. doi:10.1093/schbul/sbp103
Fletcher, P. C., & Frith, C. D. (2009). Perceiving is believing: a Bayesian approach to explaining the positive symptoms of schizophrenia. *Nature Reviews: Neuroscience, 10*(1), 48-58. doi:10.1038/nrn2536
Flückiger, R., Michel, C., Grant, P., Ruhrmann, S., Vogeley, K., Hubl, D., . . . Schultze-Lutter, F. (2019). The interrelationship between schizotypy, clinical high risk for psychosis and related symptoms: Cognitive disturbances matter. *Schizophrenia research, 210*, 188-196. doi:10.1016/j.schres.2018.12.039
Friston, K., Brown, H. R., Siemerkus, J., & Stephan, K. E. (2016). The dysconnection hypothesis (2016). *Schizophr Res, 176*(2-3), 83-94. doi:10.1016/j.schres.2016.07.014
Frith, C. D. (1992). The cognitive neuropsychology of schizophrenia. In. (Reprinted from: Not in File).
Fuchs, T. (2005a). Corporealized and disembodied minds: A phenomenological view of the body in melancholia and schizophrenia. *Philosophy, Psychiatry, & Psychology, 12*(2), 95-107.
Fuchs, T. (2005b). Delusional mood and delusional perception -- a phenomenological analysis. *Psychopathology, 38*(3), 133-139. doi:PSP2005038003133 [pii];10.1159/000085843 [doi]
Fuchs, T. (2007). The temporal structure of intentionality and its disturbance in schizophrenia. *Psychopathology, 40*(4), 229-235. doi:000101365 [pii];10.1159/000101365 [doi]
Fuchs, T. (2012). AS22-03 - The self in schizophrenia: jaspers, schneider and beyond. *European Psychiatry, 27, Supplement 1*, 1. doi:http://dx.doi.org/10.1016/S0924-9338(12)74015-4
Fuchs, T. (2015). From Self-Disorders to Ego Disorders. *Psychopathology, 48*(5), 324-331. doi:10.1159/000432404
Fuchs, T. (2017). Intercorporeality and Interaffectivity. *Phenomenology and Mind*(11). doi:10.13128/Phe_Mi-20119
Fuchs, T. (2019). The uncanny as atmosphere. In G. Francesetti, Griffero,T. [Ed] (Ed.), *Psychopathology and Atmospheres: Neither Inside nor Outside* (pp. 101-118). UK: Cambridge Scholars Publishing.
Fuchs, T., & Koch, S. C. (2014). Embodied affectivity: on moving and being moved. *Frontiers in Psychology, 5*, 508-508. doi:10.3389/fpsyg.2014.00508
Fuchs, T., & Schlimme, J. E. (2009). Embodiment and psychopathology: a phenomenological perspective. *Curr.Opin.Psychiatry, 22*(6), 570-575. doi:10.1097/YCO.0b013e3283318e5c [doi]
Fusar-Poli, P. (2017). The Clinical High-Risk State for Psychosis (CHR-P), Version II. *Schizophr Bull, 43*(1), 44-47. doi:10.1093/schbul/sbw158
Fusar-Poli, P., Bechdolf, A., Taylor, M. J., Bonoldi, I., Carpenter, W. T., Yung, A. R., & McGuire, P. (2013). At risk for schizophrenic or affective psychoses? A meta-analysis of DSM/ICD diagnostic outcomes in individuals at high clinical risk. *Schizophr Bull, 39*(4), 923-932. doi:10.1093/schbul/sbs060
Fusar-Poli, P., Bonoldi, I., Yung, A. R., Borgwardt, S., Kempton, M. J., Valmaggia, L., . . . McGuire, P. (2012). Predicting psychosis: meta-analysis of transition outcomes in individuals at high clinical risk. *Archives of general psychiatry, 69*(3), 220. doi:10.1001/archgenpsychiatry.2011.1472

Fusar-Poli, P., Borgwardt, S., Bechdolf, A., Addington, J., Riecher-Rossler, A., Schultze-Lutter, F., . . . Yung, A. (2013). The psychosis high-risk state: a comprehensive state-of-the-art review. *JAMA Psychiatry, 70*(1), 107-120. doi:10.1001/jamapsychiatry.2013.269

Fusar-Poli, P., Cappucciati, M., Borgwardt, S., Woods, S. W., Addington, J., Nelson, B., . . . McGuire, P. K. (2016). Heterogeneity of Psychosis Risk Within Individuals at Clinical High Risk: A Meta-analytical Stratification. *JAMA Psychiatry, 73*(2), 113-120. doi:10.1001/jamapsychiatry.2015.2324

Fusar-Poli, P., Cappucciati, M., De Micheli, A., Rutigliano, G., Bonoldi, I., Tognin, S., . . . McGuire, P. (2017). Diagnostic and Prognostic Significance of Brief Limited Intermittent Psychotic Symptoms (BLIPS) in Individuals at Ultra High Risk. *Schizophr Bull, 43*(1), 48-56. doi:10.1093/schbul/sbw151

Fusar-Poli, P., Cappucciati, M., Rutigliano, G., Lee, T. Y., Beverly, Q., Bonoldi, I., . . . McGuire, P. (2016). Towards a Standard Psychometric Diagnostic Interview for Subjects at Ultra High Risk of Psychosis: CAARMS versus SIPS. *Psychiatry J, 2016*, 7146341. doi:10.1155/2016/7146341

Fusar-Poli, P., Cappucciati, M., Rutigliano, G., Schultze-Lutter, F., Bonoldi, I., Borgwardt, S., . . . McGuire, P. (2015). At risk or not at risk? A meta-analysis of the prognostic accuracy of psychometric interviews for psychosis prediction. *World Psychiatry, 14*(3), 322-332. doi:10.1002/wps.20250

Fusar-Poli, P., Carpenter, W. T., Woods, S. W., & McGlashan, T. H. (2014). Attenuated Psychosis Syndrome: Ready for DSM-5.1? *Annual Review of Clinical Psychology, 10*, 155-192. doi:10.1146/annurev-clinpsy-032813-153645

Fusar-Poli, P., Davies, C., Solmi, M., Brondino, N., De Micheli, A., Kotlicka-Antczak, M., . . . Radua, J. (2019). Preventive Treatments for Psychosis: Umbrella Review (Just the Evidence). *Front Psychiatry, 10*, 764-764. doi:10.3389/fpsyt.2019.00764

Fusar-Poli, P., Nelson, B., Valmaggia, L., Yung, A. R., & McGuire, P. K. (2014). Comorbid depressive and anxiety disorders in 509 individuals with an at-risk mental state: impact on psychopathology and transition to psychosis. *Schizophr Bull, 40*(1), 120-131. doi:10.1093/schbul/sbs136

Fusar-Poli, P., Papanastasiou, E., Stahl, D., Rocchetti, M., Carpenter, W., Shergill, S., & McGuire, P. (2015). Treatments of Negative Symptoms in Schizophrenia: Meta-Analysis of 168 Randomized Placebo-Controlled Trials. *Schizophr Bull, 41*(4), 892-899. doi:10.1093/schbul/sbu170

Fusar-Poli, P., Rocchetti, M., Sardella, A., Avila, A., Brandizzi, M., Caverzasi, E., . . . McGuire, P. (2015). Disorder, not just state of risk: Meta-analysis of functioning and quality of life in people at high risk of psychosis. *Br J Psychiatry, 207*(3), 198-206. doi:10.1192/bjp.bp.114.157115

Fusar-Poli, P., Salazar de Pablo, G., Correll, C. U., Meyer-Lindenberg, A., Millan, M. J., Borgwardt, S., . . . Arango, C. (2020). Prevention of Psychosis: Advances in Detection, Prognosis, and Intervention. *JAMA Psychiatry*. doi:10.1001/jamapsychiatry.2019.4779

Fusar-Poli, P., Schultze-Lutter, F., Cappucciati, M., Rutigliano, G., Bonoldi, I., Stahl, D., . . . McGuire, P. (2016). The Dark Side of the Moon: Meta-analytical Impact of Recruitment Strategies on Risk Enrichment in the Clinical High Risk State for Psychosis. *Schizophr Bull, 42*(3), 732-743. doi:10.1093/schbul/sbv162

Fusar-Poli, P., Tantardini, M., De Simone, S., Ramella-Cravaro, V., Oliver, D., Kingdon, J., . . . McGuire, P. (2017). Deconstructing vulnerability for psychosis: Meta-analysis of environmental risk factors for psychosis in subjects at ultra high-risk. *European*

psychiatry : the journal of the Association of European Psychiatrists, 40, 65-75. doi:10.1016/j.eurpsy.2016.09.003
Fusar-Poli, P., Yung, A. R., McGorry, P., & van Os, J. (2014). Lessons learned from the psychosis high-risk state: towards a general staging model of prodromal intervention. *Psychol Med, 44*(1), 17-24. doi:10.1017/s0033291713000184
Fux, L., Walger, P., Schimmelmann, B. G., & Schultze-Lutter, F. (2013). The Schizophrenia Proneness Instrument, Child and Youth version (SPI-CY): Practicability and discriminative validity. *Schizophr Res, 146*(1), 69-78. doi:10.1016/j.schres.2013.02.014
Gallagher, S. (2005). *How the body shapes the mind*. Oxford: Clarendon Press.
Gallese, V., & Ferri, F. (2015). Schizophrenia, bodily selves, and embodied simulation. In. Oxford: Oxford: Oxford University Press.
Gallese, V., & Sinigaglia, C. (2010). The bodily self as power for action. *Neuropsychologia, 48*(3), 746-755. doi:10.1016/j.neuropsychologia.2009.09.038
Gamma, F., Goldstein, J. M., Seidman, L. J., Fitzmaurice, G. M., Tsuang, M. T., & Buka, S. L. (2014). Early intermodal integration in offspring of parents with psychosis. *Schizophr Bull, 40*(5), 992-1000. doi:10.1093/schbul/sbt111
Gao, W. J., Yang, S. S., Mack, N. R., & Chamberlin, L. A. (2021). Aberrant maturation and connectivity of prefrontal cortex in schizophrenia-contribution of NMDA receptor development and hypofunction. *Molecular Psychiatry*. doi:10.1038/s41380-021-01196-w
Gaweda, L., Goritz, A. S., & Moritz, S. (2018). Mediating role of aberrant salience and self-disturbances for the relationship between childhood trauma and psychotic-like experiences in the general population. *Schizophr Res*. doi:10.1016/j.schres.2018.11.034
Gaweda, L., Pionke, R., Krezolek, M., Prochwicz, K., Klosowska, J., Frydecka, D., . . . Nelson, B. (2018). Self-disturbances, cognitive biases and insecure attachment as mechanisms of the relationship between traumatic life events and psychotic-like experiences in non-clinical adults - A path analysis. *Psychiatry Res, 259*, 571-578. doi:10.1016/j.psychres.2017.11.009
Gaweda, L., Prochwicz, K., Adamczyk, P., Frydecka, D., Misiak, B., Kotowicz, K., . . . Nelson, B. (2018). The role of self-disturbances and cognitive biases in the relationship between traumatic life events and psychosis proneness in a non-clinical sample. *Schizophr Res, 193*, 218-224. doi:10.1016/j.schres.2017.07.023
Gray, J. A. (1998). Integrating schizophrenia. *Schizophr Bull, 24*(2), 249-266. doi:10.1093/oxfordjournals.schbul.a033324
Gross, G. (1989). The 'basic' symptoms of schizophrenia. *Br.J.Psychiatry Suppl*(7), 21-25.
Gross, G., Huber, G., Klosterkkotter, J., & Linz, M. (1987). *BSABS: Bonner Skala für die Beurteilung von Basissymptomen Bonn Scale for the Assessment of Basic Symptoms* (G. Gross Ed.). London: Springer.
Guralnik, O., Schmeidler, J., & Simeon, D. (2000). Feeling unreal: cognitive processes in depersonalization. *Am J Psychiatry, 157*(1), 103-109. doi:10.1176/ajp.157.1.103
Hackshaw, A. (2008). Small studies: strengths and limitations. *European Respiratory Journal, 32*(5), 1141-1143. doi:10.1183/09031936.00136408
Handest, P., & Parnas, J. (2005). Clinical characteristics of first-admitted patients with ICD-10 schizotypal disorder. *Br.J.Psychiatry Suppl, 187*(48), s49-s54. doi:187/48/s49 [pii];10.1192/bjp.187.48.s49 [doi]
Hanssen, M., Peeters, F., Krabbendam, L., Radstake, S., Verdoux, H., & van Os, J. (2003). How psychotic are individuals with non-psychotic disorders? *Social Psychiatry and Psychiatric Epidemiology, 38*(3), 149-154. doi:10.1007/s00127-003-0622-7

Haug, E., Lien, L., Raballo, A., Bratlien, U., Oie, M., Andreassen, O. A., . . . Moller, P. (2012). Selective aggregation of self-disorders in first-treatment DSM-IV schizophrenia spectrum disorders. *Journal of Nervous and Mental Disease, 200*(7), 632-636. doi:10.1097/NMD.0b013e31825bfd6f

Haug, E., Melle, I., Andreassen, O. A., Raballo, A., Bratlien, U., Oie, M., . . . Moller, P. (2012). The association between anomalous self-experience and suicidality in first-episode schizophrenia seems mediated by depression. *Comprehensive Psychiatry, 53*(5), 456-460. doi:10.1016/j.comppsych.2011.07.005

Haug, E., Oie, M., Andreassen, O. A., Bratlien, U., Nelson, B., Aas, M., . . . Melle, I. (2015). Anomalous self-experience and childhood trauma in first-episode schizophrenia. *Comprehensive Psychiatry, 56*, 35-41. doi:10.1016/j.comppsych.2014.10.005

Haug, E., Oie, M., Andreassen, O. A., Bratlien, U., Raballo, A., Nelson, B., . . . Melle, I. (2014). Anomalous self-experiences contribute independently to social dysfunction in the early phases of schizophrenia and psychotic bipolar disorder. *Comprehensive Psychiatry, 55*(3), 475-482. doi:10.1016/j.comppsych.2013.11.010

Haug, E., Oie, M., Melle, I., Andreassen, O. A., Raballo, A., Bratlien, U., . . . Moller, P. (2011). The association between self-disorders and neurocognitive dysfunction in schizophrenia. *Schizophr.Res.* doi:S0920-9964(11)00613-X [pii];10.1016/j.schres.2011.11.015 [doi]

Haug, E., Oie, M. G., Andreassen, O. A., Bratlien, U., Romm, K. L., Moller, P., & Melle, I. (2016). The Association between Anomalous Self-experiences, Self-esteem and Depressive Symptoms in First Episode Schizophrenia. *Frontiers in Human Neuroscience, 10*, 557. doi:10.3389/fnhum.2016.00557

Hawkins, K. A., McGlashan, T. H., Quinlan, D., Miller, T. J., Perkins, D. O., Zipursky, R. B., . . . Woods, S. W. (2004). Factorial structure of the Scale of Prodromal Symptoms. *Schizophr Res, 68*(2-3), 339-347. doi:10.1016/s0920-9964(03)00053-7

Healey, K. M., Penn, D. L., Perkins, D., Woods, S. W., Keefe, R. S. E., & Addington, J. (2017). Latent Profile Analysis and Conversion to Psychosis: Characterizing Subgroups to Enhance Risk Prediction. *Schizophr Bull*. doi:10.1093/schbul/sbx080

Heinssen, R. K., & Insel, T. R. (2015). Preventing the onset of psychosis: not quite there yet. *Schizophr Bull, 41*(1), 28-29. doi:10.1093/schbul/sbu161

Heinz, A., Murray, G. K., Schlagenhauf, F., Sterzer, P., Grace, A. A., & Waltz, J. A. (2019). Towards a Unifying Cognitive, Neurophysiological, and Computational Neuroscience Account of Schizophrenia. *Schizophr Bull, 45*(5), 1092-1100. doi:10.1093/schbul/sby154

Hemsley, D. R. (1994). A cognitive model for schizophrenia and its possible neural basis. *Acta Psychiatrica Scandinavica. Supplementum, 384*, 80-86. doi:10.1111/j.1600-0447.1994.tb05895.x

Hengartner, M. P., Heekeren, K., Dvorsky, D., Walitza, S., Rossler, W., & Theodoridou, A. (2017). Course of psychotic symptoms, depression and global functioning in persons at clinical high risk of psychosis: Results of a longitudinal observation study over three years focusing on both converters and non-converters. *Schizophr Res, 189*, 19-26. doi:10.1016/j.schres.2017.01.040

Herz, M. I., & Melville, C. (1980). Relapse in schizophrenia. *Am J Psychiatry, 137*(7), 801-805. doi:10.1176/ajp.137.7.801

Hildebrand, M. (2015). The Psychometric Properties of the Drug Use Disorders Identification Test (DUDIT): A Review of Recent Research. *Journal of Substance Abuse Treatment, 53*, 52-59. doi:10.1016/j.jsat.2015.01.008

Hilsenroth, M. J., Ackerman, S. J., Blagys, M. D., Baumann, B. D., Baity, M. R., Smith, S. R., . . . Holdwick, D. J., Jr. (2000). Reliability and validity of DSM-IV axis V. *Am.J.Psychiatry, 157*(11), 1858-1863.

Howes, O. D., & Kapur, S. (2009). The dopamine hypothesis of schizophrenia: version III--the final common pathway. *Schizophr Bull, 35*(3), 549-562. doi:10.1093/schbul/sbp006

Huber, G., & Gross, G. (1989). The concept of basic symptoms in schizophrenic and schizoaffective psychoses. *Recenti Prog.Med., 80*(12), 646-652.

Hunter, E. C., Sierra, M., & David, A. S. (2004). The epidemiology of depersonalisation and derealisation. A systematic review. *Social Psychiatry and Psychiatric Epidemiology, 39*(1), 9-18. doi:10.1007/s00127-004-0701-4

Hur, J. W., Kwon, J. S., Lee, T. Y., & Park, S. (2014). The crisis of minimal self-awareness in schizophrenia: a meta-analytic review. *Schizophr Res, 152*(1), 58-64. doi:10.1016/j.schres.2013.08.042

Hurlimann, F., Kupferschmid, S., & Simon, A. E. (2012). Cannabis-induced depersonalization disorder in adolescence. *Neuropsychobiology, 65*(3), 141-146. doi:10.1159/000334605

Husserl, E. (1931). *Ideas: general introduction to pure phenomenology.* (W. Gibson, Trans.). Oxford, England: Macmillan.

Häfner, H., Maurer, K., Löffler, W., & Riecher-Rössler, A. (1993). The Influence of Age and Sex on the Onset and Early Course of Schizophrenia. *Br J Psychiatry, 162*(1), 80-86. doi:10.1192/bjp.162.1.80

Irarrazaval, L. (2013). Psychotherapeutic implications of self disorders in schizophrenia. *American Journal of Psychotherapy, 67*(3), 277-292. doi:10.1176/appi.psychotherapy.2013.67.3.277

Jaspers, K., Hoenig, J., & Hamilton, M. W. (1997a). *General psychopathology, Vol. 1*. Baltimore, MD: Johns Hopkins University Press; US.

Jaspers, K., Hoenig, J., & Hamilton, M. W. (1997b). *General psychopathology, Vol. 2*. Baltimore, MD: Johns Hopkins University Press; US.

Juckel, G., Sass, L., & Heinz, A. (2003). Anhedonia, self-experience in schizophrenia, and implications for treatment. *Pharmacopsychiatry, 36 Suppl 3*, S176-S180. doi:10.1055/s-2003-45127 [doi]

Kapur, S. (2003). Psychosis as a state of aberrant salience: a framework linking biology, phenomenology, and pharmacology in schizophrenia. *Am.J.Psychiatry, 160*(1), 13-23.

Kaymaz, N., Drukker, M., Lieb, R., Wittchen, H. U., Werbeloff, N., Weiser, M., . . . van Os, J. (2012). Do subthreshold psychotic experiences predict clinical outcomes in unselected non-help-seeking population-based samples? A systematic review and meta-analysis, enriched with new results. *Psychol Med, 42*(11), 2239-2253. doi:10.1017/s0033291711002911

Kernberg, O. (2017). A Psychoanalytic Theory of Personality Disorders. In *Aggressivity, Narcissism, and Self-Destructiveness in the Psychotherapeutic Relationship: New Developments in the Psychopathology and Psychotherapy of Severe Personality Disorders* (pp. 3-26). New Haven: New Haven: Yale University Press.

Kernberg, O. F., & Michels, R. (2009). Borderline personality disorder. *The American Journal of Psychiatry, 166*(5), 505-508.

Kimura, B. (2001). Cogito and I: A bio-logical approach. [References]. *Philosophy, Psychiatry, & Psychology*(4), 331-336. doi:http://dx.doi.org/10.1353/ppp.2002.0019

Kirkpatrick, B., Fenton, W. S., Carpenter, W. T., Jr., & Marder, S. R. (2006). The NIMH-MATRICS consensus statement on negative symptoms. *Schizophr Bull, 32*(2), 214-219. doi:10.1093/schbul/sbj053

Klosterkotter, J. (1992). The meaning of basic symptoms for the genesis of the schizophrenic nuclear syndrome. *Japanese Journal of Psychiatry and Neurology, 46*(3), 609-630.
Klosterkotter, J., Hellmich, M., Steinmeyer, E. M., & Schultze-Lutter, F. (2001). Diagnosing schizophrenia in the initial prodromal phase. *Arch.Gen.Psychiatry, 58*(2), 158-164. doi:yoa9274 [pii]
Koren, D., Lacoua, L., Rothschild-Yakar, L., & Parnas, J. (2016). Disturbances of the Basic Self and Prodromal Symptoms Among Young Adolescents From the Community: A Pilot Population-Based Study. *Schizophr Bull*. doi:10.1093/schbul/sbw010
Koren, D., Reznik, N., Adres, M., Scheyer, R., Apter, A., Steinberg, T., & Parnas, J. (2013). Disturbances of basic self and prodromal symptoms among non-psychotic help-seeking adolescents. *Psychol Med, 43*(7), 1365-1376. doi:10.1017/s0033291712002322
Koren, D., Rothschild-Yakar, L., Lacoua, L., Brunstein-Klomek, A., Zelezniak, A., Parnas, J., & Shahar, G. (2017). Attenuated psychosis and basic self-disturbance as risk factors for depression and suicidal ideation/behaviour in community-dwelling adolescents. *Early Interv Psychiatry*. doi:10.1111/eip.12516
Koren, D., Tzivoni, Y., Schalit, L., Adres, M., Reznik, N., Apter, A., & Parnas, J. (2019). Basic self-disorders in adolescence predict schizophrenia spectrum disorders in young adulthood: A 7-year follow-up study among non-psychotic help-seeking adolescents. *Schizophr Res*. doi:10.1016/j.schres.2019.12.022
Korzekwa, M. I., Dell, P. F., Links, P. S., Thabane, L., & Fougere, P. (2009). Dissociation in borderline personality disorder: a detailed look. *J Trauma Dissociation, 10*(3), 346-367. doi:10.1080/15299730902956838
Koutsouleris, N., Kambeitz-Ilankovic, L., Ruhrmann, S., Rosen, M., Ruef, A., Dwyer, D. B., . . . Borgwardt, S. (2018). Prediction Models of Functional Outcomes for Individuals in the Clinical High-Risk State for Psychosis or With Recent-Onset Depression: A Multimodal, Multisite Machine Learning Analysis. *JAMA Psychiatry, 75*(11), 1156-1172. doi:10.1001/jamapsychiatry.2018.2165
Kraepelin, E. (1896). *Psychiatrie* (4 ed.): Leipzig, Germany: Barth.
Kraguljac, N. V., & Lahti, A. C. (2021). Neuroimaging as a Window Into the Pathophysiological Mechanisms of Schizophrenia. *Front Psychiatry, 12*, 613764. doi:10.3389/fpsyt.2021.613764
Laing, R. D. (1965). *The divided self: An existential study in sanity and madness*. Oxford, England: Penguin Books; England.
Lee, T. Y., Kim, S. N., Correll, C. U., Byun, M. S., Kim, E., Jang, J. H., . . . Kwon, J. S. (2014). Symptomatic and functional remission of subjects at clinical high risk for psychosis: a 2-year naturalistic observational study. *Schizophrenia research, 156*(2-3), 266-271. doi:10.1016/j.schres.2014.04.002
Lee, W. E., Kwok, C. H., Hunter, E. C., Richards, M., & David, A. S. (2012). Prevalence and childhood antecedents of depersonalization syndrome in a UK birth cohort. *Social Psychiatry and Psychiatric Epidemiology, 47*(2), 253-261. doi:10.1007/s00127-010-0327-7
Lilienfeld, S. O., & Treadway, M. T. (2016). Clashing Diagnostic Approaches: DSM-ICD Versus RDoC. *Annual Review of Clinical Psychology, 12*, 435-463. doi:10.1146/annurev-clinpsy-021815-093122
Lim, J., Rekhi, G., Rapisarda, A., Lam, M., Kraus, M., Keefe, R. S. E., & Lee, J. (2015). Impact of psychiatric comorbidity in individuals at Ultra High Risk of psychosis - Findings from the Longitudinal Youth at Risk Study (LYRIKS). *Schizophrenia research, 164*(1-3), 8-14. doi:10.1016/j.schres.2015.03.007

Lin, A., Wood, S. J., Nelson, B., Beavan, A., McGorry, P., & Yung, A. R. (2015). Outcomes of nontransitioned cases in a sample at ultra-high risk for psychosis. *Am J Psychiatry, 172*(3), 249-258. doi:10.1176/appi.ajp.2014.13030418

Linscott, R., & van Os, J. (2013). An updated and conservative systematic review and meta-analysis of epidemiological evidence on psychotic experiences in children and adults: on the pathway from proneness to persistence to dimensional expression across mental disorders. In (Vol. 43, pp. 1133-1149). Cambridge: Cambridge University Press.

Loewy, R. L., Pearson, R., Vinogradov, S., Bearden, C. E., & Cannon, T. D. (2011). Psychosis risk screening with the Prodromal Questionnaire--brief version (PQ-B). *Schizophr Res, 129*(1), 42-46. doi:10.1016/j.schres.2011.03.029

Lyngberg, K., Buchy, L., Liu, L., Perkins, D., Woods, S., & Addington, J. (2015). Patterns of premorbid functioning in individuals at clinical high risk of psychosis. *Schizophr Res, 169*(1), 209-213. doi:10.1016/j.schres.2015.11.004

Madeira, L., Bonoldi, I., Rocchetti, M., Brandizzi, M., Samson, C., Azis, M., . . . Fusar-Poli, P. (2016). Prevalence and implications of Truman symptoms in subjects at ultra high risk for psychosis. *Psychiatry Res, 238*, 270-276. doi:10.1016/j.psychres.2016.02.001

Madeira, L., Carmenates, S., Costa, C., Linhares, L., Stanghellini, G., Figueira, M. L., & Sass, L. (2017). Basic Self-Disturbances beyond Schizophrenia: Discrepancies and Affinities in Panic Disorder - An Empirical Clinical Study. *Psychopathology, 50*(2), 157-168. doi:10.1159/000457803

Martin, B., Wittmann, M., Franck, N., Cermolacce, M., Berna, F., & Giersch, A. (2014). Temporal structure of consciousness and minimal self in schizophrenia. *Frontiers in Psychology, 5*, 1175. doi:10.3389/fpsyg.2014.01175

Mayer-Gross, W., Slater, E., & Roth, M. (1960). *Clinical psychiatry., 2nd ed*. Oxford, England: Williams and Wilkins; England.

Mayo, D., Corey, S., Kelly, L. H., Yohannes, S., Youngquist, A. L., Stuart, B. K., . . . Loewy, R. L. (2017). The Role of Trauma and Stressful Life Events among Individuals at Clinical High Risk for Psychosis: A Review. *Front Psychiatry, 8*, 55. doi:10.3389/fpsyt.2017.00055

McGhie, A., & Chapman, J. (1961). Disorders of attention and perception in early schizophrenia. *British Journal of Medical Psychology, 34*, 103-116. doi:10.1111/j.2044-8341.1961.tb00936.x

McGlashan, T. H., Walsh, B., & Woods, S. (2010). *The psychosis-risk syndrome: handbook for diagnosis and follow-up*. Oxford: Oxford University Press.

McGlashan, T. H., Zipursky, R. B., Perkins, D., Addington, J., Miller, T., Woods, S. W., . . . Breier, A. (2006). Randomized, double-blind trial of olanzapine versus placebo in patients prodromally symptomatic for psychosis. *Am.J.Psychiatry, 163*(5), 790-799. doi:163/5/790 [pii];10.1176/appi.ajp.163.5.790 [doi]

McGorry, P. D., Nelson, B., Amminger, G. P., Bechdolf, A., Francey, S. M., Berger, G., . . . Yung, A. R. (2009). Intervention in individuals at ultra high risk for psychosis: a review and future directions. *J.Clin.Psychiatry, 70*(9), 1206-1212. doi:10.4088/JCP.08r04472 [doi]

McGorry, P. D., Yung, A. R., & Phillips, L. J. (2003). The "close-in" or ultra high-risk model: a safe and effective strategy for research and clinical intervention in prepsychotic mental disorder. *Schizophr Bull, 29*(4), 771-790. doi:10.1093/oxfordjournals.schbul.a007046

Medford, N., Baker, D., Hunter, E., Sierra, M., Lawrence, E., Phillips, M. L., & David, A. S. (2003). Chronic depersonalization following illicit drug use: a controlled analysis of 40 cases. *Addiction, 98*(12), 1731-1736.

Medford, N., Sierra, M., Stringaris, A., Giampietro, V., Brammer, M. J., & David, A. S. (2016). Emotional Experience and Awareness of Self: Functional MRI Studies of Depersonalization Disorder. *Frontiers in Psychology, 7*, 432. doi:10.3389/fpsyg.2016.00432

Mei, C., van der Gaag, M., Nelson, B., Smit, F., Yuen, H. P., Berger, M., . . . McGorry, P. D. (2021). Preventive interventions for individuals at ultra high risk for psychosis: An updated and extended meta-analysis. *Clin Psychol Rev*, 102005. doi:10.1016/j.cpr.2021.102005

Merleau-Ponty, M. (2002). Selections from Phenomenology of Perception. In A. Noe, Thompson, E. (Ed.), *Vision and mind: Selected readings in the philosophy of perception* (pp. 15-34). Cambridge, MA, US: MIT Press; US.

Michal, M., Duven, E., Giralt, S., Dreier, M., Muller, K. W., Adler, J., . . . Wolfling, K. (2015). Prevalence and correlates of depersonalization in students aged 12-18 years in Germany. *Social Psychiatry and Psychiatric Epidemiology, 50*(6), 995-1003. doi:10.1007/s00127-014-0957-2

Michel, C., Ruhrmann, S., Schimmelmann, B. G., Klosterkotter, J., & Schultze-Lutter, F. (2018). Course of clinical high-risk states for psychosis beyond conversion. *European Archives of Psychiatry and Clinical Neuroscience, 268*(1), 39-48. doi:10.1007/s00406-016-0764-8

Miller, T. J., McGlashan, T. H., Rosen, J. L., Cadenhead, K., Cannon, T., Ventura, J., . . . Woods, S. W. (2003). Prodromal assessment with the structured interview for prodromal syndromes and the scale of prodromal symptoms: predictive validity, interrater reliability, and training to reliability. *Schizophr.Bull., 29*(4), 703-715.

Miller, T. J., McGlashan, T. H., Rosen, J. L., Somjee, L., Markovich, P. J., Stein, K., & Woods, S. W. (2002). Prospective diagnosis of the initial prodrome for schizophrenia based on the Structured Interview for Prodromal Syndromes: preliminary evidence of interrater reliability and predictive validity. *Am.J.Psychiatry, 159*(5), 863-865.

Miller, T. J., McGlashan, T. H., Woods, S. W., Stein, K., Driesen, N., Corcoran, C. M., . . . Davidson, L. (1999). Symptom assessment in schizophrenic prodromal states. *Psychiatr.Q., 70*(4), 273-287.

Minkowski, E. (1987). The essential disorder underlying schizophrenia and schizophrenic thought. In J. Cutting, Shepherd, M. (Ed.), *The Clinical Roots of the Schizophrenia Concept: Translations of Seminal European Contributions on Schizophrenia* (pp. 188-212). New York, USA: Cambridge University Press.

Mishara, A., Bonoldi, I., Allen, P., Rutigliano, G., Perez, J., Fusar-Poli, P., & McGuire, P. (2016). Neurobiological Models of Self-Disorders in Early Schizophrenia. *Schizophr Bull, 42*(4), 874-880. doi:10.1093/schbul/sbv123

Mishara, A. L. (2010). Klaus Conrad (1905-1961): delusional mood, psychosis, and beginning schizophrenia. *Schizophr.Bull., 36*(1), 9-13. doi:sbp144 [pii];10.1093/schbul/sbp144 [doi]

Misiak, B., Krefft, M., Bielawski, T., Moustafa, A. A., Sasiadek, M. M., & Frydecka, D. (2017). Toward a unified theory of childhood trauma and psychosis: A comprehensive review of epidemiological, clinical, neuropsychological and biological findings. *Neuroscience and Biobehavioral Reviews, 75*, 393-406. doi:10.1016/j.neubiorev.2017.02.015

Moller, P., Haug, E., Raballo, A., Parnas, J., & Melle, I. (2011). Examination of anomalous self-experience in first-episode psychosis: interrater reliability. *Psychopathology, 44*(6), 386-390. doi:10.1159/000325173

Moller, P., & Husby, R. (2000). The initial prodrome in schizophrenia: searching for naturalistic core dimensions of experience and behavior. *Schizophr.Bull., 26*(1), 217-232.

Moos, R. H., Nichol, A. C., & Moos, B. S. (2002). Global Assessment of Functioning Ratings and the Allocation and Outcomes of Mental Health Services. *Psychiatric Services, 53*(6), 730-737. doi:10.1176/appi.ps.53.6.730

Moritz, S., Gawęda, Ł., Heinz, A., & Gallinat, J. (2019). Four reasons why early detection centers for psychosis should be renamed and their treatment targets reconsidered: we should not catastrophize a future we can neither reliably predict nor change. *Psychol Med, 49*(13), 2134-2140. doi:10.1017/s0033291719001740

Moskowitz, A., & Heim, G. (2011). Eugen Bleuler's Dementia praecox or the group of schizophrenias (1911): a centenary appreciation and reconsideration. *Schizophr.Bull., 37*(3), 471-479. doi:sbr016 [pii];10.1093/schbul/sbr016 [doi]

Myin-Germeys, I., & van Os, J. (2007). Stress-reactivity in psychosis: evidence for an affective pathway to psychosis. *Clin.Psychol.Rev., 27*(4), 409-424. doi:S0272-7358(06)00117-6 [pii];10.1016/j.cpr.2006.09.005 [doi]

Nath, M., Wong, T. P., & Srivastava, L. K. (2021). Neurodevelopmental insights into circuit dysconnectivity in schizophrenia. *Progress in Neuro-Psychopharmacology and Biological Psychiatry, 104*, 110047. doi:10.1016/j.pnpbp.2020.110047

Nelson, B., Lavoie, S., Gawęda, Ł., Li, E., Sass, L. A., Koren, D., . . . Whitford, T. J. (2020). The neurophenomenology of early psychosis: An integrative empirical study. *Consciousness and Cognition, 77*, 102845. doi:10.1016/j.concog.2019.102845

Nelson, B., Li, E., Cicero, D. C., Gaweda, L., Hartmann, J. A., Koren, D., . . . Lavoie, S. (2018). The construct validity of the Inventory of Psychotic-Like Anomalous Self-Experiences (IPASE) as a measure of minimal self-disturbance: Preliminary data. *Early Interv Psychiatry*. doi:10.1111/eip.12711

Nelson, B., Parnas, J., & Sass, L. A. (2014). Disturbance of minimal self (ipseity) in schizophrenia: clarification and current status. *Schizophr Bull, 40*(3), 479-482. doi:10.1093/schbul/sbu034

Nelson, B., & Raballo, A. (2015). Basic Self-Disturbance in the Schizophrenia Spectrum: Taking Stock and Moving Forward. *Psychopathology, 48*(5), 301-309. doi:10.1159/000437211

Nelson, B., Thompson, A., & Yung, A. R. (2012). Basic self-disturbance predicts psychosis onset in the ultra high risk for psychosis "prodromal" population. *Schizophr Bull, 38*(6), 1277-1287. doi:10.1093/schbul/sbs007

Nelson, B., Whitford, T. J., Lavoie, S., & Sass, L. A. (2014a). What are the neurocognitive correlates of basic self-disturbance in schizophrenia? Integrating phenomenology and neurocognition: Part 2 (aberrant salience). *Schizophr Res, 152*(1), 20-27. doi:10.1016/j.schres.2013.06.033

Nelson, B., Whitford, T. J., Lavoie, S., & Sass, L. A. (2014b). What are the neurocognitive correlates of basic self-disturbance in schizophrenia?: Integrating phenomenology and neurocognition. Part 1 (Source monitoring deficits). *Schizophr Res, 152*(1), 12-19. doi:10.1016/j.schres.2013.06.022

Nelson, B., Yung, A. R., Bechdolf, A., & McGorry, P. D. (2008). The phenomenological critique and self-disturbance: implications for ultra-high risk ("prodrome") research. *Schizophr.Bull., 34*(2), 381-392. doi:sbm094 [pii];10.1093/schbul/sbm094 [doi]

Nischk, D., Dölker, C., Rusch, J., & Merz, P. (2015). From theory to clinical practice: a phenomenologically inspired intervention for patients with schizophrenia. *Psychopathology, 48*(2), 127-136. doi:10.1159/000369888

Niznikiewicz, M. A. (2019). Neurobiological approaches to the study of clinical and genetic high risk for developing psychosis. *Psychiatry Res, 277*, 17-22. doi:10.1016/j.psychres.2019.02.009

Nordgaard, J., Handest, P., Vollmer-Larsen, A., Saebye, D., Pedersen, J. T., & Parnas, J. (2017). Temporal persistence of anomalous self-experience: A 5years follow-up. *Schizophr Res, 179*, 36-40. doi:10.1016/j.schres.2016.10.001

Nordgaard, J., Nilsson, L. S., Saebye, D., & Parnas, J. (2017). Self-disorders in schizophrenia-spectrum disorders: a 5-year follow-up study. *European Archives of Psychiatry and Clinical Neuroscience*. doi:10.1007/s00406-017-0837-3

Nordgaard, J., & Parnas, J. (2014). Self-disorders and the schizophrenia spectrum: a study of 100 first hospital admissions. *Schizophr Bull, 40*(6), 1300-1307. doi:10.1093/schbul/sbt239

Nordgaard, J., Revsbech, R., & Henriksen, M. G. (2015). Self-Disorders, Neurocognition and Rationality in Schizophrenia: A Preliminary Study. *Psychopathology, 48*(5), 310-316. doi:10.1159/000435892

Norgaard, J., & Parnas, J. (2012). A semi structured, phenomenologically-oriented psychiatric interview: descriptive congruence in assessing anomalous subjective experience and mental status. *Clinical neuropsychiatry, 9*(3), 123.

Norman, R. M., & Malla, A. K. (1995). Prodromal symptoms of relapse in schizophrenia: a review. *Schizophr Bull, 21*(4), 527-539. doi:10.1093/schbul/21.4.527

Northoff, G., Heinzel, A., de Greck, M., Bermpohl, F., Dobrowolny, H., & Panksepp, J. (2006). Self-referential processing in our brain--a meta-analysis of imaging studies on the self. *Neuroimage, 31*(1), 440-457. doi:10.1016/j.neuroimage.2005.12.002

Northoff, G., & Qin, P. (2011). How can the brain's resting state activity generate hallucinations? A 'resting state hypothesis' of auditory verbal hallucinations. *Schizophr Res, 127*(1-3), 202-214. doi:10.1016/j.schres.2010.11.009

Northoff, G., & Stanghellini, G. (2016). How to Link Brain and Experience? Spatiotemporal Psychopathology of the Lived Body. *Frontiers in Human Neuroscience, 10*, 76-76. doi:10.3389/fnhum.2016.00172

Oliver, D., Reilly, T. J., Baccaredda Boy, O., Petros, N., Davies, C., Borgwardt, S., . . . Fusar-Poli, P. (2020). What Causes the Onset of Psychosis in Individuals at Clinical High Risk? A Meta-analysis of Risk and Protective Factors. *Schizophr Bull, 46*(1), 110-120. doi:10.1093/schbul/sbz039

Panksepp, J., & Biven, L. (2012). *The Archaeology of mind : neuroevolutionary origins of human emotions*. New York: W.W. Norton.

Park, H. Y., Park, K., Seo, E., Koo, S. J., Bang, M., Park, J. Y., . . . An, S. K. (2020). Reduced activation of the ventromedial prefrontal cortex during self-referential processing in individuals at ultra-high risk for psychosis. *Aust N Z J Psychiatry, 54*(5), 528-538. doi:10.1177/0004867419898529

Parnas, J. (2003). Self and schizophrenia: a phenomenological perspective. In T. Kircher & A. David (Eds.), *The Self in Neuroscience and Psychiatry* (pp. 217-241). New York: Cambridge University Press. (Reprinted from: In File).

Parnas, J. (2011). A disappearing heritage: the clinical core of schizophrenia. *Schizophr.Bull., 37*(6), 1121-1130.

Parnas, J., & Bovet, P. (1991). Autism in schizophrenia revisited. *Compr.Psychiatry, 32*(1), 7-21. doi:0010-440X(91)90065-K [pii]

Parnas, J., Bovet, P., & Zahavi, D. (2002). Schizophrenic autism: clinical phenomenology and pathogenetic implications. *World Psychiatry, 1*(3), 131-136.

Parnas, J., Carter, J., & Nordgaard, J. (2016). Premorbid self-disorders and lifetime diagnosis in the schizophrenia spectrum: a prospective high-risk study. *Early Interv Psychiatry, 10*(1), 45-53. doi:10.1111/eip.12140

Parnas, J., & Handest, P. (2003). Phenomenology of anomalous self-experience in early schizophrenia. *Compr.Psychiatry, 44*(2), 121-134. doi:10.1053/comp.2003.50017 [doi];S0010440X03000373 [pii]

Parnas, J., Handest, P., Jansson, L., & Saebye, D. (2005). Anomalous subjective experience among first-admitted schizophrenia spectrum patients: empirical investigation. *Psychopathology, 38*(5), 259-267. doi:PSP2005038005259 [pii];10.1159/000088442 [doi]

Parnas, J., Handest, P., Saebye, D., & Jansson, L. (2003). Anomalies of subjective experience in schizophrenia and psychotic bipolar illness. *Acta Psychiatr.Scand., 108*(2), 126-133. doi:105 [pii]

Parnas, J., & Henriksen, M. G. (2014). Disordered self in the schizophrenia spectrum: a clinical and research perspective. *Harvard Review of Psychiatry, 22*(5), 251-265. doi:10.1097/hrp.0000000000000040

Parnas, J., Jansson, L., Sass, L. A., & Handest, P. (1998). Self-experience in the prodromal phases of schizophrenia: A pilot study of first-admissions. *Neurology Psychiatry and Brain Research, 6*(2), 97-106.

Parnas, J., & Jansson, L. B. (2015). Self-Disorders: Clinical and Conceptual Implications for the Diagnostic Concept of Schizophrenia. *Psychopathology, 48*(5), 332-338. doi:10.1159/000437232

Parnas, J., Moller, P., Kircher, T., Thalbitzer, J., Jansson, L., Handest, P., & Zahavi, D. (2005). EASE: Examination of Anomalous Self-Experience. *Psychopathology, 38*(5), 236-258. doi:PSP2005038005236 [pii];10.1159/000088441 [doi]

Parnas, J., Raballo, A., Handest, P., Jansson, L., Vollmer-Larsen, A., & Saebye, D. (2011). Self-experience in the early phases of schizophrenia: 5-year follow-up of the Copenhagen Prodromal Study. *World Psychiatry, 10*(3), 200-204.

Parnas, J., Sass, L. A., & Zahavi, D. (2013). Rediscovering psychopathology: the epistemology and phenomenology of the psychiatric object. *Schizophr Bull, 39*(2), 270-277. doi:10.1093/schbul/sbs153

Pedersen, G., Hagtvet, K. A., & Karterud, S. (2007). Generalizability studies of the Global Assessment of Functioning-Split version. *Comprehensive Psychiatry, 48*(1), 88-94. doi:10.1016/j.comppsych.2006.03.008

Pedersen, G., & Karterud, S. (2012). The symptom and function dimensions of the Global Assessment of Functioning (GAF) scale. *Comprehensive Psychiatry, 53*(3), 292-298. doi:10.1016/j.comppsych.2011.04.007

Pérez-Álvarez, M., García-Montes, J. M., Vallina-Fernández, O., Perona-Garcelán, S., & Cuevas-Yust, C. (2011). New life for schizophrenia psychotherapy in the light of phenomenology. *Clin. Psychol. Psychother, 18*(3), 187-201. doi:10.1002/cpp.716

Phillips, M. L., & Sierra, M. (2003). Depersonalization disorder: a functional neuroanatomical perspective. *Stress, 6*(3), 157-165. doi:10.1080/1025389031000138538

Piskulic, D., Addington, J., Cadenhead, K. S., Cannon, T. D., Cornblatt, B. A., Heinssen, R., . . . McGlashan, T. H. (2012a). Negative symptoms in individuals at clinical high risk of psychosis. *Psychiatry Res.*

Piskulic, D., Addington, J., Cadenhead, K. S., Cannon, T. D., Cornblatt, B. A., Heinssen, R., . . . McGlashan, T. H. (2012b). Negative symptoms in individuals at clinical high risk of psychosis. *Psychiatry Res, 196*(2-3), 220-224. doi:10.1016/j.psychres.2012.02.018

Polari, A., Lavoie, S., Yuen, H. P., Amminger, P., Berger, G., Chen, E., . . . Nelson, B. (2018). Clinical trajectories in the ultra-high risk for psychosis population. *Schizophr Res, 197*, 550-556. doi:10.1016/j.schres.2018.01.022

Popovic, D., Schmitt, A., Kaurani, L., Senner, F., Papiol, S., Malchow, B., . . . Falkai, P. (2019). Childhood Trauma in Schizophrenia: Current Findings and Research Perspectives. *Frontiers in Neuroscience, 13*, 274. doi:10.3389/fnins.2019.00274

Postmes, L., Sno, H. N., Goedhart, S., van der Stel, J., Heering, H. D., & de Haan, L. (2014). Schizophrenia as a self-disorder due to perceptual incoherence. *Schizophr Res, 152*(1), 41-50. doi:10.1016/j.schres.2013.07.027

Raballo, A., Pappagallo, E., Dell' Erba, A., Lo Cascio, N., Patane, M., Gebhardt, E., . . . Fiori Nastro, P. (2016). Self-Disorders and Clinical High Risk for Psychosis: An Empirical Study in Help-Seeking Youth Attending Community Mental Health Facilities. *Schizophr Bull, 42*(4), 926-932. doi:10.1093/schbul/sbv223

Raballo, A., & Parnas, J. (2010). The Silent Side of the Spectrum: Schizotypy and the Schizotaxic Self. *Schizophr.Bull.* doi:sbq008 [pii];10.1093/schbul/sbq008 [doi]

Raballo, A., & Parnas, J. (2012). Examination of anomalous self-experience: initial study of the structure of self-disorders in schizophrenia spectrum. *Journal of Nervous and Mental Disease, 200*(7), 577-583. doi:10.1097/NMD.0b013e31825bfb41

Raballo, A., Poletti, M., Preti, A., & Parnas, J. (2021). The Self in the Spectrum: A Meta-analysis of the Evidence Linking Basic Self-Disorders and Schizophrenia. *Schizophr Bull*. doi:10.1093/schbul/sbaa201

Raballo, A., Saebye, D., & Parnas, J. (2009). Looking at the Schizophrenia Spectrum Through the Prism of Self-disorders: An Empirical Study. *Schizophr.Bull.* doi:sbp056 [pii];10.1093/schbul/sbp056 [doi]

Rasmussen, A. R., Reich, D., Lavoie, S., Li, E., Hartmann, J. A., McHugh, M., . . . Nelson, B. (2020). The relation of basic self-disturbance to self-harm, eating disorder symptomatology and other clinical features: Exploration in an early psychosis sample. *Early Interv Psychiatry, 14*(3), 275-282. doi:10.1111/eip.12850

Read, J., Fosse, R., Moskowitz, A., & Perry, B. (2014). The traumagenic neurodevelopmental model of psychosis revisited. *Neuropsychiatry, 4*(1), 65-79. doi:10.2217/npy.13.89

Reutens, S., Nielsen, O., & Sachdev, P. (2010). Depersonalization disorder. *Curr Opin Psychiatry, 23*(3), 278-283. doi:10.1097/YCO.0b013e3283387ab4

Rietschel, L., Lambert, M., Karow, A., Zink, M., Müller, H., Heinz, A., . . . Bechdolf, A. (2017). Clinical high risk for psychosis: gender differences in symptoms and social functioning. *Early Interv Psychiatry, 11*(4), 306-313. doi:10.1111/eip.12240

Robinson, J. D., Wagner, N. F., & Northoff, G. (2016). Is the Sense of Agency in Schizophrenia Influenced by Resting-State Variation in Self-Referential Regions of the Brain? *Schizophr Bull, 42*(2), 270-276. doi:10.1093/schbul/sbv102

Rosen, J. L., Woods, S. W., Miller, T. J., & McGlashan, T. H. (2002). Prospective observations of emerging psychosis. *J.Nerv.Ment.Dis., 190*(3), 133-141.

Ruhrmann, S., Schultze-Lutter, F., Salokangas, R. K., Heinimaa, M., Linszen, D., Dingemans, P., . . . Klosterkötter, J. (2010). Prediction of psychosis in adolescents and young adults at high risk: results from the prospective European prediction of psychosis study. *Arch Gen Psychiatry, 67*(3), 241-251. doi:10.1001/archgenpsychiatry.2009.206

Ryan, A. T., Addington, J., Bearden, C. E., Cadenhead, K. S., Cornblatt, B. A., Mathalon, D. H., . . . Walker, E. F. (2017). Latent class cluster analysis of symptom ratings identifies distinct subgroups within the clinical high risk for psychosis syndrome. *Schizophr Res*. doi:10.1016/j.schres.2017.12.001

Salami, A., Andreu-Perez, J., & Gillmeister, H. (2020). Symptoms of depersonalisation/derealisation disorder as measured by brain electrical activity: A

systematic review. *Neuroscience and Biobehavioral Reviews, 118*, 524-537. doi:10.1016/j.neubiorev.2020.08.011
Sass, L. (2003). Self-disturbance in schizophrenia: hyperreflexivity and diminished self-affection. In T. Kircher & A. David (Eds.), *The Self in Neuroscience and Psychiatry* (pp. 242-271). New York: Cambridge University Press. (Reprinted from: In File).
Sass, L., Borda, J. P., Madeira, L., Pienkos, E., & Nelson, B. (2018). Varieties of Self Disorder: A Bio-Pheno-Social Model of Schizophrenia. *Schizophr Bull, 44*(4), 720-727. doi:10.1093/schbul/sby001
Sass, L., & Byrom, G. (2015). Phenomenological and neurocognitive perspectives on delusions: A critical overview. *World Psychiatry, 14*(2), 164-173. doi:10.1002/wps.20205
Sass, L., Pienkos, E., & Nelson, B. (2013). Introspection and schizophrenia: a comparative investigation of anomalous self experiences. *Consciousness and Cognition, 22*(3), 853-867. doi:10.1016/j.concog.2013.05.004
Sass, L., Pienkos, E., Nelson, B., & Medford, N. (2013). Anomalous self-experience in depersonalization and schizophrenia: a comparative investigation. *Consciousness and Cognition, 22*(2), 430-441. doi:10.1016/j.concog.2013.01.009
Sass, L. A. (1992). *Madness and modernism: insanity in the light of modern art, literature, and thought*. New York: BasicBooks.
Sass, L. A. (2001). Self and world in schizophrenia: Three classic approaches. [References]. *Philosophy, Psychiatry, & Psychology*(4), 251-270. doi:http://dx.doi.org/10.1353/ppp.2002.0026
Sass, L. A. (2003a). "Negative symptoms", schizophrenia, and the self. [References]. *International Journal of Psychology & Psychological Therapy*(2), 153-180.
Sass, L. A. (2003b). Self-disturbance in schizophrenia: Hyperreflexivity and diminished self-affection. [References]. In (pp. 242-271). (Reprinted from: Not in File).
Sass, L. A. (2014). Self-disturbance and schizophrenia: structure, specificity, pathogenesis (Current issues, New directions). *Schizophr Res, 152*(1), 5-11. doi:10.1016/j.schres.2013.05.017
Sass, L. A., & Borda, J. P. (2015). Phenomenology and neurobiology of self disorder in schizophrenia: Secondary factors. *Schizophr Res, 169*(1-3), 474-482. doi:10.1016/j.schres.2015.09.025
Sass, L. A., & Parnas, J. (2003). Schizophrenia, consciousness, and the self. *Schizophr.Bull., 29*(3), 427-444.
Scharfetter, C. (2008). Ego-fragmentation in schizophrenia: A severe dissociation of self-experience. In *Moskowitz, Andrew [Ed]; Schafer, Ingo [Ed]; Dorahy, Martin J [Ed] (2008) Psychosis, trauma and dissociation: Emerging perspectives on severe psychopathology (pp 51-64) xxi, 358 pp Wiley-Blackwell*.
Schlosser, D. A., Campellone, T. R., Biagianti, B., Delucchi, K. L., Gard, D. E., Fulford, D., . . . Vinogradov, S. (2015). Modeling the role of negative symptoms in determining social functioning in individuals at clinical high risk of psychosis. *Schizophrenia research, 169*(1-3), 204-208. doi:10.1016/j.schres.2015.10.036
Schlosser, D. A., Jacobson, S., Chen, Q., Sugar, C. A., Niendam, T. A., Li, G., . . . Cannon, T. D. (2012). Recovery from an at-risk state: clinical and functional outcomes of putatively prodromal youth who do not develop psychosis. *Schizophrenia bulletin, 38*(6), 1225-1233. doi:10.1093/schbul/sbr098
Schmidt, S. J., Schultze-Lutter, F., Schimmelmann, B. G., Maric, N. P., Salokangas, R. K., Riecher-Rossler, A., . . . Ruhrmann, S. (2015). EPA guidance on the early intervention in clinical high risk states of psychoses. *European Psychiatry, 30*(3), 388-404. doi:10.1016/j.eurpsy.2015.01.013

Schneider, K. (1959). *Clinical psychopathology. (Trans. by M. W. Hamilton), 5th ed*. Oxford, England: Grune & Stratton.
Schultze-Lutter, F. (2009). Subjective symptoms of schizophrenia in research and the clinic: the basic symptom concept. *Schizophr.Bull., 35*(1), 5-8. doi:sbn139 [pii];10.1093/schbul/sbn139 [doi]
Schultze-Lutter, F., Addington, J., Ruhrmann, S., & Klosterkotter, J. (2007). *Schizophrenia proneness instrument: Adult version (SPI-A)*. Roma: Giovanni Fioriti Editore.
Schultze-Lutter, F., Klosterkötter, J., Picker, H., Steinmeyer, E.-M., & Ruhrmann, S. (2007). Predicting first-episode psychosis by basic symptom criteria. *Clinical neuropsychiatry, 4*(1), 11-22.
Schultze-Lutter, F., Michel, C., Schmidt, S. J., Schimmelmann, B. G., Maric, N. P., Salokangas, R. K., . . . Klosterkotter, J. (2015). EPA guidance on the early detection of clinical high risk states of psychoses. *European Psychiatry, 30*(3), 405-416. doi:10.1016/j.eurpsy.2015.01.010
Schultze-Lutter, F., Ruhrmann, S., & Klosterkotter, J. (2006). Can schizophrenia be predicted phenomenologically? [References]. In J. O. Johannessen (Ed.), *Evolving psychosis* (pp. 104-123). New York, USA: Routledge/Taylor & Francis Group; US.
Selten, J. P., van der Ven, E., Rutten, B. P., & Cantor-Graae, E. (2013). The social defeat hypothesis of schizophrenia: an update. *Schizophr Bull, 39*(6), 1180-1186. doi:10.1093/schbul/sbt134
Seth, A. K., & Friston, K. J. (2016). Active interoceptive inference and the emotional brain. *Philosophical Transactions of the Royal Society of London. Series B: Biological Sciences, 371*(1708). doi:10.1098/rstb.2016.0007
Shepherd, A. M., Laurens, K. R., Matheson, S. L., Carr, V. J., & Green, M. J. (2012). Systematic meta-review and quality assessment of the structural brain alterations in schizophrenia. *Neuroscience and Biobehavioral Reviews, 36*(4), 1342-1356. doi:10.1016/j.neubiorev.2011.12.015
Sierra, M., & Berrios, G. E. (1998). Depersonalization: neurobiological perspectives. *Biological Psychiatry, 44*(9), 898-908.
Sierra, M., & Berrios, G. E. (2000). The Cambridge Depersonalization Scale: a new instrument for the measurement of depersonalization. *Psychiatry Res, 93*(2), 153-164.
Sierra, M., & David, A. S. (2011). Depersonalization: a selective impairment of self-awareness. *Consciousness and Cognition, 20*(1), 99-108. doi:10.1016/j.concog.2010.10.018
Sierra, M., Medford, N., Wyatt, G., & David, A. S. (2012). Depersonalization disorder and anxiety: a special relationship? *Psychiatry Res, 197*(1-2), 123-127. doi:10.1016/j.psychres.2011.12.017
Silverstein, S. M., & Keane, B. P. (2011). Perceptual organization impairment in schizophrenia and associated brain mechanisms: review of research from 2005 to 2010. *Schizophr Bull, 37*(4), 690-699. doi:10.1093/schbul/sbr052
Simeon, D., Gross, S., Guralnik, O., Stein, D. J., Schmeidler, J., & Hollander, E. (1997). Feeling unreal: 30 cases of DSM-III-R depersonalization disorder. *Am J Psychiatry, 154*(8), 1107-1113. doi:10.1176/ajp.154.8.1107
Simeon, D., Guralnik, O., Knutelska, M., & Nelson, D. (2004). Dissection of Schizotypy and Dissociation in Depersonalization Disorder. *Journal of trauma & dissociation, 5*(4), 111-119. doi:10.1300/J229v05n04_07
Simeon, D., & Hamilton, H. K. (2008). Depersonalization disorder and schizotypal personality disorder. In *Moskowitz, Andrew [Ed]; Schafer, Ingo [Ed]; Dorahy, Martin J [Ed] (2008) Psychosis, trauma and dissociation: Emerging perspectives on severe psychopathology (pp 209-220) xxi, 358 pp Wiley-Blackwell*.

Simeon, D., Knutelska, M., Nelson, D., & Guralnik, O. (2003). Feeling unreal: a depersonalization disorder update of 117 cases. *Journal of Clinical Psychiatry, 64*(9), 990-997.

Simeon, D., Kozin, D. S., Segal, K., & Lerch, B. (2009). Is depersonalization disorder initiated by illicit drug use any different? A survey of 394 adults. *Journal of Clinical Psychiatry, 70*(10), 1358-1364. doi:10.4088/JCP.08m04370

Simon, A. E., Borgwardt, S., Riecher-Rossler, A., Velthorst, E., de Haan, L., & Fusar-Poli, P. (2013). Moving beyond transition outcomes: meta-analysis of remission rates in individuals at high clinical risk for psychosis. *Psychiatry Res, 209*(3), 266-272. doi:10.1016/j.psychres.2013.03.004

Simons, H. (2009). *Case study research in practice*. Los Angeles: SAGE.

Škodlar, B., & Henriksen, M. G. (2019). Toward a Phenomenological Psychotherapy for Schizophrenia. *Psychopathology, 52*(2), 117-125. doi:10.1159/000500163

Skodlar, B., & Parnas, J. (2010). Self-disorder and subjective dimensions of suicidality in schizophrenia. *Compr.Psychiatry, 51*(4), 363-366. doi:S0010-440X(09)00136-9 [pii];10.1016/j.comppsych.2009.11.004 [doi]

Solmi, M., Radua, J., Olivola, M., Croce, E., Soardo, L., Salazar de Pablo, G., . . . Fusar-Poli, P. (2021). Age at onset of mental disorders worldwide: large-scale meta-analysis of 192 epidemiological studies. *Molecular Psychiatry*. doi:10.1038/s41380-021-01161-7

Stafford, M. R., Jackson, H., Mayo-Wilson, E., Morrison, A. P., & Kendall, T. (2013). Early interventions to prevent psychosis: systematic review and meta-analysis. *BMJ, 346*, f185. doi:10.1136/bmj.f185

Stanghellini, G. (2000). Vulnerability to schizophrenia and lack of common sense. *Schizophr.Bull., 26*(4), 775-787.

Stanghellini, G. (2009). Embodiment and schizophrenia. *World Psychiatry, 8*(1), 56-59.

Stanghellini, G., & Ballerini, M. (2011a). What is it like to be a person with schizophrenia in the social world? A first-person perspective study on Schizophrenic dissociality--part 1: state of the art. *Psychopathology, 44*(3), 172-182. doi:000322637 [pii];10.1159/000322637 [doi]

Stanghellini, G., & Ballerini, M. (2011b). What is it like to be a person with Schizophrenia in the social world? A first-person perspective study on Schizophrenic Dissociality--part 2: methodological issues and empirical findings. *Psychopathology, 44*(3), 183-192. doi:000322638 [pii];10.1159/000322638 [doi]

Stanghellini, G., & Lysaker, P. H. (2007). The psychotherapy of schizophrenia through the lens of phenomenology: intersubjectivity and the search for the recovery of first- and second-person awareness. *Am.J.Psychother., 61*(2), 163-179.

Stein, D. J., & Simeon, D. (2009). Cognitive-affective neuroscience of depersonalization. *CNS Spectr, 14*(9), 467-471.

Stern, D. N. (1985). *The interpersonal world of the infant : a view from psychoanalysis and developmental psychology*. New York: Basic Books.

Stilo, S. A., & Murray, R. M. (2019). Non-Genetic Factors in Schizophrenia. *Curr Psychiatry Rep, 21*(10), 100. doi:10.1007/s11920-019-1091-3

Strauss, G. P., & Cohen, A. S. (2017). A Transdiagnostic Review of Negative Symptom Phenomenology and Etiology. *Schizophr Bull, 43*(4), 712-719. doi:10.1093/schbul/sbx066

Strauss, G. P., Pelletier-Baldelli, A., Visser, K. F., Walker, E. F., & Mittal, V. A. (2020). A review of negative symptom assessment strategies in youth at clinical high-risk for psychosis. *Schizophrenia Research, 222*, 104-112. doi:https://doi.org/10.1016/j.schres.2020.04.019

Subotnik, K. L., & Nuechterlein, K. H. (1988). Prodromal signs and symptoms of schizophrenic relapse. *Journal of Abnormal Psychology, 97*(4), 405-412. doi:10.1037//0021-843x.97.4.405

Svendsen, I. H., Oie, M. G., Moller, P., Nelson, B., Haug, E., & Melle, I. (2019). Basic self-disturbances independently predict recovery in psychotic disorders: A seven year follow-up study. *Schizophr Res*. doi:10.1016/j.schres.2019.08.009

Svendsen, I. H., Oie, M. G., Moller, P., Nelson, B., Melle, I., & Haug, E. (2018). Stability in basic self-disturbances and diagnosis in a first treated psychosis: A seven year follow-up study. *Schizophr Res, 202*, 274-280. doi:10.1016/j.schres.2018.07.011

Süllwold, L., & Huber, G. (1986a). *Schizophrene Basisstörungen* (Vol. 42). Berlin, Heidelberg: Berlin, Heidelberg: Springer Berlin / Heidelberg.

SÜLlwold, L., & Huber, G. (1986b). Schizophrene Basisstörungen: frankfurter Beschwerde-Fragebogen. III. *Monographien aus dem Gesamtgebiete der Psychiatrie, 42*, 145-170.

Szily, E., & Keri, S. (2009). Anomalous subjective experience and psychosis risk in young depressed patients. *Psychopathology, 42*(4), 229-235. doi:000218520 [pii];10.1159/000218520 [doi]

Tanaka, S. (2018). What is it like to be disconnected from the body?: A phenomenological account of disembodiment in depersonalization/derealization disorder. *Journal of Consciousness Studies, 25*(5-6), 239-262.

Teicher, M. H., & Parigger, A. (2015). The 'Maltreatment and Abuse Chronology of Exposure' (MACE) scale for the retrospective assessment of abuse and neglect during development. *PloS One, 10*(2), e0117423-e0117423. doi:10.1371/journal.pone.0117423

Thompson, E., Millman, Z. B., Okuzawa, N., Mittal, V., DeVylder, J., Skadberg, T., . . . Schiffman, J. (2015). Evidence-based early interventions for individuals at clinical high risk for psychosis: a review of treatment components. *Journal of Nervous and Mental Disease, 203*(5), 342-351. doi:10.1097/nmd.0000000000000287

Thompson, K., & Chanen, A. (2019). The Age of Onset of Personality Disorders. In (pp. 183-201).

Tikka, M., Luutonen, S., Ilonen, T., Tuominen, L., Kotimäki, M., Hankala, J., & Salokangas, R. K. R. (2013). Childhood trauma and premorbid adjustment among individuals at clinical high risk for psychosis and normal control subjects: Childhood trauma and premorbid adjustment. *Early Intervention in Psychiatry, 7*(1), 51-57. doi:10.1111/j.1751-7893.2012.00391.x

Titchener, E. B. (1909). *A text-book of psychology : Pt. 1* (Rev. ed. ed. Vol. Pt. 1). New York: Macmillan.

Torbet, G., Schulze, D., Fiedler, A., & Reuter, B. (2015). Assessment of self-disorders in a non-clinical population: Reliability and association with schizotypy. *Psychiatry Res, 228*(3), 857-865. doi:10.1016/j.psychres.2015.05.011

Trotman, H. D., Holtzman, C. W., Walker, E. F., Addington, J. M., Bearden, C. E., Cadenhead, K. S., . . . McGlashan, T. H. (2014). Stress exposure and sensitivity in the clinical high-risk syndrome: initial findings from the North American Prodrome Longitudinal Study (NAPLS). *Schizophr Res, 160*(1-3), 104-109. doi:10.1016/j.schres.2014.09.017

Tschacher, W., Giersch, A., & Friston, K. (2017). Embodiment and Schizophrenia: A Review of Implications and Applications. *Schizophr Bull, 43*(4), 745-753. doi:10.1093/schbul/sbw220

Uhlhaas, P. J., & Silverstein, S. M. (2005). Perceptual organization in schizophrenia spectrum disorders: empirical research and theoretical implications. *Psychological Bulletin, 131*(4), 618-632. doi:10.1037/0033-2909.131.4.618

Valmaggia, L. R., Stahl, D., Yung, A. R., Nelson, B., Fusar-Poli, P., McGorry, P. D., & McGuire, P. K. (2013). Negative psychotic symptoms and impaired role functioning predict transition outcomes in the at-risk mental state: a latent class cluster analysis study. *Psychological medicine, 43*(11), 2311-2325. doi:10.1017/S0033291713000251

van der Gaag, M., Smit, F., Bechdolf, A., French, P., Linszen, D. H., Yung, A. R., . . . Cuijpers, P. (2013). Preventing a first episode of psychosis: meta-analysis of randomized controlled prevention trials of 12 month and longer-term follow-ups. *Schizophr Res, 149*(1-3), 56-62. doi:10.1016/j.schres.2013.07.004

van Huijstee, J., & Vermetten, E. (2018). The Dissociative Subtype of Post-traumatic Stress Disorder: Research Update on Clinical and Neurobiological Features. *Current Topics in Behavioral Neurosciences, 38*, 229-248. doi:10.1007/7854_2017_33

van Os, J., & Guloksuz, S. (2017). A critique of the "ultra-high risk" and "transition" paradigm. *World Psychiatry, 16*(2), 200-206. doi:10.1002/wps.20423

van Os, J., & Linscott, R. J. (2012). Introduction: The extended psychosis phenotype--relationship with schizophrenia and with ultrahigh risk status for psychosis. *Schizophr Bull, 38*(2), 227-230. doi:10.1093/schbul/sbr188

van Os, J., Linscott, R. J., Myin-Germeys, I., Delespaul, P., & Krabbendam, L. (2009). A systematic review and meta-analysis of the psychosis continuum: evidence for a psychosis proneness-persistence-impairment model of psychotic disorder. *Psychol Med, 39*(2), 179-195. doi:10.1017/s0033291708003814

van Os, J., Pries, L. K., Ten Have, M., de Graaf, R., van Dorsselaer, S., Delespaul, P., . . . Guloksuz, S. (2020). Evidence, and replication thereof, that molecular-genetic and environmental risks for psychosis impact through an affective pathway. *Psychol Med*, 1-13. doi:10.1017/s0033291720003748

Varese, F., Smeets, F., Drukker, M., Lieverse, R., Lataster, T., Viechtbauer, W., . . . Bentall, R. P. (2012). Childhood adversities increase the risk of psychosis: a meta-analysis of patient-control, prospective- and cross-sectional cohort studies. *Schizophr Bull, 38*(4), 661-671. doi:10.1093/schbul/sbs050

Varghese, D., Scott, J., Welham, J., Bor, W., Najman, J., O'Callaghan, M., . . . McGrath, J. (2011). Psychotic-like experiences in major depression and anxiety disorders: a population-based survey in young adults. *Schizophr Bull, 37*(2), 389-393. doi:10.1093/schbul/sbp083

Velthorst, E., Nieman, D. H., Becker, H. E., van de, F. R., Dingemans, P. M., Klaassen, R., . . . Linszen, D. H. (2009). Baseline differences in clinical symptomatology between ultra high risk subjects with and without a transition to psychosis. *Schizophr.Res., 109*(1-3), 60-65. doi:S0920-9964(09)00068-1 [pii];10.1016/j.schres.2009.02.002 [doi]

Vollmer-Larsen, A., Handest, P., & Parnas, J. (2007). Reliability of measuring anomalous experience: the Bonn Scale for the Assessment of Basic Symptoms. *Psychopathology, 40*(5), 345-348. doi:000106311 [pii];10.1159/000106311 [doi]

Waszczuk, M. A., Eaton, N. R., Krueger, R. F., Shackman, A. J., Waldman, I. D., Zald, D. H., . . . Kotov, R. (2020). Redefining phenotypes to advance psychiatric genetics: Implications from hierarchical taxonomy of psychopathology. *Journal of Abnormal Psychology, 129*(2), 143-161. doi:10.1037/abn0000486

Werbeloff, N., Drukker, M., Dohrenwend, B. P., Levav, I., Yoffe, R., van Os, J., . . . Weiser, M. (2012). Self-reported attenuated psychotic symptoms as forerunners of severe mental disorders later in life. *Archives of general psychiatry, 69*(5), 467. doi:10.1001/archgenpsychiatry.2011.1580

Wiberg, M., & Sundstrom, A. (2009). A Comparison of Two Approaches to Correction of Restriction of Range in Correlation Analysis. *Practical Assessment, Research & Evaluation, 14*(5), 1-9.

Wiltink, S., Velthorst, E., Nelson, B., McGorry, P. M., & Yung, A. R. (2015). Declining transition rates to psychosis: the contribution of potential changes in referral pathways to an ultra-high-risk service. *Early Interv Psychiatry, 9*(3), 200-206. doi:10.1111/eip.12105

Woodberry, K. A., Shapiro, D. I., Bryant, C., & Seidman, L. J. (2016). Progress and Future Directions in Research on the Psychosis Prodrome: A Review for Clinicians. *Harvard Review of Psychiatry, 24*(2), 87-103. doi:10.1097/hrp.0000000000000109

Woods, S. W., Addington, J., Cadenhead, K. S., Cannon, T. D., Cornblatt, B. A., Heinssen, R., . . . McGlashan, T. H. (2009). Validity of the prodromal risk syndrome for first psychosis: findings from the North American Prodrome Longitudinal Study. *Schizophr.Bull., 35*(5), 894-908. doi:sbp027 [pii];10.1093/schbul/sbp027 [doi]

Woods, S. W., Walsh, B. C., Addington, J., Cadenhead, K. S., Cannon, T. D., Cornblatt, B. A., . . . McGlashan, T. H. (2014). Current status specifiers for patients at clinical high risk for psychosis. *Schizophr Res, 158*(1-3), 69-75. doi:10.1016/j.schres.2014.06.022

Wright, A. C., Browne, J., Skiest, H., Bhiku, K., Baker, J. T., & Cather, C. (2021). The relationship between conventional clinical assessments and momentary assessments of symptoms and functioning in schizophrenia spectrum disorders: A systematic review. *Schizophr Res, 232*, 11-27. doi:10.1016/j.schres.2021.04.010

Yang, L. H., Link, B. G., Ben-David, S., Gill, K. E., Girgis, R. R., Brucato, G., . . . Corcoran, C. M. (2015). Stigma related to labels and symptoms in individuals at clinical high-risk for psychosis. *Schizophr Res, 168*(1-2), 9-15. doi:10.1016/j.schres.2015.08.004

Yung, A. R., & McGorry, P. D. (1996). The prodromal phase of first-episode psychosis: past and current conceptualizations. *Schizophr Bull, 22*(2), 353-370. doi:10.1093/schbul/22.2.353

Yung, A. R., McGorry, P. D., McFarlane, C. A., Jackson, H. J., Patton, G. C., & Rakkar, A. (1996). Monitoring and care of young people at incipient risk of psychosis. *Schizophr Bull, 22*(2), 283-303. doi:10.1093/schbul/22.2.283

Yung, A. R., Nelson, B., McGorry, P. D., Wood, S. J., & Lin, A. (2018). Persistent negative symptoms in individuals at Ultra High Risk for psychosis. *Schizophr Res*. doi:10.1016/j.schres.2018.10.019

Yung, A. R., Nelson, B., Thompson, A. D., & Wood, S. J. (2010). Should a "Risk Syndrome for Psychosis" be included in the DSMV? *Schizophr.Res.* doi:S0920-9964(10)01187-4 [pii];10.1016/j.schres.2010.03.017 [doi]

Yung, A. R., Phillips, L. J., Yuen, H. P., Francey, S. M., McFarlane, C. A., Hallgren, M., & McGorry, P. D. (2003). Psychosis prediction: 12-month follow up of a high-risk ("prodromal") group. *Schizophr.Res., 60*(1), 21-32. doi:S0920996402001676 [pii]

Yung, A. R., Phillips, L. J., Yuen, H. P., & McGorry, P. D. (2004). Risk factors for psychosis in an ultra high-risk group: psychopathology and clinical features. *Schizophr.Res., 67*(2-3), 131-142. doi:10.1016/S0920-9964(03)00192-0 [doi];S0920996403001920 [pii]

Yung, A. R., Wood, S. J., Malla, A., Nelson, B., McGorry, P., & Shah, J. (2019). The reality of at risk mental state services: a response to recent criticisms. *Psychol Med*, 1-7. doi:10.1017/s003329171900299x

Yung, A. R., Yuen, H. P., McGorry, P. D., Phillips, L. J., Kelly, D., Dell'Olio, M., . . . Buckby, J. (2005). Mapping the onset of psychosis: the Comprehensive Assessment of At-Risk Mental States. *Aust.N.Z.J.Psychiatry, 39*(11-12), 964-971. doi:ANP1714 [pii];10.1111/j.1440-1614.2005.01714.x [doi]

Zhang, T., Tang, X., Li, H., Woodberry, K. A., Kline, E. R., Xu, L., . . . Wang, J. (2020). Clinical subtypes that predict conversion to psychosis: A canonical correlation

analysis study from the ShangHai At Risk for Psychosis program. *Aust N Z J Psychiatry, 54*(5), 482-495. doi:10.1177/0004867419872248

Errata

The printed edition of this thesis is a reprint of the originally submitted thesis to the University of Oslo, October 2021. The printed version is identical to the original version except for the following changes:

Page	*Line*	*Original text*	*Corrected text*
12	11	Ultra-high risk	Ultra-High Risk
13	4	1. **INTRODUCTION**	**1. INTRODUCTION** (text moved to the left)
15	1	«basic symptoms»	'basic symptoms'
17	17-18	'Basic symptoms'	'basic symptoms'
18	27	Psychosis-Risk Symptoms	Psychosis-risk Symptoms
40	12-13	… based on the EASE (Inventory of Psychotic-Like Anomalous Self-Experiences (, psychotic-like experiences and psychosis proneness…	… based on the EASE: Inventory of Psychotic-like Anomalous Self-Experiences (IPASE)), were associated with psychotic-like experiences and psychosis proneness …
43	17	*"prediction error"*	*'prediction error'*
46	1	**2 AIMS**	**2. AIMS**
47	1	**3 METHODS**	**3. METHODS**
48	18	c linical	clinical
49	19	"non-progressive symptoms group"	'non-progressive symptoms group'
56	2-3	short form	Short Form
56	33	(CDSS)(D. Addington ...	(CDSS) (D. Addington …
57	28	… illness discomfort …	… illness, discomfort …
60	1	**4 RESULTS/SUMMARY OF PAPERS**	**4. RESULTS/SUMMARY OF PAPERS**
65	1	**5 DISCUSSION**	**5. DISCUSSION**
67	22-23	… with stable or a small decline in EASE levels …	… with stable EASE levels or a small decline in these levels …
70	32	include	includes
74	8	... study of non-clinical sample …	… study of a non-clinical sample …
77	3-5	The findings in our study II, studies by Sass and colleagues on published descriptions of depersonalization (L. Sass, Pienkos, Nelson, et al., 2013), intense introspection cases (L. Sass, Pienkos, & Nelson, 2013), and a study in a sample …	The findings in our study II, and in the studies by Sass and colleagues on published descriptions of depersonalization (L. Sass, Pienkos, Nelson, et al., 2013) and intense introspection cases (L. Sass, Pienkos, & Nelson, 2013), and in a panic disorder sample …
77	12	… differences, at the …	… differences at the …
77	16	… e.g. sense of …	… e.g. a sense of …

77	24-25	… spectrum is generally more *state-like*… drug use, physiological or somatic conditions …	… spectrum are generally more *state-like*… drug use or physiological/somatic conditions …
89	11	… SIPS interviews, and symptom descriptions …	… SIPS interviews and symptom descriptions …
89	28	br ief	brief
92	17	An example from study II is the descriptions…	An example from study II are the descriptions…
98	1	**6 Conclusion**	**6. CONCLUSION**
101	1	**7. References**	**7. REFERENCES**

I

Comprehensive Psychiatry 93 (2019) 65–72

Contents lists available at ScienceDirect

Comprehensive Psychiatry

journal homepage: www.elsevier.com/locate/comppsych

Anomalous self-experiences are strongly associated with negative symptoms in a clinical high-risk for psychosis sample

Tor Gunnar Værnes [a,b,*], Jan Ivar Røssberg [c], Paul Møller [d]

[a] Early Intervention in Psychosis Advisory Unit for South-East Norway, TIPS Sør-Øst, Division of Mental Health and Addiction, Oslo University Hospital, Oslo, Norway.
[b] NORMENT, Norwegian Centre for Mental Disorders Research, University of Oslo, Norway.
[c] Division of Psychiatric Treatment Research, Oslo University Hospital and Institute of Clinical Medicine, University of Oslo, Norway
[d] Dept. for Mental Health Research and Development, Division of Mental Health and Addiction, Vestre Viken Hospital Trust, Norway.

ARTICLE INFO

Available online xxxx

Keywords:
Basic self-disturbance
anomalous self-experiences
clinical high-risk for psychosis
schizophrenia spectrum disorders
negative symptoms
cognitive disturbances

ABSTRACT

Objective: Anomalous self-experiences (ASE) are considered as central features of the schizophrenia spectrum disorders and prodromal schizophrenia. We investigated total and single-item prevalence of these phenomena in a clinical high-risk (CHR) for psychosis sample, and associations with conventional psychosis-risk symptoms, present and childhood global/psychosocial functioning, and childhood trauma.
Methods: The sample ($n = 38$) included 31 CHR, according to ultra-high risk or cognitive basic symptoms (COGDIS) criteria, and seven with non-progressive attenuated positive symptoms. Psychopathological evaluations included the Examination of Anomalous Self-Experience (EASE), Structured Clinical Interview for Prodromal Syndromes (SIPS), Schizophrenia Proneness Instrument – Adult (SPI-A) (only the COGDIS-criteria), a diagnostic interview (SCID-I), Global Assessment of Functioning – Split version (S-GAF), Premorbid Adjustment Scale (PAS) and Childhood Trauma Questionnaire (CTQ).
Results: The mean total EASE score was in line with reports from other CHR samples, and was particularly enhanced in schizotypal personality disorder and in subjects fulfilling COGDIS-criteria. The four most frequent EASE-items were present in two-thirds or more of the participants. EASE total was significantly associated with negative and disorganization symptoms. A multiple regression analysis revealed that the level of negative symptoms explained most of the variance in EASE total.
Conclusions: These results corroborates other findings that anomalous self-experiences are frequent and important features in CHR conditions and in the schizophrenia spectrum. The strong associations with negative symptoms and cognitive disturbances (COGDIS) should be investigated in longitudinal studies to address causality, psychopathological pathways and schizophrenia spectrum specificity. The weaker correlation between EASE total and positive symptoms may partly be related to a restricted range of positive symptoms.
© 2019 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

1. Introduction

Phenomenologically oriented perspectives focusing on characteristic subjective aspects of signs and symptoms have enriched our understanding of the psychopathology of schizophrenia spectrum disorders and prodromal conditions [1]. After the contemporary reintroduction of this perspective [2,3], a model was introduced claiming that the core pathogenic feature of schizophrenia is a self-disorder marked by structural distortions of subjectivity ("ipseity") and consciousness [4]. This self-disorder is also termed an *ipseity disturbance* or *basic self-disturbance* (BSD), and involves and articulates a range of mutually implicative *anomalous self-experiences* (ASE). These include a diminished sense of presence and existence, hyperreflexivity, diminished sense of agency and ownership to experiences and actions, feelings of unreality, and severe "common sense" disturbances [4,5]. This basic self-disturbance may further constitute a core psychopathological drive for the development of a full "Gestalt", comprising both positive, negative and disorganization symptoms in the schizophrenia spectrum and in prodromal states [4,6–8].

A semi-structured interview, the Examination of Anomalous Self-Experience (EASE), aims to specifically and comprehensively assess aspects of this self-disorder. Using EASE and related instruments, it has been demonstrated that ASE aggregate in the schizophrenia spectrum, including schizotypal and prodromal conditions [2,3,9–18], are frequent in clinical high-risk (CHR) states for psychosis, and predict conversion to schizophrenia spectrum disorders [19–24]. The CHR construct includes both "ultra-high risk" states and states characterized by "basic symptoms" high-risk criteria [25]. Basic self-disturbance has thus been

* Corresponding author at: Oslo University Hospital, Division of Mental Health and Addiction, TIPS Sør-Øst, Postbox 4956, Nydalen, 0424 Oslo, Norway.
E-mail address: uxvrnt@ous-hf.no (T.G. Værnes).

https://doi.org/10.1016/j.comppsych.2019.07.003
0010-440X/© 2019 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

suggested as a strong phenotypic trait marker of vulnerability for schizophrenia spectrum disorders [20,22,26].

Although there is considerable support for this phenotypic marker, the evidence from CHR studies needs to be expanded. Assessing the total prevalence of ASE, as well as the relative occurrence of specific ASE phenomena (single EASE-items) in CHR, may add to the evidence base regarding the early development and aggregation of these phenomena in CHR, and contribute to refine the methods for clinical risk assessment. To our knowledge, only one CHR study, with a small sample size ($n = 11$), have investigated and reported the occurrence of specific ASE [19], and further studies are needed.

There are also still few studies which have examined the relationships between ASE and symptoms/functioning in CHR. Raballo and co-workers found significant associations between the presence of such experiences and attenuated positive symptoms, as well as with cognitive or cognitive-perceptive basic symptoms. However, they did not examine the relationship between ASE and negative or other symptoms [21]. Koren and co-workers found significant associations between ASE and positive, negative and disorganization symptoms, but no correlation with a non-specific symptom scale, in a sample of 82 help-seeking adolescents. Correlations were not reported for the 24 CHR subjects in this sample [23]. A study by Comparelli and co-workers showed a significant correlation between ASE and global functioning in a group of 45 CHR subjects, as did the study by Raballo and co-workers [21,24]. However, the Comparelli study did not find significant correlations with positive, negative, disorganization and general symptoms (after Bonferroni correction). Koren's group found that social functioning, but not role functioning, was significantly more impaired in a combined "CHR and ASE syndrome" group than in a group assessed as not at risk, while a study by Nelson and co-workers did not find an association between total level of self-disturbances and psychosocial functioning in CHR [20,23]. To sum up, there is a lack of clarity about the relationship between ASE and different variants of symptom and functioning measures in CHR.

To increase our psychopathological understanding of self-disorders in the broad and diverse field of CHR conditions, there is also a need to investigate the role of background factors like childhood trauma and psychosocial functioning during childhood. Significant associations have been found between traumatic life events and ASE in a first episode schizophrenia sample (only females) [27], and in three studies on non-clinical samples [28–30], but this is not explored in CHR-studies. Associations between ASE and early psychosocial functioning are to our knowledge not examined in previous studies neither in CHR nor in other mental disorders and conditions.

In light of the lack of clarity of the relationships between ASE, other clinical characteristics and background factors in CHR, we set up a study to:

1. Investigate the total level of ASE, as well as the *relative occurrence of single EASE items*, in CHR and some intimately related conditions (with non-progressive attenuated psychotic symptoms).

2. Investigate in these conditions the associations between ASE and clinical characteristics (i.e. positive, negative, disorganization and general symptoms, and global functioning), and background factors (i.e. childhood trauma and psychosocial functioning during childhood).

2. Methods

2.1. Participants

The current study is part of the Norwegian Thematically Organized Psychosis (TOP) study, and was approved by a Regional Committee for Medical Research Ethics in Norway. The main target group was subjects between 15 and 30 years fulfilling CHR criteria. However, we also included subjects in the same age range with long-standing, non-progressive attenuated positive symptoms, i.e. not fulfilling CHR criteria with respect to a recent onset or progression [31]. Exclusion criteria were: present or previous psychotic disorder according to DSM-IV Axis I criteria (schizophrenia and other psychotic disorders), antipsychotic treatment (current or for ≥4 weeks lifetime, equivalent to a dose of ≥5 mg Olanzapin per day), organic cause for presentation, intellectual disability (IQ < 70), clearly substance-induced CHR-symptoms, and inability to speak Norwegian. Other non-psychotic comorbid DSM-IV disorders were not exclusionary, and some individuals had more than one diagnosis.

The sample was recruited from adult and child/adolescent outpatient clinics at Oslo University Hospital, Vestre Viken Hospital Trust and Akershus University Hospital. The participants were consecutively recruited from June 2012 to December 2015. The final sample comprised 38 patients.

2.2. Procedure and measures

Clinicians at the recruitment facilities were encouraged to refer patients to the study if they clinically suspected risk of psychosis. At first meeting, the patients were given information about the study, and a preliminary clinical screening was conducted. The patients participated in the study on the condition of an informed written consent (for 12 patients below 18 years the parents consented as well). The screening and all the clinical interviews were conducted by the first author, TGV. Interviews with the Structured Interview for Prodromal Syndromes (SIPS) [32,33] and the Examination of Anomalous Self-Experience (EASE) [34] were videotaped.

2.2.1. Clinical high-risk according to Criteria of Prodromal Syndromes

The SIPS was used to decide inclusion in the study, by formally assessing CHR status, as well as present or previous psychosis. The main target group was patients fulfilling the Criteria of Prodromal Syndromes in the SIPS. These criteria comprise three categories: 1) Attenuated Positive Symptom syndrome (APS), i.e. sub-threshold positive symptoms with onset or worsening of symptoms last year, 2) Brief Intermittent Psychotic Symptom syndrome (BIPS), i.e. recent, short lasting, spontaneously remitting episodes of psychotic symptoms, and 3) Genetic Risk and Deterioration syndrome (GRD), i.e. significant decline in functioning last year combined with schizotypal personality disorder or having a first-degree relative with psychotic disorder [32].

Additionally we included patients presenting with longstanding, non-progressive attenuated positive symptoms (a score from 3 to 5 on one or more positive symptoms on the Scale of Prodromal Symptoms (SOPS), with an onset more than one year ago and no worsening of these symptoms the last year). We included this group, to reflect 1) the very close phenomenological resemblance to the CHR group fulfilling the high-risk criteria in the SIPS, and 2) the naturalistic referencing in our study, to specialized outpatient units on the basis of a clinical suspicion of high risk for psychosis. TGV has been trained for SIPS by attending a course led by a Norwegian SIPS expert, TK Larsen. To establish inter-rater reliability, TGV scored nine SIPS case vignettes from the North American Prodrome Longitudinal Study (NAPLS) study [67], and compared these to the final scores from the NAPLS raters. The CHR-status agreement between TGV and these raters was 100%. Excellent reliability was found also with respect to the scores of positive symptoms. The single measure ICC was 0.95 with a 95% confidence interval from 0.82 to 0.99 (two-way mixed effects model, absolute agreement, calculated by SPSS version 25).

2.2.2. Assessment of severity of psychosis-risk symptoms

The Scale of Prodromal Symptoms (SOPS) was used to assess the severity of symptoms in four continuous subscales: *positive* (five symptoms), *negative* (six symptoms), *disorganization* (four symptoms) and *general* (four symptoms), ranging from 0 (= absent) to 6 (= psychotic/extreme) for each symptom. General symptoms include sleep disturbances, dysphoric mood, motor disturbances and impaired tolerance to normal stress. Level of severity of positive, negative, disorganization and

general symptoms was measured by summing the item scores in each subscale.

2.2.3. Assessment of anomalous self-experiences

Following SIPS, the patients were assessed for ASE with the Examination of Anomalous Self-Experience (EASE). The EASE is a symptom checklist for semi-structured phenomenological exploration of experiential anomalies, organized in the domains of disturbed stream of consciousness, self-awareness and presence, corporeality, self-demarcation and existential reorientation [34]. The EASE-items were scored according to a continuous 0–4 Likert scale, and later converted into dichotomous scores (1 = definitely present, all severity levels, and 0 = absent or questionably present). TGV has been trained by one of the authors of EASE, PM, and is a certified EASE rater. To investigate interrater reliability, he scored nine videotaped EASE-interviews from a study by Haug et al. [14] and compared EASE total scores to the scores of two raters: Haug and PM. Single measures ICC was 0.62 with a 95% confidence interval from 0.24 to 0.88, which indicated moderate reliability (two-way mixed effects model, absolute agreement) [35].

2.2.4. Clinical high-risk according to cognitive basic symptoms high-risk criteria

CHR status based on the criteria in the SIPS was supplemented with the cognitive basic symptoms criteria (COGDIS), as described in the Schizophrenia Proneness Instrument – Adult Version (SPI-A) [36]. The EASE was used as a proxy tool to explore the presence and severity of these criteria, however adhering strictly to the SPI-A descriptions. Seven of the nine symptoms comprising the COGDIS criteria overlap considerably with descriptions of EASE-items (EASE-items 1.1, 1.3, 1.4, 1.12.1, 1.12.2, 1.17 and 5.1) [34,36]. The two remaining symptoms (disturbance of receptive speech, disturbance of abstract thinking) were explored both as a part of SIPS/SOPS (particularly P5 Conceptual Disorganization and N5 Decreased Ideational Richness) and the EASE (particularly 2.12 Loss of Common Sense/Perplexity/Lack of Natural Evidence).

2.2.5. Diagnoses and present global functioning

Diagnoses were established using a full version of the Structured Clinical Interview for DSM-IV-Axis I disorders: SCID-I [37]. During the assessment period, TGV discussed diagnoses on a regular basis with PM and JIR, two experienced psychiatrists and researchers. TGV has attended the TOP study SCID-I training and reliability program. The SIPS checklist was applied for the DSM-IV diagnosis Schizotypal Personality Disorder. Present global functioning was assessed with Global Assessment of Functioning - Split version (S-GAF); a scale divided into a symptom and a function score, ranging from 0 (severe symptoms and dysfunction) to 100 (no symptoms, superior functioning) [38].

2.2.6. Childhood trauma and early psychosocial functioning

Childhood trauma was assessed using a Norwegian version of the Childhood Trauma Questionnaire, short form (CTQ-SF), which is a self-report inventory covering experiences of maltreatment before the age of 18 [39]. It comprises 28 items, yielding scores on 5 subscales of trauma: physical abuse, sexual abuse, emotional abuse, emotional neglect, and physical neglect [40]. Psychosocial functioning during childhood was assessed using the Premorbid Adjustment Scale (PAS), based on semi-structured interviews with the participants [41]. We used the childhood (0–11 years) scores from four domains (sociability and withdrawal, peer relationships, scholastic performance and adaption to school) in the analyses of this study.

2.3. Statistical analyses

All analyses were performed with the statistical package SPSS, version 25.0. All analyses including EASE total scores were based on the sum of dichotomous EASE scores on all the main items, sub-items excluded. Differences in total or subscale EASE, SOPS, GAF, CTQ and PAS scores between subgroups in the sample were analyzed using an independent samples *t*-test or the non-parametric alternative: the Mann-Whitney *U* test. Bivariate associations between EASE and continuous psychopathological variables were analyzed, either using Pearson correlation coefficient for normally distributed scores or Spearman rho correlation coefficient for scores on variables not normally distributed. Due to the restriction of range of SOPS positive symptoms in the included participants, the correlation with EASE total is expected to be an underestimation of the correlation in the help-seeking population in general [42]. We corrected for multiple comparisons, using Bonferroni adjustments, i.e. with a *p*-value of 0.004 as the level of statistical significance (calculated on the basis of comparisons with thirteen variables, 0.05/13 = 0.004). However, due to the exploratory nature of the study, we also report results significant according to nominal *p*-values ($p < .05$), and performed a standard linear multiple regression analysis based on these results. This regression analysis included EASE total as the dependent variable and four variables showing nominally significant associations with EASE total ($p < .05$, $r = 0.31$ to 0.66, medium to large effect sizes) in the bivariate correlation analyses as independent variables. Preliminary analyses were conducted to ensure no violations of normality, linearity, multicollinearity and homoscedasticity. The purpose of the regression analysis was to investigate the variance and predictive values of each of the independent variables included in the model.

3. Results

3.1. Risk criteria, demographics and clinical characteristics

The sample ($n = 38$) consisted of 31 subjects fulfilling CHR-criteria and seven defined as non-progressive attenuated positive symptom subjects. Among the 31 CHR subjects, 28 fulfilled criteria for an Attenuated Positive Symptom syndrome (APS), and three fulfilled the COGDIS-criteria only. Ten of the 28 APS subjects fulfilled COGDIS-criteria too, and one simultaneously fulfilled the Genetic Risk and Deterioration syndrome (GRD) criteria.

Table 1 presents demographic characteristics and primary diagnoses, EASE total, SOPS subscale and S-GAF scores for the 31 CHR and the 7 subjects with non-progressive positive symptoms subjects separately, and for all 38 combined. In addition to the sum of dichotomous EASE scores, we also presents the sum of EASE Likert scale scores (0–4) in Table 1, in order to compare the results with two other CHR-studies only reporting the sum of the EASE Likert scale scores [20,24]. Not unexpectedly, the CHR group was significantly younger than the non-progressive positive symptoms group, but did not differ significantly regarding years of education. The most common primary clinical diagnoses in the total sample were mood disorders (40%), followed by anxiety disorders (24%).

3.1.1. Total level of ASE (mean EASE total score)

In the full sample ($n = 38$), the mean EASE total score (sum of dichotomized scores) was 15.45 ± 8.31, and not significantly associated with any of the demographic variables (age, gender, country of birth, years of education, currently employed/at school, civil status). There were no significant differences between the CHR and the non-progressive positive symptoms group in EASE total scores (CHR: 15.65 ± 8.91, non-progressive: 14.57 ± 5.32; t (36) = −0.42, $p = .68$). With respect to DSM-IV diagnoses, schizotypal personality disorder was associated with the highest EASE total score ($n = 6$, mean EASE total: 22.00 ± 3.41), significantly and considerably higher than the remaining sample ($n = 32$, mean EASE total: 14.22 ± 8.40; t (36) = −3.82, $p = .001$).

In the CHR-group ($n = 31$), subjects fulfilling COGDIS criteria ($n = 13$) had significantly higher levels of EASE total scores (20.85 ± 8.05) compared to subjects not fulfilling these criteria ($n = 18$, EASE total: 11.89 ± 7.65, t (29) = 3.15, $p = .004$). The mean difference in EASE

Table 1
Sample demographics, diagnoses, SOPS subscale, EASE total and S-GAF scores.

	Total sample	CHR	Non-progressive symptoms
Number of patients	38	31	7
Demographics			
Mean age (years ± SD)	19.8 ± 3.4	19.0 ± 3.3	23.1 ± 3.7
Gender, Male, n (%)	24 (63)	18 (58)	6 (86)
Born in Norway, n (%)	34 (90)	27 (87)	7 (100)
Employed or studying, n (%)	20 (53)	17 (55)	3 (43)
Total years education	11.6	11.4	12.6
Married or cohabitant, n (%)	2 (5)	2 (6)	0 (0)
Diagnoses, n (%)			
Mood disorders	15 (40)	13 (42)	2 (29)
Anxiety disorders	9 (24)	7 (23)	2 (29)
Other Axis I disorders[a]	6 (16)	4 (13)	2 (29)
Schizotypal pers. dis.	6 (16)	5 (16)	1 (14)
No DSM-IV-TR diagnosis	2 (5)	2 (7)	0 (0)
EASE total score, dichotomized, mean ± SD	15.45 ± 8.31	15.65 ± 8.90	14.57 ± 5.32
EASE total score, Likert scale, mean ± SD	50.84 ± 26.91	52.00 ± 29.00	45.71 ± 14.96
SOPS positive, mean ± SD	10.13 ± 3.50	10.55 ± 3.61	8.29 ± 2.36
SOPS negative, mean ± SD	12.95 ± 6.92	13.00 ± 6.95	12.71 ± 7.30
SOPS disorg., mean ± SD	6.92 ± 3.27	6.94 ± 3.37	6.86 ± 3.02
SOPS general, mean ± SD	8.00 ± 3.47	8.16 ± 3.34	7.29 ± 4.23
GAF Split version, mean ± SD			
GAF symptom	52.79 ± 10.04	52.00 ± 12.56	56.06 ± 9.48
GAF function	55.76 ± 11.03	55.45 ± 10.96	57.14 ± 12.10

[a] Other Axis 1 disorders include Cannabis dependence (1), Dissociative disorder NOS (1) and Depersonalization disorder (4).

total score between the two groups was 8.96 (95% *CI*: 3.14–14.78, eta squared = 0.25). Even if removing the EASE-items directly overlapping with COGDIS-items, a marked effect remained, though somewhat smaller (t (29) = 2.34, $p = .026$, eta squared = 0.16).

3.2. The relative occurrence of single EASE items

Table 2 presents the 11 most frequent baseline EASE-items in the total sample, those present in >45% of the participants (45–82%). In the CHR group only ($N = 31$), exactly the same items were the most frequent. Although present in all subjects, item 2.13 Anxiety is not included in the table because it is a non-specific symptom, more loosely associated with the concept of basic self-disturbance. The four most frequent items were ruminations/obsessions (1.6), distorted first-person perspective (2.2), diminished presence (2.4), and derealization (2.5), each reported by 66–82% of the participants.

3.3. Associations between ASE, clinical characteristics and background factors

Scores on SOPS subscales, S-GAF, CTQ and PAS did not differ significantly between the CHR group and the non-progressive positive symptoms group. Hence, we present pairwise correlations between EASE total scores and these variables for the full sample. Higher EASE total scores were associated ($p < .05$) with higher SOPS positive (r = 0.31), SOPS negative (r = 0.66) and SOPS disorganization (r = 0.54) scores, as well as with a higher score on the CTQ subscale Emotional neglect ($r = 0.43$). After Bonferroni-correction ($p < .004$) only the association between EASE total and SOPS negative, and between EASE total and SOPS disorganization scores, retained statistical significance (Table 3). Neither present functioning (S-GAF) nor childhood functioning scores (PAS; 0–11 years) were significantly associated with EASE total. We were also interested in the same correlations, but limited to the 11 most frequent EASE items (listed in Table 2). Using the Bonferroni-adjusted *p*-value, the total score on "EASE Top11" was also significantly correlated with SOPS negative (r = 0.49, $p < .004$), but not with the other variables (Table 3).

Table 2
Top 11 EASE-items (present in ≥45% of the total sample, $n = 38$). Anxiety (2.13) excluded.

EASE-items	Item present, number of participants (%)
1.6 Ruminations, obsessions	31 (82)
2.2 Distorted first-person perspective	26 (68)
2.4 Diminished presence	25 (66)
2.5 Derealization	25 (66)
1.3 Thought pressure	23 (61)
2.1 Diminished sense of basic self	19 (50)
1.1 Thought interference	18 (47)
1.10 Inability to discriminate modalities of experience	18 (47)
2.6 Hyperreflectivity	18 (47)
3.7 Cenesthetic experiences	18 (47)
5.5 World feels as if not truly real	17 (45)

3.3.1. The strongest loadings on EASE

A standard multiple regression analysis was performed with EASE total as the dependent variable, and four variables significantly associated with EASE total, according to the nominal p-value ($p < .05$), as the independent variables, i.e. SOPS positive, SOPS negative, SOPS disorganization and CTQ Emotional Neglect. The total variance of the model including these variables explained 47.4% of the variance in the EASE total score (adjusted R Square). Only SOPS negative explained a significant amount of the variance in the model (beta = 0.701, $p < .01$).

To address the potential problem of spurious correlations, we repeated the correlation analysis regarding the association between SOPS negative and EASE total, removing certain overlapping symptoms and items from this analysis. This association however remained strong ($r = 0.58$, $p < .001$) even if we removed four EASE-items (1.11, 2.16, 2.17, 2.18) resembling the description of certain SOPS negative symptoms (particularly N1, N2 and N4) from the correlation analysis, as well as the one negative SOPS symptom which seemed to resemble the EASE descriptions of self-disturbances the most: N4 Experience of Emotions and Self (e.g. including loss of sense of self).

4. Discussion

In the present study, the mean EASE total score was in line with reports from other CHR samples [20,21,24]. The level was particularly enhanced in subjects fulfilling schizotypal personality disorder criteria and COGDIS criteria. The 11 most frequent items were present in >45% of the participants, including top four items, present in 66 to 82% of the participants. A multiple regression analysis revealed that SOPS negative

Table 3
Correlations between EASE total, EASE top11, SOPS subscales, GAF symptom, GAF function, CTQ and PAS childhood (0–11 yrs).

	SOPS Pos	SOPS Neg	SOPS Dis	SOPS Gen	GAF Sympt	GAF Funct	CTQ Phys. abuse	CTQ Sex. abuse	CTQ Em. abuse.	CTQ Em. negl	CTQ Phys. negl.	CTQ Total	PAS Childh.
EASE total	0.34*a	0.66**a	0.54**b	.28a	-.18a	-.30a	-.05b	.11b	.05b	0.43*b	.09b	.25b	.13a
EASE top11	.20a	0.49**a	0.32*b	.18a	-.06a	-.23a	.01b	-.12b	.12b	0.41*b	.05b	.28b	-.07a

a = Pearson two-tailed.
b = Spearman two-tailed.
* $p < .05$.
** $p < .004$ (Bonferroni-adjusted).

symptoms made by far the strongest statistically significant contribution to the variance in EASE total scores.

4.1. Level of ASE

The high level of ASE in subjects with DSM-IV schizotypal personality disorder is in line with results from other studies on schizotypal disorders (diagnosed according to ICD-10 or DSM-IV criteria) [11,16,18]. Although limited by the small number of these patients in our sample ($n = 6$), the results corroborates earlier findings that basic self-disturbance is highly characteristic of all schizophrenia spectrum conditions [10,12,14,15,18].

Subjects fulfilling COGDIS criteria in this and the CHR study by Raballo and co-workers [21] also had high levels of ASE. This indicates that cognitive disturbances typically constitute a core part of markedly self-disturbed individuals. The high EASE total scores are not explained by a simple overlap between COGDIS criteria and EASE-items, because the significant association remained when removing the directly overlapping EASE-items from the analyses. Assuming that ASE and conventional symptomatic manifestations may constitute interrelated aspects of a more comprehensive psychopathological Gestalt, constituting a self-disorder, the EASE assessment in CHR conditions may be of considerable clinical importance. The co-presence of cognitive disturbances and other disturbances in the basic sense of self may reflect a CHR-subgroup particularly vulnerable with respect to schizophrenia spectrum disorders, as both the COGDIS criteria and high levels of ASE have been demonstrated to be associated with an increased risk of these disorders [20,22,43]. In addition, assessing ASE may result in a more comprehensive clinical picture, and give rise to a more dynamic and integrated psychopathological understanding of the patient [5,44,45], also relevant for treatment.

The lack of difference in EASE total, SOPS subscales and S-GAF scores between those categorized as CHR versus the group with non-progressive positive symptoms probably reflects that all subjects were referred to the study on the basis of a clinically based suspicion of increased risk for psychosis. This is also supported by the fact that the most frequently reported EASE-items (Table 2) were identical for the two groups. Considering the medical history of the subjects with non-progressive symptoms, they had most probably fulfilled CHR criteria at an earlier stage, and may thus be conceptualized as non-remitting CHR subjects. In prospective CHR-studies, this relatively stable category is indeed quite common among non-converters to psychosis [46,47].

4.2. Profiles of ASE

The assessment of certain clusters of EASE-items may supplement and refine the methods for the assessment of risk for psychosis and schizophrenia spectrum disorders [23]. It might thus be clinically useful to start looking at EASE data in more detail, to explore profiles of ASE in risk cohorts. We therefore report the 11 most frequent baseline EASE-items (not including 2.13 Anxiety), all present in >45% of the subjects in Table 2. There are considerable overlaps with a CHR study by Davidsen [19]. Among the 13 most common EASE-items in that study, seven were among the most frequent items in our study (EASE-items 1.1, 1.3, 1.10, 2.1, 2.2, 2.4 and 3.7). In a study by Nordgaard and co-workers assessing 48 schizophrenia and schizotypal patients, six of the top 12 items (seven out of 13 if including 2.13 Anxiety) overlapped with our top items (EASE-items 1.3, 1.6, 2.6, 2.1, 2.5 and 3.7) [10]. Three of the top items in our study are among the top items in all three studies (EASE-items 1.3, 2.1, 3.7), and 10 of our top items are among the most frequent in *either* the Davidsen CHR study or the Nordgaard schizophrenia spectrum study [10,19]. Additionally, four of our top-11 items (1.3, 2.1, 2.2, 2.6) are also among the ten EASE-items suggested as most prototypically reflecting disorders of the basic self in a study by Koren and co-workers [23].

It is crucial to bear in mind that ASE are not discrete symptoms, but aspects of a phenomenological entirety, a Gestalt. Risk evaluation cannot be performed based on one or a few EASE-items, but must always take the full picture into consideration. Still, the preliminary impression from investigations till now indicates that certain clusters of EASE-items most prevalent in CHR might also be among the most prevalent in schizophrenia spectrum disorders. This is anyway in line with considering self-disorders as trait-like features, developing continuously from pre-psychosis to psychosis [44]. We may only speculate that a high prevalence of these EASE-items in CHR subjects may indicate a more schizophrenia spectrum-related risk-profile. Examples of this kind of continuous development of a disordered self has previously been demonstrated in an extensive naturalistic case study [48]. However, most CHR subjects do not develop psychosis, and it is off the mark to consider CHR conditions in general as “schizophrenia light” [25]. Hence, further investigations of the trait- or state character of ASE, and level of specificity for groups of EASE-items as risk markers, are still needed.

4.3. ASE and their relationship with symptoms, childhood trauma, present and early functioning

This study indicates that negative symptoms and cognitive disturbances (presence of COGDIS criteria) may be tightly interwoven with ASE in CHR and intimately related conditions. It could be argued that these strong associations are due to overlapping items in the scales used for assessing these symptoms and experiences, i.e. that they reflect spurious relationships. However, these associations remained strong and significant even after removing those items most obviously overlapping, implying that this is probably not a sufficient explanation. The results are moreover in line with the findings in a study on a diagnostically heterogeneous sample of 100 patients, including approximately two-thirds with schizophrenia spectrum disorders [11]. The strong correlation between scores on the eleven most frequent EASE-items in the sample (EASE Top11) and SOPS negative symptoms may point to a strong affinity between these symptoms, but further studies are needed to investigate whether these findings may generalize to CHR conditions. Of course, so far, we can neither conclude firmly that a basic self-disturbance is driving the development of other symptoms in our sample, given the purely correlational data.

After Bonferroni-correction, positive symptoms (SOPS positive) did not correlate significantly with ASE in this sample. However, it is important to keep in mind that the weaker correlation with positive symptoms may be due to the restricted range of positive symptoms in our

sample. This is a common problem in predictive validity studies where the criterion variable is restricted in range [42]. This may at least partly explain the stronger correlations between the SOPS positive symptoms and EASE total in the study by Raballo and co-workers [21]. This study included a help-seeking sample not restricted with respect to positive symptoms, consisting both of CHR- and other help-seeking subjects, and analyzed these correlations in the total sample. Possibly, differences between the studies also reflect other differences in sample characteristics, even if the participants share positive symptoms of varying severity. In the heterogeneous help-seeking population many subjects may share symptoms like suspiciousness or perceptual abnormalities, but these symptoms are trans-diagnostic phenomena involving a variety of psychopathological mechanisms [49–53], not necessarily including the operation of a basic self-disturbance in all subjects.

The strong association between negative symptoms and ASE is interesting in light of the conceptualization in early European continental psychiatric literature of a certain kind of "*autism*" as an essential feature or 'trouble générateur' of schizophrenia [44,54,55]. In this theoretical context, autism involves a "deficit in the basic, non-reflective attunement between the person and his world" [54,55] or a loss of "common sense" [56], and prototypically manifests in the negative syndrome of schizophrenia [4,56]. In more recent phenomenological theory, this core feature is assumed to be intimately related to diminished self-presence/self-affection and hyperreflexivity, and thus implies a self-disorder characterized by a basic self-disturbance [4,55]. Given the cross-sectional design, the present data cannot tell us if the negative and other symptoms in our sample are *caused* by this core feature. On the other hand, to ask whether "autism" or a basic self-disturbance causes other symptoms may not necessarily be an adequate question to ask. Some symptoms, e.g. anhedonia and blunted affect, may constitute more or less simultaneous symptomatic *expressions* of more primary pathogenic features, among which basic self-disturbance may be prominent [55]. Still, other symptoms may be more appropriately characterized as compensatory mental events (i.e. effects, like delusional ideas or social withdrawal), dealing with a more primary disturbance.

Although common in the schizophrenia spectrum, the co-presence of ASE and negative symptoms in our sample may not necessarily imply an impending schizophrenia spectrum disorder. Some of the subjects in this sample may have been characterized by a depersonalized condition outside of the schizophrenia spectrum, which may occur as a primary disorder (DSM-5 Depersonalization/Derealization disorder, four of the participants were diagnosed with this disorder) or as a secondary feature of e.g. depressive and anxiety disorders [57,58]. Depersonalized conditions are not only characterized by feelings of unrealness and detachment, but also by a diminished sense of agency and emotional numbing [59]. These experiences manifest as symptoms overlapping with several kinds of ASE as described in the EASE [60,61]. The emotional numbing include different degrees of attenuated emotional experience (even though commonly showing emotions), including lack of feelings of affection towards family and friends [62,63]. It cannot be precluded that emotionally numb subjects in the sample may have been assessed as having "negative" symptoms like SOPS N1 Social anhedonia and N4 Experience of emotions and the self. Descriptions of these SOPS symptoms seem to overlap with descriptions of emotional numbness, e.g. "Passively goes along with most social activities in a disinterested or mechanical way" (N1), "Sense of distance when talking to others…" (N4) and "Emotions disappearing, difficulty feeling happy or sad" (N4).

4.3.1. Childhood trauma

We found a link between the CTQ subscale Emotional neglect and ASE using a nominal p-value ($p < .05$), but this correlation was insignificant after Bonferroni-correction. Still, this finding is worth mentioning considering the exploratory nature of this study, and in light of other studies finding significant associations between the experience of traumatic events/childhood trauma and self-disturbances. These include three studies of non-clinical samples (total $n = 1992$) [28–30], as well as one study of patients with first episode schizophrenia (only in females, $n = 27$) [27]. Although limited by the cross-sectional design of these studies, these results are interesting in light of a recently revised version of the self-disorder/ipseity disturbance model of schizophrenia. The model postulates that in addition to primary, trait-like ASE, characterizing schizophrenia, secondary forms of basic self-disturbance may occur both in the schizophrenia spectrum and in certain depersonalized conditions outside of this spectrum. These secondary forms are considered to constitute short-term or long-term *reactions* to external adversities and trauma [64–66]. This model, and the preliminary results regarding associations between ASE and trauma variables, point to the need of longitudinal studies to investigate the interaction between these factors.

4.3.2. Present and childhood functioning

Neither present global functioning (S-GAF) nor childhood functioning (PAS) were significantly associated with ASE. The lack of a significant association with present functioning is in line with one CHR study (measuring functioning with the Social and Occupational Functioning Scale, SOFAS) [20], but in disagreement with two other CHR studies (using GAF, not the split version) [21,24]. However, the strong correlation ($p < .01$) between EASE total and some of the SOPS negative symptoms, including symptoms like N1 Social Anhedonia, N2 Avolition and N6 Occupational Functioning, actually points to aspects of functioning affected in a significant amount of the participants.

4.4. Limitations

It could be argued that the use of EASE as a proxy tool to investigate COGDIS is a dubious method. However, when assessing these criteria we strictly adhered to the descriptions of them in the SPI-A. Due to the young age of several of the participants, assessments did not include an evaluation of personality disorders, except from the SIPS checklist of DSM-IV schizotypal personality disorder. Another limitation is the moderate interrater reliability of videotaped EASE-interviews which was based on pre-study scoring from another study. This should be considered in the context of our running supervisory post-scoring discussions (with EASE author PM) of almost all EASE-interviews, throughout the study.

As already described, the cross-sectional design limits the kind of analyses possible to carry out, and does not provide grounds for causal inferences. The exploratory nature of the study with the relatively small number of participants, and the lack of a control group, also limits the feasibility of comparative analyses and the generalizability of the study. If we had included a comparison group of non-CHR patients, we could have been more confident in concluding that the differences in the strength of relationships between EASE total and the other variables are not statistical artefacts, e.g. due to a more restricted range of positive symptoms in the included CHR subjects.

5. Conclusions

This study corroborates other studies finding that ASE are frequent in CHR and in the schizophrenia spectrum. The finding that the total level of ASE was extra enhanced in subjects with cognitive disturbances (fulfilling COGDIS criteria), may point to a CHR-subgroup particularly vulnerable to schizophrenia spectrum disorders. The strong association with negative symptoms is not previously reported in a CHR-sample. This finding is interesting in light of early models of "autism" as the "trouble générateur" of the symptoms of schizophrenia, but the cross-sectional design implies that we cannot draw the conclusion that this "autism" or basic self-disturbance drives symptom development in the sample. Longitudinal studies in clinical samples are needed to

investigate associations between ASE and negative symptoms, and between ASE and cognitive disturbances, to further address questions of causality, psychopathological pathways and schizophrenia spectrum specificity. The weaker correlation between ASE and positive symptoms may at least partly be due to range restriction of positive symptoms. Hence, future studies should investigate this association in samples not limited by this kind of range restriction.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial or not-for-profit sectors.

References

[1] Sass LA, Parnas J. Phenomenology of self-disturbances in schizophrenia: Some research findings and directions. [References]. Philosophy, Psychiatry, & Psychology. 2001:347–56.
[2] Parnas J, Jansson L, Sass LA, Handest P. Self-experience in the prodromal phases of schizophrenia: a pilot study of first-admissions. Neurol Psychiatry Brain Res 1998; 6:97–106.
[3] Moller P, Husby R. The initial prodrome in schizophrenia: searching for naturalistic core dimensions of experience and behavior. SchizophrBull 2000;26:217–32.
[4] Sass LA, Parnas J. Schizophrenia, consciousness, and the self. SchizophrBull 2003;29: 427–44.
[5] Sass LA. Self-disturbance and schizophrenia: structure, specificity, pathogenesis (current issues, new directions). Schizophr Res 2014;152:5–11.
[6] Nelson B, Parnas J, Sass LA. Disturbance of minimal self (ipseity) in schizophrenia: clarification and current status. Schizophr Bull 2014;40:479–82.
[7] Sass L, Parnas J, Zahavi D. Phenomenological psychopathology and schizophrenia: Contemporary approaches and misunderstandings. [References]. Philosophy, Psychiatry, & Psychology. 2011:1–23.
[8] Sass LA. Self-disturbance in schizophrenia: Hyperreflexivity and diminished self-affection. [References]. 2003. p. 242–71.
[9] Nordgaard J, Handest P, Vollmer-Larsen A, Saebye D, Pedersen JT, Parnas J. Temporal persistence of anomalous self-experience: a 5years follow-up. Schizophr Res 2017; 179:36–40.
[10] Nordgaard J, Nilsson LS, Saebye D, Parnas J. Self-disorders in schizophrenia-spectrum disorders: a 5-year follow-up study. Eur Arch Psychiatry Clin Neurosci 2018;268: 713–8.
[11] Nordgaard J, Parnas J. Self-disorders and the schizophrenia spectrum: a study of 100 first hospital admissions. Schizophr Bull 2014;40:1300–7.
[12] Parnas J, Handest P, Jansson L, Saebye D. Anomalous subjective experience among first-admitted schizophrenia spectrum patients: empirical investigation. Psychopathology 2005;38:259–67.
[13] Parnas J, Handest P, Saebye D, Jansson L. Anomalies of subjective experience in schizophrenia and psychotic bipolar illness. Acta Psychiatr Scand 2003;108:126–33.
[14] Haug E, Lien L, Raballo A, Bratlien U, Oie M, Andreassen OA, et al. Selective aggregation of self-disorders in first-treatment DSM-IV schizophrenia spectrum disorders. J Nerv Ment Dis 2012;200:632–6.
[15] Hur JW, Kwon JS, Lee TY, Park S. The crisis of minimal self-awareness in schizophrenia: a meta-analytic review. Schizophr Res 2014;152:58–64.
[16] Handest P, Parnas J. Clinical characteristics of first-admitted patients with ICD-10 schizotypal disorder. Br J Psychiatry Suppl 2005;187:s49–54.
[17] Raballo A, Parnas J. The silent side of the Spectrum: Schizotypy and the Schizotaxic self. SchizophrBull 2011;37:1017–26.
[18] Raballo A, Saebye D, Parnas J. Looking at the schizophrenia spectrum through the prism of self-disorders: an empirical study. SchizophrBull 2011;37:344–51.
[19] Davidsen KA. Anomalous self-experience in adolescents at risk of psychosis. Clinical and conceptual elucidation. Psychopathology 2009;42:361–9.
[20] Nelson B, Thompson A, Yung AR. Basic self-disturbance predicts psychosis onset in the ultra high risk for psychosis "prodromal" population. Schizophr Bull.2012:Feb.
[21] Raballo A, Pappagallo E. Dell' Erba a, Lo Cascio N, Patane M, Gebhardt E, et al. Self-disorders and clinical high risk for psychosis: an empirical study in help-seeking youth attending community mental health facilities. Schizophr Bull 2016;42: 926–32.
[22] Parnas J, Raballo A, Handest P, Jansson L, Vollmer-Larsen A, Saebye D. Self-experience in the early phases of schizophrenia: 5-year follow-up of the Copenhagen prodromal study. World Psychiatry 2011;10:200–4.
[23] Koren D, Reznik N, Adres M, Scheyer R, Apter A, Steinberg T, et al. Disturbances of basic self and prodromal symptoms among non-psychotic help-seeking adolescents. Psychol Med 2013;43:1365–76.
[24] Comparelli A, Corigliano V, De Carolis A, Pucci D, Angelone M, Di Pietro S, et al. Anomalous self-experiences and their relationship with symptoms, neurocognition, and functioning in at-risk adolescents and young adults. Compr Psychiatry 2016;65:44–9.
[25] Fusar-Poli P, Borgwardt S, Bechdolf A, Addington J, Riecher-Rossler A, Schultze-Lutter F, et al. The psychosis high-risk state: a comprehensive state-of-the-art review. JAMA Psychiat 2013;70:107–20.
[26] Nelson B, Raballo A. Basic self-disturbance in the schizophrenia spectrum: taking stock and moving forward. Psychopathology 2015;48:301–9.
[27] Haug E, Oie M, Andreassen OA, Bratlien U, Nelson B, Aas M, et al. Anomalous self-experience and childhood trauma in first-episode schizophrenia. Compr Psychiatry 2015;56:35–41.
[28] Gaweda L, Goritz AS. Moritz S. Schizophr Res: Mediating role of aberrant salience and self-disturbances for the relationship between childhood trauma and psychotic-like experiences in the general population; 2018.
[29] Gaweda L, Pionke R, Krezolek M, Prochwicz K, Klosowska J, Frydecka D, et al. Self-disturbances, cognitive biases and insecure attachment as mechanisms of the relationship between traumatic life events and psychotic-like experiences in non-clinical adults - a path analysis. Psychiatry Res 2018;259:571–8.
[30] Gaweda L, Prochwicz K, Adamczyk P, Frydecka D, Misiak B, Kotowicz K, et al. The role of self-disturbances and cognitive biases in the relationship between traumatic life events and psychosis proneness in a non-clinical sample. Schizophr Res 2018; 193:218–24.
[31] McGlashan TH, Walsh B, Woods S. The psychosis-risk syndrome: Handbook for diagnosis and follow-up. Oxford: Oxford University Press; 2010.
[32] Miller TJ, McGlashan TH, Rosen JL, Cadenhead K, Cannon T, Ventura J, et al. Prodromal assessment with the structured interview for prodromal syndromes and the scale of prodromal symptoms: predictive validity, interrater reliability, and training to reliability. SchizophrBull 2003;29:703–15.
[33] Miller TJ, McGlashan TH, Woods SW, Stein K, Driesen N, Corcoran CM, et al. Symptom assessment in schizophrenic prodromal states. PsychiatrQ 1999;70:273–87.
[34] Parnas J, Moller P, Kircher T, Thalbitzer J, Jansson L, Handest P, et al. EASE: examination of anomalous self-experience. Psychopathology 2005;38:236–58.
[35] Koo TK, Li MY. A guideline of selecting and reporting Intraclass correlation coefficients for reliability research. J Chiropr Med 2016;15:155–63.
[36] Schultze-Lutter F, Addington J, Ruhrmann S, Klosterkotter J. Schizophrenia proneness instrument: Adult version (SPI-A). Giovanni Fioriti Editore: Roma; 2007.
[37] First MB. Structured clinical interview for DSM-IV Axis I disorders (SCID-I): clinician version: User's guide for the Structured clinical interview for DSM-IV Axis I disorders. Washington, D.C: American Psychiatric Press; 1997.
[38] Pedersen G, Hagtvet KA, Karterud S. Generalizability studies of the global assessment of functioning-split version. Compr Psychiatry 2007;48:88–94.
[39] Bernstein DP, Stein JA, Newcomb MD, Walker E, Pogge D, Ahluvalia T, et al. Development and validation of a brief screening version of the childhood trauma questionnaire. Child Abuse Negl 2003;27:169–90.
[40] Bernstein DP, Ahluvalia T, Pogge D, Handelsman L. Validity of the childhood trauma questionnaire in an adolescent psychiatric population. J Am Acad Child Adolesc Psychiatry 1997;36:340–8.
[41] Cannon-Spoor HE, Potkin SG, Wyatt RJ. Measurement of premorbid adjustment in chronic schizophrenia. Schizophr Bull 1982;8:470–84.
[42] Marie W, Anna S. A comparison of two approaches to correction of restriction of range in correlation analysis. Pract Assess Res Eval 2009;14:1–9.
[43] Fusar-Poli P, Bechdolf A, Taylor MJ, Bonoldi I, Carpenter WT, Yung AR, et al. At risk for schizophrenic or affective psychoses? A meta-analysis of DSM/ICD diagnostic outcomes in individuals at high clinical risk. Schizophr Bull 2013;39:923–32.
[44] Parnas J. A disappearing heritage: the clinical core of schizophrenia. SchizophrBull 2011;37:1121–30.
[45] Parnas J, Jansson LB. Self-disorders: clinical and conceptual implications for the diagnostic concept of schizophrenia. Psychopathology 2015;48:332–8.
[46] Addington J, Liu L, Buchy L, Cadenhead KS, Cannon TD, Cornblatt BA, et al. North American Prodrome Longitudinal Study (NAPLS 2): the prodromal symptoms. J Nerv Ment Dis 2015;203:328–35.
[47] Simon AE, Borgwardt S, Riecher-Rossler A, Velthorst E, de Haan L, Fusar-Poli P. Moving beyond transition outcomes: meta-analysis of remission rates in individuals at high clinical risk for psychosis. Psychiatry Res 2013;209:266–72.
[48] Moller P. Duration of untreated psychosis: are we ignoring the mode of initial development?. An extensive naturalistic case study of phenomenal continuity in first-episode schizophrenia. Psychopathology 2001;34:8–14.
[49] Laroi F, Sommer IE, Blom JD, Fernyhough C, Ffytche DH, Hugdahl K, et al. The characteristic features of auditory verbal hallucinations in clinical and nonclinical groups: state-of-the-art overview and future directions. Schizophr Bull 2012;38:724–33.
[50] Elahi A, Perez Algorta G, Varese F, McIntyre JC, Bentall RP. Do paranoid delusions exist on a continuum with subclinical paranoia? A multi-method taxometric study. Schizophr Res 2017;190:77–81.
[51] Bebbington P, Freeman D. Transdiagnostic extension of delusions: schizophrenia and beyond. Schizophr Bull 2017;43:273–82.
[52] Upthegrove R, Broome MR, Caldwell K, Ives J, Oyebode F, Wood SJ. Understanding auditory verbal hallucinations: a systematic review of current evidence. Acta Psychiatr Scand 2016;133:352–67.
[53] Bentall RP, de Sousa P, Varese F, Wickham S, Sitko K, Haarmans M, et al. From adversity to psychosis: pathways and mechanisms from specific adversities to specific symptoms. Soc Psychiatry Psychiatr Epidemiol 2014;49:1011–22.
[54] La Minkowski E. Schizophrènie. Psychopathologie des Schizoides et des Schizophrènes.: Paris. Payot: France; 1927.
[55] Parnas J, Bovet P, Zahavi D. Schizophrenic autism: clinical phenomenology and pathogenetic implications. World Psychiatry 2002;1:131–6.
[56] Blankenburg W, Mishara AT. First steps toward a psychopathology of "common sense". Philos Psychiatry Psychol 2001;8:303–15.
[57] Reutens S, Nielsen O, Sachdev P. Depersonalization disorder. Curr Opin Psychiatry 2010;23:278–83.
[58] Hunter EC, Sierra M, David AS. The epidemiology of depersonalisation and derealisation. A systematic review. Soc Psychiatry Psychiatr Epidemiol 2004;39:9–18.

[59] Sierra M, David AS. Depersonalization: a selective impairment of self-awareness. Conscious Cogn 2011;20:99–108.
[60] Sass L, Pienkos E, Nelson B, Medford N. Anomalous self-experience in depersonalization and schizophrenia: a comparative investigation. Conscious Cogn 2013;22:430–41.
[61] Vaernes TG, Rossberg JI, Moller P. Anomalous self-experiences: markers of schizophrenia vulnerability or symptoms of depersonalization disorder? A phenomenological investigation of two cases. Psychopathology 2018:1–12.
[62] Simeon D, Kozin DS, Segal K, Lerch B, Dujour R, Giesbrecht T. De-constructing depersonalization: further evidence for symptom clusters. Psychiatry Res 2008;157:303–6.
[63] Sierra M, Berrios GE. The Cambridge Depersonalization Scale: a new instrument for the measurement of depersonalization. Psychiatry Res 2000;93:153–64.
[64] Borda JP, Sass LA. Phenomenology and neurobiology of self disorder in schizophrenia: primary factors. Schizophr Res 2015;169:464–73.
[65] Sass LA, Borda JP. Phenomenology and neurobiology of self disorder in schizophrenia: secondary factors. Schizophr Res 2015;169:474–82.
[66] Sass L, Borda JP, Madeira L, Pienkos E, Nelson B. Varieties of self disorder: a bio-pheno-social model of schizophrenia. Schizophr Bull 2018;44:720–7.
[67] Addington J, Cadenhead KS, Cannon TD, et al. North American Prodrome Longitudinal Study: a collaborative multisite approach to prodromal schizophrenia Research. Schizophr Bull 2007;33(3):665–72.

III

Psychiatry Research 300 (2021) 113942

Contents lists available at ScienceDirect

Psychiatry Research

journal homepage: www.elsevier.com/locate/psychres

Basic self-disturbance in subjects at clinical high risk for psychosis: Relationship with clinical and functional outcomes at one year follow-up

Tor Gunnar Værnes [a,b,*], Jan Ivar Røssberg [c,d], Ingrid Melle [d], Barnaby Nelson [e,f], Kristin Lie Romm [a,d], Paul Møller [g]

[a] Early Intervention in Psychosis Advisory Unit for South-East Norway, Division of Mental Health and Addiction, Oslo University Hospital, Oslo, Norway
[b] NORMENT, Division of Mental Health and Addiction, Oslo University Hospital, Oslo, Norway
[c] Psychiatric Research Unit, Division of Mental Health and Addiction, Oslo University Hospital, Oslo, Norway
[d] Institute of Clinical Medicine, Faculty of Medicine, University of Oslo, Oslo, Norway
[e] Orygen, Parkville, Victoria, Australia
[f] Centre for Youth Mental Health, the University of Melbourne, Parkville, Victoria, Australia
[g] Department for Mental Health Research and Development, Division of Mental Health and Addiction, Vestre Viken Hospital Trust, Drammen, Norway

ARTICLE INFO

Keywords:
Anomalous self-experience
Risk
UHR
Schizophrenia
Schizotypal
Remission
Phenomenology

ABSTRACT

Basic self-disturbance (BSD) is assumed to drive symptom development in schizophrenia spectrum disorders and in clinical high-risk (CHR) for psychosis. We investigated the relationship between BSD at baseline, assessed with the Examination of Anomalous Self-Experience (EASE), and symptoms and functional outcome after one year in 32 patients, including 26 CHR and six with non-progressive attenuated psychotic symptoms. Correlations between baseline BSD levels and positive, negative and disorganization symptoms, and global functioning level at follow-up were significant. Hierarchical regression analyses revealed that higher levels of baseline BSD predicted more severe positive symptoms and lower global functioning at follow-up, after adjusting for baseline positive symptoms and functioning. Subjects who were not in symptomatic and functional remission after one year had higher levels of BSD and negative symptoms, and lower functioning level, at baseline. Baseline BSD in participants with schizophrenia spectrum diagnoses at follow-up (9 of 12 were schizotypal personality disorder) were at the levels seen in schizotypal disorders in previous studies, but not significantly different from the other participants. Early identification and assessment of BSD may constitute a useful prognostic tool and a signal for therapeutic targets in CHR conditions. Further CHR studies investigating these relationships with larger samples are recommended.

1. Introduction

Criteria for clinical high-risk (CHR) for psychosis have been established to predict and hopefully prevent a first episode of psychosis, and these criteria have increasingly been implemented in clinical research and practice during the last two decades (Fusar-Poli, 2017; Schultze--Lutter et al., 2015). CHR criteria are currently defined in two ways based on two different approaches to the CHR concept: 1) the ultra-high risk (UHR) criteria and 2) the basic symptoms high-risk criteria. The UHR criteria aims to detect imminent risk of psychosis, while the basic symptoms criteria were developed to detect risk of psychosis as early as possible in the development of the illness (Schultze-Lutter et al., 2015). UHR criteria include the presence of 1) 'attenuated' psychotic symptoms (APS), 2) brief limited psychotic symptoms (BLIPS) and/or 3) functional decline in combination with genetic predisposition or in the context of schizotypal personality disorder (Schultze-Lutter et al., 2015; Yung et al., 2008). Two interview measures are widely used for these main UHR criteria, the Structured Interview for Psychosis-Risk Syndromes (SIPS), including the Scale of Psychosis-Risk Symptoms (SOPS) (McGlashan et al., 2010; Miller et al., 2002) and the Comprehensive Assessment of At-Risk Mental State (CAARMS) (Yung et al., 2005). Basic symptoms high-risk criteria involve subjectively experienced non-delusional changes and disturbances of thought and perception. They are defined and assessed with the Schizophrenia Proneness Instrument, Adult (SPI-A) or Child & Youth version (SPI-CY), and include the cognitive-perceptive basic symptoms (COPER) and the cognitive

* Corresponding author at: Oslo University Hospital, Division of Mental Health and Addiction, TIPS Sør-Øst, Postbox 4956, Nydalen, 0424Oslo, Norway
E-mail address: uxvrnt@ous-hf.no (T.G. Værnes).

https://doi.org/10.1016/j.psychres.2021.113942
Received 9 July 2020; Accepted 11 April 2021
Available online 18 April 2021
0165-1781/© 2021 The Authors. Published by Elsevier B.V. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).

disturbances (COGDIS) criteria (Schultze-Lutter et al., 2007). The COGDIS criteria have the strongest evidence-base regarding prediction of psychosis among these two sets of criteria (Schultze-Lutter et al., 2015).

The clinical outcome in subjects meeting CHR criteria is heterogeneous and includes 1) transition to psychosis, 2) maintenance or recurrence/relapse of a high-risk state, 3) remission and recovery from the high-risk state, as well as 4) variable outcomes with respect to functioning and other non-psychotic disorders (Beck et al., 2019a; Polari et al., 2018). Even though about a third remits from attenuated psychotic symptoms and functionally recovers, the majority of CHR subjects not transitioning to psychosis have enduring clinical needs and suffer from psychosocial impairments (Addington et al., 2011; Addington et al., 2015; Beck et al., 2019a; Beck et al., 2019b; Lee et al., 2014; Lim et al., 2015; Lin et al., 2015; Schlosser et al., 2012). Traditionally, prospective CHR studies have focused mostly on the prediction and prevention of psychosis, but recent years have witnessed an increased focus on the various non-transitioning outcomes and their predictors. This is important in order to improve early identification and differentiation of clinical sub-types, and to develop and implement targeted intervention strategies (Ferrarelli and Mathalon, 2020; Lim et al., 2015; Mechelli et al., 2017; Polari et al., 2018).

Representing a third concept, though closely related to the basic symptoms concept, certain kinds of *anomalous self-experiences* have been demonstrated to be frequent in the initial prodrome of schizophrenia in retrospective studies (Møller and Husby, 2000; Parnas et al., 1998; Raballo et al., 2021), and to characterize schizophrenia spectrum disorders (Nelson and Raballo, 2015; Parnas and Henriksen, 2014). High levels of these phenomena have been found to predict transition to psychosis in an UHR sample, and to characterize schizophrenia spectrum cases in this sample, irrespective of psychosis transition (Nelson et al., 2012). Anomalous self-experiences have further been shown to aggregate in CHR samples (Comparelli et al., 2016; Davidsen, 2009; Nelson et al., 2012; Raballo et al., 2016; Vaernes et al., 2019) and to predict future psychosis-risk symptoms (Koren, 2012) and schizophrenia spectrum disorders (SSDs) (Koren et al., 2020) in non-psychotic help--seeking adolescents. These phenomena thus seems to constitute a promising additional clinical predictor of SSDs in CHR conditions (Nelson and Raballo, 2015; Nelson et al., 2012). To assist researchers and clinicians, an instrument for a phenomenological exploration of BSD has been developed, the Examination of Anomalous Self-Experience (EASE) (Parnas et al., 2005).

In a phenomenologically oriented model of schizophrenia spectrum psychopathology, such anomalies are assumed to be intimately interrelated aspects or manifestations of a 'core' disturbance affecting the most 'basic' or 'minimal' sense of self, i.e. a *'basic self-disturbance'* (BSD) (Parnas, 2011; Parnas and Handest, 2003; Parnas et al., 2005a; Sass and Parnas, 2003). This 'basic self-disturbance model', also termed the 'ipseity disturbance model', describes a weakening of (the sense of) subjectivity and first-person perspective, including a diminished sense of 'mineness' of experience and action, an exaggerated self-consciousness ('hyperreflexivity'), and a weakening of feeling naturally and self-evidently immersed in the world (Nelson et al., 2014; Nelson and Raballo, 2015; Parnas and Henriksen, 2014; Sass et al., 2018; Sass, 2014; Sass and Parnas, 2003). The positive, negative and disorganization symptoms common to the SSDs are presumed to emerge and progress as interrelated features and transformations of BSD (Parnas, 2011; Raballo and Parnas, 2010; Sass and Parnas, 2003).

Moreover, the exploration of BSD phenomena could help to identify non-transitioning CHR subjects with high likeliness of *non-remission*. BSD may underlie ongoing, potentially shifting and varying, symptomatic manifestations (Sass, 2014), in addition to enduring functional impairments in non-remitting CHR conditions(). Some of these conditions may meet DSM or ICD criteria for schizotypal disorders (Boldrini et al., 2019; Schlosser et al., 2012), which are commonly assumed to belong to the schizophrenia spectrum (American Psychiatric Association, 2013; World Health Organization, 1992; Parnas and Jansson, 2015; Schultze-Lutter et al, 2019).

We aimed to investigate in a one-year follow-up study whether the clinical and functional trajectories in CHR subjects, were associated with, and predicted by, the severity of BSD at baseline. It is still a paucity of prospective CHR studies investigating this, particularly with respect to clinical and functional remission.

Our research questions were:

1) Is the severity of BSD at baseline in CHR subjects associated with the following features after one year:
   a positive, negative, disorganization and general symptoms (according to SIPS/SOPS), and global functioning?
   b clinical and functional remission?
   c meeting DSM-IV criteria for a schizophrenia spectrum disorder?
2) Is clinical and functional outcome after one year in CHR subjects predicted by the severity of BSD at baseline?

2. Methods

2.1. Setting and participants

Help-seeking individuals between 15 and 29 years were consecutively recruited from child/adolescent and adult outpatient units in Oslo and adjacent catchment areas (Oslo University Hospital, Diakonhjemmet Hospital, Vestre Viken Hospital Trust and Akershus University Hospital) during the years 2012-2015. The study was part of the Norwegian Thematically Organized Psychosis (TOP) study, and was approved by the Regional Committee for Medical Research Ethics in Norway. All patients gave written informed consent. For those below 18 years, parents consented as well.

Patients were referred to the study by their treating clinicians if they clinically suspected high risk of psychosis. Inclusion criteria were: 1) meeting UHR criteria as described in the SIPS (Miller et al., 2003), or 2) meeting basic symptoms high-risk criteria (COGDIS) (Schultze-Lutter et al., 2007), or 3) being in a 'non-progressive symptoms group'. The latter meaning they had at least one stable attenuated positive symptom (score 3 to 5 on the SOPS (Miller et al., 2003)) with an onset more than a year ago, with no progression during this period. We included this group to reflect the naturalistic 'real world' clinical referral pattern, considered as at-risk by their treating clinician and thus referred to our study. They would possibly have met UHR criteria in the CAARMS instrument, which do not require, in contrast with the SIPS, onset or increased severity of attenuated positive symptoms in the last year (Yung et al., 2005). Exclusion criteria were: present or previous psychotic episode, current antipsychotic treatment or for $\geq$ 4 weeks lifetime (dose equivalent to $\geq$ 5 mg Olanzapine per day), organic or clearly substance-induced CHR symptoms, intellectual disability (IQ $<$ 70), and inability to speak Norwegian.

Fifty-three individuals were interviewed (preliminary screening) for eligibility in the study. Thirteen of these were excluded either due to meeting the exclusion criteria at the initial screening or during the baseline assessments ($n = 7$), or because they declined to participate in or complete all assessments ($n = 6$). Two individuals were also excluded after the baseline assessments because they were reassessed as not meeting the inclusion criteria. The baseline sample thus comprised 38 participants, including 31 subjects meeting ultra-high risk and/or COGDIS criteria (i.e. CHR), and seven in the non-progressive symptoms group.

2.2. Measures

2.2.1. Baseline assessments

The included participants were first interviewed at baseline with the SIPS/SOPS (Miller et al., 2003; Miller et al., 2002) (Norwegian version 5.0, Jan. 2012). The presence and severity of each symptom was

assessed on the SOPS, a 0 (absent) to 6 (psychotic or extreme) Likert scale. The SOPS is organized in four subscales, comprising positive, negative, disorganization and general symptoms (Miller et al., 1999). The SIPS/SOPS was used both to assess UHR and non-progressive symptoms group criteria, and the severity of symptoms on each of the four SOPS subscales. The timeframe for assessing SOPS symptom severity was last month.

CHR status was supplementary assessed according to the COGDIS criteria (Schultze-Lutter et al., 2007). Adhering strictly to the descriptions in the SPI-A, we used the EASE (Parnas et al., 2005b) interview as a proxy instrument to explore the presence and severity of the COGDIS criteria. There is a near-complete overlap between certain item descriptions in the EASE and in the instruments developed for assessing basic symptoms, the Bonn Scale for the Assessment of Basic Symptoms (BSABS), and basic symptoms high-risk criteria (SPI-A) (Gross et al., 1987; Parnas et al., 2005b; Schultze-Lutter et al., 2007).

We explored life-time experiences of BSD phenomena with the EASE (Parnas et al., 2005b). The EASE covers 57 items distributed to five domains (1) cognition and stream of consciousness, (2) self-awareness and presence, (3) bodily experiences, (4) demarcation/ transitivism, and (5) existential reorientation. To compare with other studies using the EASE e.g. (Koren et al., 2019; Nordgaard and Parnas, 2014; Raballo et al., 2018; Raballo et al., 2016), the scores on each of the 57 main EASE-items (excluding subtypes scores) were converted from continuous 0-4 Likert scale scores to dichotomous scores representing the presence (1 = definitely present, all severity levels) or absence (0 = absent or questionably present) of BSD phenomena. The dichotomous scores of all the main items were then summed up, giving an EASE total score, reflecting the overall severity of the BSD.

We established diagnoses by using a full version of the Structured Interview for DSM-IV-Axis I disorders: SCID-I (First, 1997). A SIPS checklist was applied to assess the DSM-IV diagnosis Schizotypal Personality Disorder (SPD) (Miller et al., 2003). Other Axis II diagnoses were not assessed.

Global functioning (during the last week) was assessed with the Global Assessment of Functioning (GAF) – split version, a scale divided in a function (GAF-F) and a symptom (GAF-S) score, ranging from 0 (most severe dysfunction and symptoms) to 100 (no symptoms, excellent functioning) (Pedersen et al., 2007). We only report the GAF-F score because the use of a measure of functioning not conflated by symptomatic severity is recommended for studies of remission (Lee et al., 2014).

2.2.2. Follow-up assessments

Between baseline and follow-up, participants were offered treatment as usual at their local services, including psychotherapy, other psychosocial interventions and medication. In the case of suspected transition to psychosis between baseline and follow-up (reported from the therapist), this was confirmed or disconfirmed by TGV, according to the criteria for a psychotic syndrome in the SIPS (Miller et al., 2003; Miller et al., 2002). A differential diagnostic assessment followed, according to DSM-IV criteria. This assessment was based on information from clinical records and interviews with the SCID-I A-D modules. The non-transitioning participants did not undergo a new differential diagnostic assessment with the SCID-I at or before follow-up. However, the SIPS SPD checklist was used at follow-up for a reassessment of the criteria for this disorder for all participants. Subjects meeting SPD criteria or criteria for DSM-IV schizophrenia, schizophreniform disorder or schizoaffective disorder were considered to belong to the schizophrenia spectrum group at follow-up.

At the one-year follow-up, we reassessed positive, negative, disorganization and general symptoms (SIPS/SOPS) (based on symptom severity last month), and the level of global functioning (GAF-F) (during the last week). We defined full remission as a score of ≤ 2 on all SOPS positive symptoms, together with a good level of functioning (GAF-F $\geq$70) or improved functioning ($\geq$10-point improvement on GAF-F compared to baseline functioning). Both participants in the CHR group and in the non-progressive symptoms group were assessed according to these remission criteria, as they did not differ with respect to baseline symptom severity and functioning level (as reported previously (Vaernes et al., 2019)). We focused on remission/non-remission of SOPS positive symptoms at follow-up rather than remission/non-remission of COGDIS criteria. This was due to the assumption that basic symptoms high-risk phenomena precede the attenuated positive symptoms defining UHR states (Jimeno et al., 2020; Schultze-Lutter et al., 2015), and the considerable overlap between several of the COGDIS items and items in the EASE (Parnas et al., 2005b; Schultze-Lutter et al., 2007)

All interviews at baseline and follow-up were conducted by TGV, who had participated in "gold-standard" training in the use of SIPS/SOPS, EASE and SCID-I, including supervision by PM, one of the authors and certified instructors of the EASE. SIPS/SOPS inter-rater reliability (IRR) was tested by comparing scores on nine case vignettes with final scores of raters from the North American Prodrome Longitudinal Study (NAPLS). UHR status agreement was 100 %, and SOPS positive symptom scores IRR was excellent (single measure ICC: 0.95, 95 % CI [0.82, 0.99], two-way mixed effects model, absolute agreement). Regarding EASE, IRR was established by scoring nine videotaped EASE-interviews from a study by Haug and colleagues (Haug et al., 2012), and then comparing these scores with the scores from Haug and PM. IRR was moderate (single measure ICC of 0.62, 95 % CI [0.24, 0.88], two-way mixed effects model, absolute agreement). Diagnoses, CHR status and EASE scores were regularly discussed throughout the assessment period with PM and JIR, both experienced psychiatrists and researchers.

2.3. Statistical analysis

Mean and standard deviations for continuous variables and percentages for categorical variables are reported. We used the sum scores on the EASE scale (based on the sum of dichotomous (0-1) scores on all EASE main items) in the analyses involving the continuous EASE total variable. Analysis of SOPS subscale scores were based on summing the 0-6 scores for each item constituting the four symptom domains. The non-parametric Wilcoxon signed rank test for repeated measures was used to analyze differences in continuous clinical variables between baseline and follow-up.

Bivariate correlations between baseline EASE total score and sum scores on the four SOPS subscales and the GAF-F score at follow-up were analyzed, using Pearson correlation or Spearman rho correlation for variables not normally distributed. Four SOPS subscale change variables and a GAF-F change variable were calculated (baseline minus follow-up score). A bivariate correlation analysis between baseline EASE total and these five change variables were performed.

The independent samples *t*-test, or the non-parametric alternative Mann-Whitney *U* test for data without normal distribution, was used to analyze differences in baseline EASE total scores and other continuous baseline variables between subjects in remission and the non-remitting subjects. The Fisher's exact test was used to analyze subgroup differences in baseline categorical variables. In these analyses, we treated COGDIS both as a categorical variable (meeting or not meeting COGDIS criteria), and as a continuous variable measuring severity (sum score of all nine items, each rated on a 0-6 frequency/severity scale, excluding specifier ratings 7-9).

To investigate whether meeting or not meeting DSM-IV criteria for a schizophrenia spectrum disorder at follow-up was associated with baseline EASE total scores, we used the independent samples *t*-test.

Blockwise hierarchical multiple regression tests were used to examine whether BSD at baseline explained a significant amount of the variance in the follow-up outcome variables. We entered the baseline equivalent of the follow-up variable in the first block (e.g. SOPS positive at baseline, if SOPS positive at follow-up was the dependent variable), adjusting for the influence of this baseline variable, and then we entered EASE total in the second block. Due to the small sample size, we report

adjusted R^2 values. For all regression analyses, preliminary analyses were conducted to check for any violations of normality, linearity, multicollinearity and homoscedasticity. No such violations were found.

The significance level was set to $p < 0.05$, two-sided, for all the statistical tests. All analyses were conducted with SPSS version 25.0.

3. Results

3.1. Demographics and clinical characteristics

Of the 38 participants included at baseline, 32 completed the one-year follow-up assessments (attrition rate 15.8%), including 26 CHR and six from the non-progressive symptoms group. The follow-up period had a median length of 13 months (range 12-18). The six drop-outs did not differ from the other participants on any of the demographic or clinical baseline variables. Four participants (10.5% of the original sample), all CHR, transitioned to a psychotic episode between baseline and follow-up. Clinical trajectories from baseline to follow-up are described in more detail in figure 1.

All SOPS subscale scores decreased significantly as mean measures from baseline to follow-up, but not the GAF-F score. Eight subjects ended their treatment during follow-up either due to their own request ($n = 2$) or because they were no longer considered to be in need of treatment by their treating team ($n = 4$) or due to unknown reasons ($n = 2$). Neither demographic characteristics at baseline nor differences in the use of antipsychotics or other medications at baseline or between baseline and follow-up nor ending treatment between baseline and follow-up, were associated with any of the clinical variables at follow-up. Having an anxiety disorder as a primary diagnosis at baseline was significantly associated with less severe SOPS negative symptoms and a higher GAF-F score at follow-up. Being diagnosed with SPD at baseline was significantly associated with more severe SOPS positive, negative and disorganization symptoms, and a lower GAF-F score at follow-up. Table 1 displays demographics and clinical characteristics of the sample completing both baseline and follow-up assessments.

3.2. Baseline EASE total was associated with symptoms and functioning at follow-up

In table 2 correlations between EASE total at baseline and clinical variables at follow-up are presented. EASE total at baseline was significantly associated with SOPS positive, negative and disorganization

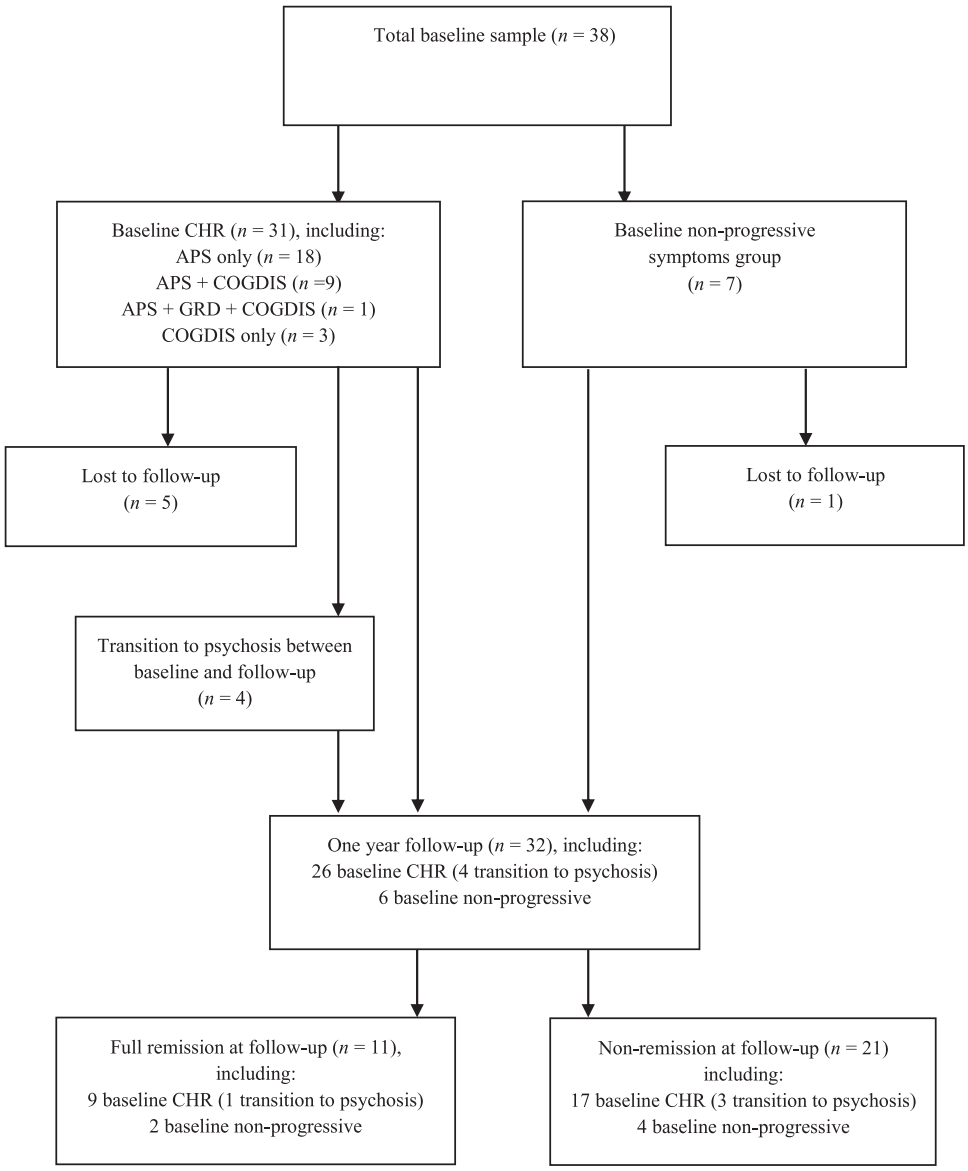


Fig. 1.. Flow chart showing CHR status at baseline, sample attrition, transition to a psychotic episode, and remission status at 1-year follow-up

Table 1.
Demographics and clinical characteristics for the sample completing assessments at baseline and one-year follow-up

Characteristics	Baseline	Follow-up	Mean difference (*SD*)	Wilcoxon's sign. rank test, *P* value
Total *N*	32			
CHR positive, *n* (%)	26 (81.3)			
Non-progressive, *n* (%)	6 (18.8)			
Gender, Male, *n* (%)	21 (65.6)			
Age, mean (*SD*)	19.9 (3.8)	21.1 (4.0)		
Born in Norway, *n* (%)	29 (90.6)			
Employed or studying, *n* (%)	17 (53.1)			
Years of education, mean (*SD*)	11.7 (1.8)			
Diagnoses, *n* (%)				
Mood disorders	13 (40.6)			
Anxiety disorders	8 (25.0)			
Other DSM-IV Axis I disorders	4 (12.5)			
Schizotypal personality disorder	5 (15.6)	9 (28.1)		
No DSM-IV diagnosis	2 (6.3)			
Medication prescribed, *n* (%)[a]				
Antipsychotics	7 (21.9)	8 (25.0)		
Antidepressants	6 (18.8)	10 (31.3)		
Anxiolytics	2 (6.3)	0		
Anticonvulsants	1 (3.1)	1 (3.1)		
Psychostimulants	1 (3.1)	1 (3.1)		
Transition psychosis, *n* (%)		4 (12.5)		
Diagnosis, psychotic episode,*n* (%)				
Schizophrenia		2 (6.3)		
Schizophreniform disorder		1 (3.1)		
Psychosis NOS (%)		1 (3.1)		
Full remission (%)		11 (34.4)		
EASE total (*SD*)	15.31 (8.01)			
SOPS positive (5 items) (*SD*)	10.41 (3.45)	6.56 (5.58)	3.84 (5.50)	0.001*
SOPS negative (6 items) (*SD*)	12.50 (7.02)	9.94 (7.39)	2.56 (4.69)	0.005*
SOPS disorganization (4 items) (*SD*)	6.91 (3.36)	5.13 (4.32)	1.78 (3.26)	0.007*
SOPS general (4 items) (*SD*)	7.59 (3.31)	4.97 (3.49)	2.63 (4,12)	0.002*
COGDIS severity (*SD*)	6.16 (5.91)			
GAF-F (*SD*)	56.31 (10.83)	59.80 (15.72)	3.53 (11.65)	0.117

* $p < 0.05$
[a]With respect to medication, the data in the follow-up column represents prescribed medication between baseline and follow-up.

subscales, and with GAF-F, but not with SOPS general, at follow-up. EASE total was also strongly associated with the GAF-F change variable, meaning that the subjects who improved the most on GAF-F had lower baseline EASE total scores. All these significant associations remained significant after excluding the four subjects who transitioned to psychosis from the correlation analyses.

Table 2.
Correlations between EASE total at baseline and SOPS subscale and GAF-F at follow-up, and with change in SOPS subscale and GAF-F from baseline to follow-up ($n = 32$).

	Correlations at 1 year follow-up ($N = 32$)									
	SOPS Pos	SOPS Neg	SOPS Dis	SOPS Gen	GAF-F	SOPS Pos change	SOPS Neg change	SOPS Dis change	SOPS Gen change	GAF-F change
Baseline EASE total	0.50**[b]	0.56**[a]	0.51**[b]	0.34[a]	-0.54**[a]	-0.26[a]	0.05[a]	-0.12[a]	-0.09[a]	0.54**[a]

*$p < 0.05$, **$p < 0.01$, [a] = Pearsons rho two-tailed, [b] = Pearson two-tailed

3.3. Baseline EASE total, SOPS negative and GAF-F were associated with remission at follow-up

Of the sample completing both assessments ($n = 32$), 13 (40.6 %) remitted symptomatically, 14 (43.8) remitted functionally, and 11 (34.4 %) reached both, i.e. full remission after one year. The 'full remission group' did not differ from the 'non-remission group' ($n = 21$) on any of the demographic variables. The non-remission group had significantly higher baseline EASE total (eta squared = 0.27, large effect size) and baseline SOPS negative scores (eta squared = 0.25, large effect size), and a lower baseline GAF-F score (eta squared = 0.19, large effect size). Interestingly, severity of baseline SOPS positive symptoms was not associated with remission of positive symptoms at follow-up. There were also no significant associations between COGDIS status at baseline (meeting COGDIS criteria or COGDIS sum score) and remission (Table 3). When excluding the four transitioning to psychosis subjects from these analyses of remission, we found the same pattern, but with somewhat lower t-values.

3.4. Baseline EASE total in subjects with or without a schizophrenia spectrum disorder at follow-up

Among the four participants who transitioned to psychosis, two were diagnosed with schizophrenia, one with schizophreniform disorder and one with psychosis NOS. Not including the psychosis NOS case, twelve subjects were diagnosed with a schizophrenia spectrum disorder at follow-up, including three transitioned cases and nine with SPD (SPD increased from five at baseline). The mean EASE total score at baseline was nominally higher in the schizophrenia spectrum group (EASE total =18.17, $SD = 6.83$, $n = 12$) than in the other participants (EASE total =13.60, $SD = 8.51$, $n = 20$), but the magnitude of this difference did not reach statistical significance (t (30) = -1.58, $p = 0.13$).

Table 3.
Demographics and clinical characteristics at baseline in remitters vs non-remitters.

Baseline demographics and clinical characteristics			Difference between remitters/non-remitters
	Remitters, N= 11 (34.4%)	Non-remitters, $N = 21$ (66.6%)	T-test (df = 30) (t)/Mann-Whitney U (U)/Fisher's exact test (P)
Male (%)	6 (54.5)	15 (71.4)	$P = 0.44$
Female (%)	5 (45.5)	6 (28.6)	
Age, mean (SD)	20.4 (4.3)	19.7 (3.7)	$t = -0.48$
Yrs education, mean (SD)	12.0 (2.2)	11.5 (1.6)	$U = 97$
Employed or studying, n (%)	7 (63,6)	10 (47.6)	$P = 0,71$
EASE total, mean (SD)	10.27 (4.88)	17.95 (8.32)	$t = 3.29$*
SOPS Positive, mean (SD)	9.64 (2.98)	10.81 (3.68)	$t = 0.91$
SOPS Negative, mean (SD)	7.73 (5.76)	15.00 (6.37)	**$t = 3.16$***
SOPS Disorg, mean (SD)	5.45 (2.21)	7.67 (3.65)	$U = 73$
SOPS General, mean (SD)	6.64 (3.17)	8.10 (3.35)	$t = 1.19$
GAF function, mean (SD)	62.64 (11.45)	53.00 (9.09)	**$t = -2.61$***
COGDIS criteria met (%)	3 (27.3)	9 (42.9)	$P = 0.47$
COGDIS criteria not met (%)	8 (72.7)	12 (57.1)	
COGDIS sum, mean (SD)	3.73 (4.29)	7.43 (6.33)	$U = 74.5$

* $p < 0.05$

3.5. The predictive value of BSD for clinical and functional outcomes

Results from the hierarchical multiple regression analyses are presented in Table 4. EASE total at baseline explained a significant amount of the variance in SOPS positive (13 %) and GAF-F scores (17 %) at follow-up, when controlling for baseline SOPS and GAF scores respectively, but not of the variance in follow-up SOPS negative and SOPS disorganization scores. These results implied that higher baseline EASE total scores predicted higher SOPS positive and lower GAF-F scores at follow-up.

4. Discussion

Summing up, this CHR study found that high levels of BSD (EASE total score) at baseline were associated with a higher severity of SOPS positive, negative and disorganization symptoms, and more severe global dysfunction, at one-year follow-up. Higher levels of BSD were also associated with less or no improvement in functioning between baseline and follow-up, and not achieving remission symptomatically (from attenuated psychotic symptoms) and functionally. These findings were not significantly affected by removing the four subjects who transitioned to psychosis from the analyses. Levels of BSD were nominally higher in subjects with schizophrenia spectrum disorders at follow-up than in the other subjects in the sample, but this difference was not statistically significant. Finally, we found that higher levels of BSD predicted more severe positive symptoms and lower level of global functioning at follow-up, when controlling for the impact of baseline positive symptoms and global functioning. The relationship between baseline BSD and these two follow-up variables were actually stronger than between baseline BSD and positive symptoms and functioning at baseline, as described in a previous study of the same sample (at that time also including the drop-outs from the present study) (Vaernes et al. 2019). Hence, these findings corroborate the status of BSD as an important clinical marker of unfavorable future outcomes in CHR, even in non-transitioning cases.

The non-remission group also presented with more severe baseline negative symptoms and functional impairments. Neither the severity of SOPS positive, disorganization and general symptoms nor the severity of COGDIS symptoms at baseline were significantly associated with remission. The lack of a significant association between baseline positive symptoms and remission should be considered in the light of the restricted range of the inclusion criterion variable (participants included on the basis of presence of attenuated positive symptoms, the majority with an APS syndrome). It is possible that this association would have been stronger in a more unrestricted sample. This may also have affected

Table 4.
Hierarchical multiple regression analyses of the ability of baseline EASE total to predict follow-up SOPS subscale and GAF-F scores, when controlling for baseline SOPS subscale and GAF-F scores.

Dependent variable	Independent variable, by step 1 and 2	B	SE	p	R^2	% increase of explained variance
SOPS pos follow-up	SOPS pos, baseline	.348	.275	.216	.079	11
	EASE total, baseline	.258	.117	.035	.185	13
SOPS neg follow-up	SOPS neg, baseline	.760	.151	.000	.610	62
	EASE total, baseline	.100	.131	.449	.605	1
SOPS disorg follow-up	SOPS disorg, baseline	.756	.195	.001	.425	44
	EASE total, baseline	.093	.081	.257	.432	2
GAF-F follow-up	GAF-F, baseline	.864	.169	.000	.440	46
	EASE total, baseline	-.804	.226	.001	.598	17

the non-significant correlation between SOPS positive at baseline and follow-up. Youn and colleagues (Youn et al., 2019) found that meeting COGDIS criteria were associated with a greater likelihood of having persistent attenuated psychotic symptoms at 12 months follow-up. Our results revealed a trend in the same direction, however below the level of statistical significance. This could be due to the small sample size, and the even smaller number of participants meeting COGDIS criteria at baseline ($n = 13$).

The significantly higher BSD level we found in non-remitting CHR-patients is compatible with findings in a seven-year follow-up study on a sample of patients with psychotic disorders (first-treatment psychosis patients). In this study, recovery (combination of full remission of psychotic symptoms and regained functioning) was significantly associated with lower baseline levels of BSD (Svendsen et al., 2019). Though the sense of basic self in the schizophrenia spectrum conditions may be unstable (Sass, 2014), and the severity of BSD may be somewhat milder longitudinally (Svendsen et al., 2018), BSD is assumed to have a trait-like character (Nordgaard et al., 2017; Parnas and Henriksen, 2014; Parnas et al., 2011). BSD may thus give rise to ongoing, but also fluctuating clinical manifestations, as postulated in the BSD model (see Nelson and Raballo, 2015; Sass, 2014). Hence, BSD may not only constitute a high-risk factor for the initial development of symptoms in CHR, but its assumed trait-like, but somewhat unstable, character may also render CHR subjects vulnerable for non-remission or recurrence/relapse of these symptoms longitudinally. In some cases signs and symptoms may develop into frank psychotic symptoms, but not in all cases (as can be seen in the schizotypal conditions).

However, we can of course not assume that the relationship between BSD and future clinical outcomes inevitably reflects the development of a schizophrenia spectrum disorder, as the majority did not meet criteria for such a disorder at follow-up. Still, this should also be considered in light of the relatively short follow-up period. Although the largest proportion of transitions to psychosis in CHR samples happens during the first year, many convert later (Fusar-Poli et al., 2013b; Nelson et al., 2013; Schultze-Lutter et al., 2015). By far, the majority of transitioning CHR cases are diagnosed with a psychotic disorder in the schizophrenia spectrum, as demonstrated in a meta-analysis (73 % versus 11 % with affective psychoses and 16 % with other psychoses) (Fusar-Poli et al., 2013a).

The results are also in line with other CHR studies finding that clinical and/or functional improvement and remission is associated with lower baseline levels of negative symptoms (Carrion et al., 2016; Schlosser et al., 2015; Schlosser et al., 2012) and better baseline psychosocial functioning (Beck et al., 2019b; Koutsouleris et al., 2018). These findings thus corroborate the significance of negative symptoms and psychosocial functioning as important prognostic markers in CHR, not only for transition to psychosis (Addington et al., 2017; Healey et al., 2017; Valmaggia et al., 2013; Zhang et al., 2020), but also for other adverse outcomes in non-transitioning cases. Hence, the co-presence of a high severity of BSD, negative symptoms and dysfunction in CHR may constitute a particularly strong prognostic risk index for symptomatic and functional non-remission, unfavorable course of disorder irrespective of diagnosis, and possibly also for transition to psychosis.

The finding that BSD predicted future positive symptoms and level of functioning, but not negative and disorganization symptoms may indicate that the future trajectories of positive symptoms and functioning levels may be more dependent on the previous severity of BSD than these other symptoms. However, this finding should be interpreted with caution. Regarding positive symptoms at follow-up, a quite large amount of the variance was unexplained by the two independent variables in the model: SOPS positive and EASE total at baseline. Considering the baseline characteristics of the non-remission group, it is likely that more severe baseline negative symptoms and functional impairments also explain a considerable amount of the variance in both positive symptoms and level of functioning at follow-up. Secondly, the proportion of the variance in SOPS positive at follow-up explained by BSD could have been lower if the baseline and follow-up SOPS positive subscale scores had been more strongly correlated. It is possible that this association would have been stronger in a more unrestricted sample with respect to the inclusion criteria.

The baseline EASE levels in the twelve cases assessed with schizophrenia spectrum diagnoses (nine with SPD) at follow-up (EASE total = 18.17 ± 6.83) were in line with previous studies of samples with schizotypal disorders (e.g 17.82 ± 6.82 in Nordgaard et al (Nordgaard and Parnas, 2014) and 17.0 ± 7.2 in Raballo and Parnas (Raballo and Parnas, 2012)). These results corroborate the status of BSD as a marker of schizophrenia spectrum conditions. Still, even though the EASE score was higher in this group than in the remaining sample, the difference did not reach statistical significance. A somewhat speculative explanation could be that some of the CHR individuals not meeting criteria for schizophrenia spectrum disorders at follow-up, were predominantly characterized by 'reactive', 'secondary' forms of anomalous self-experiences at baseline, overlapping with transdiagnostic depersonalization and derealization phenomena (Sass et al., 2018; Sass and Borda, 2015). These experiences may still fit with many of the descriptions in the EASE (Madeira et al., 2017; Sass et al., 2013; Vaernes et al., 2018). The predominance of such 'secondary' anomalies may be associated with a smaller risk of meeting criteria for schizophrenia spectrum disorders in the future (Sass et al., 2018). However, as mentioned earlier, we cannot preclude that the non-spectrum subjects in this sample will later meet criteria for a schizophrenia spectrum disorder. Finally, the relatively small sample size may play a role for the lack of a significant difference, increasing the risk for a Type II error.

The high proportion of subjects diagnosed with SPD in the sample (15.2 % at baseline, 28.1 % at follow-up) is not untypical of CHR studies. A recent meta-analytic review of 11 samples with 1313 CHR subjects found that comorbid SPD was present in 13.4 % at baseline (Boldrini et al., 2019). It may also come as no surprise that the number of SPD diagnoses increase in non-remitting, non-transitioning CHR conditions, given that schizotypal disorders are characterized by enduring sub-threshold psychotic symptoms and functional deficits (American Psychiatric Association, 2013; First, 2004; World Health Organization, 1992). It has been suggested that up to 50 % of non-converting CHR cases 'progress' to SPD or a sub-threshold variant of this disorder (Schlosser et al., 2012).

4.1. Strengths and limitations

The broad assessment, including the EASE at baseline, and all SOPS subscales domains and GAF-F at baseline and follow-up, opened up the possibility for assessing a broader range of prospective relationships between BSD, symptoms and functioning than previous CHR studies. The inclusion criteria may be seen as restricting the generalizability of the findings to other CHR individuals, because the sample also included six subjects not meeting conventional CHR time criteria. However, we controlled for this limitation by doing all analyzes with and without the non-progressive symptoms group, and the results were not affected by this. Conclusions from analyses involving the baseline SOPS positive variable, are to some degree limited by the restricted range of SOPS positive symptoms at baseline. This limitation could have been avoided by including a control group of help-seeking individuals, with no restrictions regarding positive symptoms. The lack of a control group and the limited number of participants affected the feasibility of comparative analyses and the generalizability of the findings, and may have increased the risk for both type I and type II errors. However, although we cannot conclude that the significant findings necessarily reflect indisputable effects in the general CHR population, it is of particular interest to find such effects even in such small samples. Finally, it should be noted that TGV, who did all the assessments, was not blind with respect to the baseline assessments when doing the follow-up.

4.2. Conclusion

Overall, this CHR study demonstrated that high levels of baseline BSD were associated with and predicted adverse future clinical and functional outcomes in both non-transitioning and transitioning to psychosis cases. Higher levels of BSD predicted more severe positive symptoms and a lower level of global functioning, after adjusting for baseline levels of these symptoms and functioning. Baseline BSD levels were also associated with more severe negative and disorganization symptoms, and with symptomatic and functional non-remission at the one-year follow-up. This is in line with the proposed trait-like character of BSD, and corroborates its significant status as an important supplemental clinical marker in CHR. Early identification and assessment of BSD in CHR may thus constitute an important prognostic tool and a therapeutic target in these conditions. Relationships between BSD and future clinical and functional outcomes should be further explored in more long-term prospective CHR studies, and with larger samples than the present study.

Author statement

Author statement regarding author contributions

TGV: Conceptualization, Methodology, lnvestigation, Formal Analysis, Writing - original draft, review and editing

JIR: Project Administration, Supervision, Conceptualization, Methodology, lnvestigation, Formal

Analysis, Writing - original draft, review and editing

IM: Formal Analysis, Writing - original draft, review and editing

KLR: Formal Analysis, Writing - original draft, review and editing

BN: Formal Analysis, Writing - original draft, review and editing

PM - Main supervision, Conceptualization, Methodology, lnvestigation, Writing - original draft, review and editing

The authors declare that they have seen and approved the final version of the manuscript being submitted. They warrant that the article is the authors' original work, hasn't received prior publication and isn't under consideration for publication else where.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

References

Addington, J., Cornblatt, B.A., Cadenhead, K.S., Cannon, T.D., McGlashan, T.H., Perkins, D.O., Seidman, L.J., Tsuang, M.T., Walker, E.F., Woods, S.W., Heinssen, R., 2011. At clinical high risk for psychosis: outcome for nonconverters. Am. J. Psychiatry168 (8), 800–805.

Addington, J., Liu, L., Buchy, L., Cadenhead, K.S., Cannon, T.D., Cornblatt, B.A., Perkins, D.O., Seidman, L.J., Tsuang, M.T., Walker, E.F., Woods, S.W., Bearden, C.E., Mathalon, D.H., McGlashan, T.H., 2015. North American Prodrome Longitudinal Study (NAPLS 2): The Prodromal Symptoms. J. Nerv. Ment. Dis.203 (5), 328–335.

Addington, J., Liu, L., Perkins, D.O., Carrion, R.E., Keefe, R.S.E., Woods, S.W., 2017. The Role of Cognition and Social Functioning as Predictors in the Transition to Psychosis for Youth With Attenuated Psychotic Symptoms. Schizophr. Bull.43 (1), 57–63.

American Psychiatric, A., 2013. Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5®). American Psychiatric Publishing, Washington, D.C.

Beck, K., Andreou, C., Studerus, E., Heitz, U., Ittig, S., Leanza, L., Riecher-Rossler, A., 2019a. Clinical and functional long-term outcome of patients at clinical high risk (CHR) for psychosis without transition to psychosis: A systematic review. Schizophr. Res.

Beck, K., Studerus, E., Andreou, C., Egloff, L., Leanza, L., Simon, A.E., Borgwardt, S., Riecher-Rössler, A., 2019b. Clinical and functional ultra-long-term outcome of patients with a clinical high risk (CHR) for psychosis. European Psychiatry 62, 30–37.

Boldrini, T., Tanzilli, A., Pontillo, M., Chirumbolo, A., Vicari, S., Lingiardi, V., 2019. Comorbid Personality Disorders in Individuals With an At-Risk Mental State for Psychosis: A. Meta-Analytic Review. Front. Psychiatry 10, 429.

Carrion, R.E., Demmin, D., Auther, A.M., McLaughlin, D., Olsen, R., Lencz, T., Correll, C. U., Cornblatt, B.A., 2016. Duration of attenuated positive and negative symptoms in individuals at clinical high risk: Associations with risk of conversion to psychosis and functional outcome. J. Psychiatr. Res.81 95–101.

Comparelli, A., Corigliano, V., De Carolis, A., Pucci, D., Angelone, M., Di Pietro, S., Kotzalidis, G.D., Terzariol, L., Manni, L., Trisolini, A., Girardi, P., 2016. Anomalous self-experiences and their relationship with symptoms, neuro-cognition, and functioning in at-risk adolescents and young adults. Comprehens. Psychiatry 65, 44–49.

Davidsen, K.A., 2009. Anomalous self-experience in adolescents at risk of psychosis. Clinical and conceptual elucidation. Psychopathology 42 (6), 361–369.

Ferrarelli, F., Mathalon, D., 2020. The prodromal phase: Time to broaden the scope beyond transition to psychosis? Schizophr. Res.

First, M.B., 1997. Structured clinical interview for DSM-IV Axis I disorders (SCID-I) : clinician version : User's guide for the Structured clinical interview for DSM-IV Axis I disorders. American Psychiatric Press, Washington, D.C.

First, M.B., 2004. DSM-IV-TR guidebook. American Psychiatric Pub., Washington, DC.

Fusar-Poli, P., 2017. The Clinical High-Risk State for Psychosis (CHR-P), Version II. Schizophr. Bull. 43 (1), 44–47.

Fusar-Poli, P., Bechdolf, A., Taylor, M.J., Bonoldi, I., Carpenter, W.T., Yung, A.R., McGuire, P., 2013a. At risk for schizophrenic or affective psychoses? A meta-analysis of DSM/ICD diagnostic outcomes in individuals at high clinical risk. Schizophr. Bull. 39 (4), 923–932.

Fusar-Poli, P., Borgwardt, S., Bechdolf, A., Addington, J., Riecher-Rossler, A., Schultze-Lutter, F., Keshavan, M., Wood, S., Ruhrmann, S., Seidman, L.J., Valmaggia, L., Cannon, T., Velthorst, E., De Haan, L., Cornblatt, B., Bonoldi, I., Birchwood, M., McGlashan, T., Carpenter, W., McGorry, P., Klosterkotter, J., McGuire, P., Yung, A., 2013b. The psychosis high-risk state: a comprehensive state-of-the-art review. JAMA Psychiatry 70 (1), 107–120.

Gross, G., Huber, G., Klosterkkotter, J., Linz, M., 1987. *BSABS: Bonner Skala für die Beurteilung von Basissymptomen Bonn Scale for the Assessment of Basic Symptoms Springer*, London.

Haug, E., Lien, L., Raballo, A., Bratlien, U., Oie, M., Andreassen, O.A., Melle, I., Moller, P., 2012. Selective aggregation of self-disorders in first-treatment DSM-IV schizophrenia spectrum disorders. J. Nerv. Ment. Dis.200 (7), 632–636.

Healey, K.M., Penn, D.L., Perkins, D., Woods, S.W., Keefe, R.S.E., Addington, J., 2017. Latent Profile Analysis and Conversion to Psychosis: Characterizing Subgroups to Enhance Risk Prediction. Schizophr. Bull.

Jimeno, N., Gomez-Pilar, J., Poza, J., Hornero, R., Vogeley, K., Meisenzahl, E., Haidl, T., Rosen, M., Klosterkötter, J., Schultze-Lutter, F., 2020. Main Symptomatic Treatment Targets in Suspected and Early Psychosis: New Insights From Network Analysis. Schizophr. Bull. sbz140.

Koren, D., Tziivoni, Y., Schalit, L., Adres, M., Reznik, N., Apter, A., Parnas, J., et al., 2020. Basic self-disorders in adolescence predict schizophrenia spectrum disorders in young adulthood: A 7-year follow-up study among non-psychotic help-seeking adolescents. Schizophr. Res. 216, 97–103. https://doi.org/10.1016/j.schres.2019.12.022.

Koren, D., Tzivoni, Y., Schalit, L., Adres, M., Reznik, N., Apter, A., Parnas, J., 2019. Basic self-disorders in adolescence predict schizophrenia spectrum disorders in young adulthood: A 7-year follow-up study among non-psychotic help-seeking adolescents. Schizophr. Res.

Koren, D., Reznik, N., Adres, M., Scheyer, R., Apter, A., Parnas, J., 2012. Poster #61 disturbances of the basic self as a core marker of vulnerability to schizophrenia: preliminary results from a 2-year follow-up study among non-psychotic help-seeking adolescents. Schizophr. Res.136 S207.

Koutsouleris, N., Kambeitz-Ilankovic, L., Ruhrmann, S., Rosen, M., Ruef, A., Dwyer, D.B., Paolini, M., Chisholm, K., Kambeitz, J., Haidl, T., Schmidt, A., Gillam, J., Schultze-Lutter, F., Falkai, P., Reiser, M., Riecher-Rössler, A., Upthegrove, R., Hietala, J., Salokangas, R.K.R., Pantelis, C., Meisenzahl, E., Wood, S.J., Beque, D., Brambilla, P., Borgwardt, S., 2018. Prediction Models of Functional Outcomes for Individuals in the Clinical High-Risk State for Psychosis or With Recent-Onset Depression: A Multimodal, Multisite Machine Learning Analysis. JAMA Psychiatry 75 (11), 1156–1172.

Lee, T.Y., Kim, S.N., Correll, C.U., Byun, M.S., Kim, E., Jang, J.H., Kang, D.-H., Yun, J.-Y., Kwon, J.S., 2014. Symptomatic and functional remission of subjects at clinical high risk for psychosis: a 2-year naturalistic observational study. Schizophr. Res.156 (2–3), 266–271.

Lim, J., Rekhi, G., Rapisarda, A., Lam, M., Kraus, M., Keefe, R.S.E., Lee, J., 2015. Impact of psychiatric comorbidity in individuals at Ultra High Risk of psychosis - Findings from the Longitudinal Youth at Risk Study (LYRIKS). Schizophr. Res.164 (1–3), 8–14.

Lin, A., Wood, S.J., Nelson, B., Beavan, A., McGorry, P., Yung, A.R., 2015. Outcomes of nontransitioned cases in a sample at ultra-high risk for psychosis. Am. J. Psychiatry 172 (3), 249–258.

Madeira, L., Carmenates, S., Costa, C., Linhares, L., Stanghellini, G., Figueira, M.L., Sass, L., 2017. Basic Self-Disturbances beyond Schizophrenia: Discrepancies and Affinities in Panic Disorder - An Empirical Clinical Study. Psychopathology 50 (2), 157–168.

McGlashan, T.H., Walsh, B., Woods, S., 2010. *The psychosis-risk syndrome: handbook for diagnosis and follow-up*. Oxford University Press, Oxford.

Mechelli, A., Lin, A., Wood, S., McGorry, P., Amminger, P., Tognin, S., McGuire, P., Young, J., Nelson, B., Yung, A., 2017. Using clinical information to make

individualized prognostic predictions in people at ultra high risk for psychosis. Schizophr. Res.184 32–38.
Miller, T.J., McGlashan, T.H., Rosen, J.L., Cadenhead, K., Cannon, T., Ventura, J., McFarlane, W., Perkins, D.O., Pearlson, G.D., Woods, S.W., 2003. Prodromal assessment with the structured interview for prodromal syndromes and the scale of prodromal symptoms: predictive validity, interrater reliability, and training to reliability. Schizophr. Bull. 29 (4), 703–715.
Miller, T.J., McGlashan, T.H., Rosen, J.L., Somjee, L., Markovich, P.J., Stein, K., Woods, S.W., 2002. Prospective diagnosis of the initial prodrome for schizophrenia based on the Structured Interview for Prodromal Syndromes: preliminary evidence of interrater reliability and predictive validity. Am. J. Psychiatry 159 (5), 863–865.
Miller, T.J., McGlashan, T.H., Woods, S.W., Stein, K., Driesen, N., Corcoran, C.M., Hoffman, R., Davidson, L., 1999. Symptom assessment in schizophrenic prodromal states. Psychiatr. Q. 70 (4), 273–287.
Moller, P., Husby, R., 2000. The initial prodrome in schizophrenia: searching for naturalistic core dimensions of experience and behavior. Schizophr. Bull. 26 (1), 217–232.
Nelson, B., Parnas, J., Sass, L.A., 2014. Disturbance of minimal self (ipseity) in schizophrenia: clarification and current status. Schizophr. Bull. 40 (3), 479–482.
Nelson, B., Raballo, A., 2015. Basic Self-Disturbance in the Schizophrenia Spectrum: Taking Stock and Moving Forward. Psychopathology 48 (5), 301–309.
Nelson, B., Thompson, A., Yung, A.R., 2012. Basic self-disturbance predicts psychosis onset in the ultra high risk for psychosis "prodromal" population. Schizophr. Bull. 38 (6), 1277–1287.
Nelson, B., Yuen, H., Wood, S.J., Lin, A., Spiliotacopoulos, D., Bruxner, A., Broussard, C., Simmons, M., Foley, D.L., Brewer, W., Francey, S.M., Amminger, G.P., Thompson, A., McGorry, P.D., Yung, A., 2013. Long-term Follow-up of a Group at Ultra High Risk ("Prodromal") for Psychosis The PACE 400 Study. JAMA Psychiatry 70 (8), 793–802.
Nordgaard, J., Handest, P., Vollmer-Larsen, A., Saebye, D., Pedersen, J.T., Parnas, J., 2017. Temporal persistence of anomalous self-experience: A 5years follow-up. Schizophr. Res. 179, 36–40.
Nordgaard, J., Parnas, J., 2014. Self-disorders and the schizophrenia spectrum: a study of 100 first hospital admissions. Schizophr. Bull. 40 (6), 1300–1307.
Parnas, J., 2011. A disappearing heritage: the clinical core of schizophrenia. Schizophr. Bull. 37 (6), 1121–1130.
Parnas, J., Handest, P., 2003. Phenomenology of anomalous self-experience in early schizophrenia. Compr. Psychiatry 44 (2), 121–134.
Parnas, J., Handest, P., Jansson, L., Saebye, D., 2005a. Anomalous subjective experience among first-admitted schizophrenia spectrum patients: empirical investigation. Psychopathology 38 (5), 259–267.
Parnas, J., Henriksen, M.G., 2014. Disordered self in the schizophrenia spectrum: a clinical and research perspective. Harvard Review of Psychiatry 22 (5), 251–265.
Parnas, J., Jansson, L., Sass, L.A., Handest, P., 1998. Self-experience in the prodromal phases of schizophrenia: A pilot study of first-admissions. Neurology Psychiatry and Brain Research 6 (2), 97–106.
Parnas, J., Jansson, L.B., 2015. Self-Disorders: Clinical and Conceptual Implications for the Diagnostic Concept of Schizophrenia. Psychopathology 48 (5), 332–338.
Parnas, J., Moller, P., Kircher, T., Thalbitzer, J., Jansson, L., Handest, P., Zahavi, D., 2005b. EASE: Examination of Anomalous Self-Experience. Psychopathology 38 (5), 236–258.
Parnas, J., Raballo, A., Handest, P., Jansson, L., Vollmer-Larsen, A., Saebye, D., 2011. Self-experience in the early phases of schizophrenia: 5-year follow-up of the. Copenhagen Prodromal Study. World Psychiatry 10 (3), 200–204.
Pedersen, G., Hagtvet, K.A., Karterud, S., 2007. Generalizability studies of the Global Assessment of Functioning-Split version. Comprehensive Psychiatry 48 (1), 88–94.
Polari, A., Lavoie, S., Yuen, H.P., Amminger, P., Berger, G., Chen, E., deHaan, L., Hartmann, J., Markulev, C., Melville, F., Nieman, D., Nordentoft, M., Riecher-Rossler, A., Smesny, S., Stratford, J., Verma, S., Yung, A., McGorry, P., Nelson, B., 2018. Clinical trajectories in the ultra-high risk for psychosis population. Schizophr. Res.
Raballo, A., Monducci, E., Ferrara, M., Fiori Nastro, P., Dario, C., 2018. Developmental vulnerability to psychosis: Selective aggregation of basic self-disturbance in early onset schizophrenia. Schizophr. Res.
Raballo, A., Pappagallo, E., Dell' Erba, A., Lo Cascio, N., Patane, M., Gebhardt, E., Boldrini, T., Terzariol, L., Angelone, M., Trisolini, A., Girardi, P., Fiori Nastro, P., 2016. Self-Disorders and Clinical High Risk for Psychosis: An Empirical Study in Help-Seeking Youth Attending Community Mental Health Facilities. Schizophr. Bull. 42 (4), 926–932.
Raballo, A., Parnas, J., 2010. The Silent Side of the Spectrum: Schizotypy and the Schizotaxic Self. Schizophr. Bull.
Raballo, A., Parnas, J., 2012. Examination of anomalous self-experience: initial study of the structure of self-disorders in schizophrenia spectrum. J. Nerv. Ment. Dis.200 (7), 577–583.
Raballo, A., Poletti, M., Preti, A., Parnas, J., et al., 2021. The Self in the Spectrum: A Meta-analysis of the Evidence Linking Basic Self-Disorders and Schizophrenia. Schizophr. Bull. 1–11. https://doi.org/10.1093/schbul/sbaa201. In press.
Sass, L., Borda, J.P., Madeira, L., Pienkos, E., Nelson, B., 2018. Varieties of Self Disorder: A Bio-Pheno-Social Model of Schizophrenia. Schizophr. Bull. 44 (4), 720–727.
Sass, L., Pienkos, E., Nelson, B., Medford, N., 2013. Anomalous self-experience in depersonalization and schizophrenia: a comparative investigation. Consciousness and Cognition 22 (2), 430–441.
Sass, L.A., 2014. Self-disturbance and schizophrenia: structure, specificity, pathogenesis (Current issues, New directions). Schizophr. Res. 152 (1), 5–11.
Sass, L.A., Borda, J.P., 2015. Phenomenology and neurobiology of self disorder in schizophrenia: Secondary factors. Schizophr. Res. 169 (1–3), 474–482.
Sass, L.A., Parnas, J., 2003. Schizophrenia, consciousness, and the self. Schizophr. Bull. 29 (3), 427–444.
Schlosser, D.A., Campellone, T.R., Biagianti, B., Delucchi, K.L., Gard, D.E., Fulford, D., Stuart, B.K., Fisher, M., Loewy, R.L., Vinogradov, S., 2015. Modeling the role of negative symptoms in determining social functioning in individuals at clinical high risk of psychosis. Schizophr. Res. 169 (1–3), 204–208.
Schlosser, D.A., Jacobson, S., Chen, Q., Sugar, C.A., Niendam, T.A., Li, G., Bearden, C.E., Cannon, T.D., 2012. Recovery from an at-risk state: clinical and functional outcomes of putatively prodromal youth who do not develop psychosis. Schizophr. Bull.38 (6), 1225–1233.
Schultze-Lutter, F., Addington, J., Ruhrmann, S., Klosterkotter, J., 2007. Schizophrenia proneness instrument: Adult version (SPI-A).
Schultze-Lutter, F., Michel, C., Schmidt, S.J., Schimmelmann, B.G., Maric, N.P., Salokangas, R.K., Riecher-Rossler, A., van der Gaag, M., Nordentoft, M., Raballo, A., Meneghelli, A., Marshall, M., Morrison, A., Ruhrmann, S., Klosterkotter, J., 2015. EPA guidance on the early detection of clinical high risk states of psychoses. European Psychiatry 30 (3), 405–416.
Schultze-Lutter, F., Nenadic, I., Grant, P., 2019. Psychosis and Schizophrenia-Spectrum Personality Disorders Require Early Detection on Different Symptom Dimensions. Front. Psychiatry 10, 476.
Svendsen, I.H., Oie, M.G., Moller, P., Nelson, B., Haug, E., Melle, I., 2019. Basic self-disturbances independently predict recovery in psychotic disorders: A seven year follow-up study. Schizophr. Res.
Svendsen, I.H., Oie, M.G., Moller, P., Nelson, B., Melle, I., Haug, E., 2018. Stability in basic self-disturbances and diagnosis in a first treated psychosis: A seven year follow-up study. Schizophr. Res.
Vaernes, T.G., Rossberg, J.I., Moller, P., 2018. Anomalous Self-Experiences: Markers of Schizophrenia Vulnerability or Symptoms of Depersonalization Disorder? A Phenomenological Investigation of Two Cases. Psychopathology 1–12.
Vaernes, T.G., Rossberg, J.I., Moller, P., 2019. Anomalous self-experiences are strongly associated with negative symptoms in a clinical high-risk for psychosis sample. Comprehensive Psychiatry 93, 65–72.
Valmaggia, L.R., Stahl, D., Yung, A.R., Nelson, B., Fusar-Poli, P., McGorry, P.D., McGuire, P.K., 2013. Negative psychotic symptoms and impaired role functioning predict transition outcomes in the at-risk mental state: a latent class cluster analysis study. Psychol. Med. 43 (11), 2311–2325.
World Health, O., 1992. The ICD-10 classification of mental and behavioural disorders : clinical descriptions and diagnostic guidelines.
Youn, S., Phillips, L.J., Amminger, G.P., Berger, G., Chen, E.Y.H., de Haan, L., Hartmann, J.A., Hickie, I.B., Lavoie, S., Markulev, C., McGorry, P.D., Mossaheb, N., Nieman, D.H., Nordentoft, M., Riecher-Rossler, A., Schafer, M.R., Schlogelhofer, M., Smesny, S., Thompson, A., Verma, S., Yuen, H.P., Yung, A.R., Nelson, B., 2019. Basic symptoms in young people at ultra-high risk of psychosis: Association with clinical characteristics and outcomes. Schizophr. Res.
Yung, A.R., Nelson, B., Stanford, C., Simmons, M.B., Cosgrave, E.M., Killackey, E., Phillips, L.J., Bechdolf, A., Buckby, J., McGorry, P.D., 2008. Validation of "prodromal" criteria to detect individuals at ultra high risk of psychosis: 2 year follow-up. Schizophr. Res. 105 (1–3), 10–17.
Yung, A.R., Yuen, H.P., McGorry, P.D., Phillips, L.J., Kelly, D., Dell'Olio, M., Francey, S. M., Cosgrave, E.M., Killackey, E., Stanford, C., Godfrey, K., Buckby, J., 2005. Mapping the onset of psychosis: the Comprehensive Assessment of At-Risk Mental States. Aust. N. Z. J. Psychiatry 39 (11-12), 964–971.
Zhang, T., Tang, X., Li, H., Woodberry, K.A., Kline, E.R., Xu, L., Cui, H., Tang, Y., Wei, Y., Li, C., Hui, L., Niznikiewicz, M.A., Shenton, M.E., Keshavan, M.S., Stone, W.S., Wang, J., 2020. Clinical subtypes that predict conversion to psychosis: A canonical correlation analysis study from the ShangHai At Risk for Psychosis program. Aust. N. Z. J. Psychiatry 54 (5), 482–495.

IV

Basic self-disturbance trajectories in clinical high-risk for psychosis – a one year follow-up study

Tor Gunnar Værnes[ab]*, Jan Ivar Røssberg[cd], Ingrid Melle[d], Barnaby Nelson[ef], Kristin Lie Romm[ag], Paul Møller[h]

[a] Early Intervention in Psychosis Advisory Unit for South-East Norway, Division of Mental Health and Addiction, Oslo University Hospital, Norway, [b] Norwegian Centre for Mental Disorders Research, Division of Mental Health and Addiction, Oslo University Hospital, Norway, [c] Psychiatric Research Unit, Division of Mental Health and Addiction, Oslo University Hospital, Norway, [d] Institute of Clinical Medicine, Faculty of Medicine, University of Oslo, Norway, [e] Orygen, Parkville, Victoria, Australia, [f] Centre for Youth Mental Health, the University of Melbourne, Parkville, Victoria, Australia, [g] Institute of Clinical Medicine, Norwegian Centre for Mental Disorders Research, Faculty of Medicine, University of Oslo, Norway, [h] Dept. for Mental Health Research and Development, Division of Mental Health and Addiction, Vestre Viken Hospital Trust, Norway

Abstract

Basic self-disturbance (BSD) has been proposed as a driver of symptom development in schizophrenia spectrum disorders (SSDs). In a one-year follow-up of 32 patients (15-30 years) at putative risk for psychosis, we investigated trajectories of BSD levels from baseline to follow-up, and associations between clinical characteristics at baseline and follow-up, including follow-up levels of BSD (assessed with the EASE). Clinical high-risk (CHR) for psychosis status and symptom severity were assessed with the SIPS/SOPS scales and also according to the cognitive basic symptoms high-risk criteria (COGDIS). DSM-IV diagnoses, functioning and other clinical characteristics were assessed with standard clinical instruments. Higher severity of negative symptoms and meeting COGDIS criteria at baseline were associated with higher BSD levels at follow-up. All measured at follow-up, higher BSD levels correlated with higher severity of positive, negative, disorganization and general symptoms, and with a lower level of global functioning. We found higher BSD levels at follow-up in subjects with schizotypal personality disorder (SPD) at baseline (*n* = 5) and in SSDs at follow-up (*n* = 12, including nine with SPD). Mean BSD levels decreased significantly from baseline to follow-up, but individual trajectories varied considerably. Increased BSD levels were associated with higher baseline BSD, non-remission of positive symptoms and functional decline. Overall, the current study indicates that subgroups in the CHR population with a higher risk of non-remission or deterioration may be identified by supplementing CHR criteria with assessment of BSD and negative symptoms.

Key words: basic self-disturbance/ anomalous self-experience/clinical high-risk for psychosis/UHR/COGDIS/schizophrenia spectrum/functioning/remission

* Tel.: +47 92455678
E-Mail address: uxvrnt@ous-hf.no

1. Introduction

In a phenomenological model of schizophrenia, first developed by Sass and Parnas, a core feature of this disorder is considered a self-disorder, also termed an 'ipseity disturbance' or a 'basic self-disturbance' (BSD). The model describes an instability in the basic sense of self, characterized by 'diminished self-presence', i.e. disturbances in subjectivity and implicit "ownership" of experience and action, 'hyperreflexivity', i.e. an exaggerated self-consciousness involving self-alienation, and 'disturbed grip or hold', involving loss of salience, stability and significance of objects in the field of awareness [35, 36, 62, 65, 67]. BSD is assumed to drive symptom development and articulation over the course of the schizophrenia prodrome, and to underlie and connect the seemingly disparate symptoms of all the schizophrenia spectrum disorders (SSDs) [17, 22, 42, 56, 58, 62, 65, 67, 74].

A range of studies have consecutively demonstrated that SSDs and the schizophrenia prodrome are characterized by a panoply of anomalies of self-experience, assumed to reflect BSD [8, 34, 39, 40, 44, 45, 47, 50, 56-58]. These anomalies have been shown to aggregate in SSDs compared to other diagnostic groups and healthy controls, as described in a recent meta-analysis (e.g. SSD vs. bipolar or affective disorders, Hedges g = 1.8, CI = 1.4 to 2.2, and SSD vs healthy controls, Hedges g = 1.8, CI = 1.5 to 2.0 [57].

In order to detect, and hopefully prevent, development of psychotic disorders, clinical high-risk (CHR) criteria for psychosis are extensively used in research and clinical settings [21, 69, 72]. The CHR concept is currently based on two different sets of criteria: (1) the ultra-high risk (UHR) criteria, and (2) the basic symptoms high-risk criteria [19, 72]. Several studies have demonstrated that BSD phenomena are common in CHR samples [13, 14, 37, 54, 77], although less frequent than in SSDs [57]. However, prospective studies of BSD in CHR samples are sparse. One study found that a higher level of BSD was associated with transition

to psychosis in an UHR sample. Being diagnosed with SSDs (including both psychotic SSDs and schizotypal or schizoid personality disorder) was also associated with higher BSD levels [37]. In a seven-year follow-up study of non-psychotic help-seeking adolescents, future SSD diagnoses were significantly predicted by level of BSD [24]. Finally, in a previous communication from the current research project, we found that non-remission of attenuated psychotic symptoms and functional deficits was associated with higher baseline levels of BSD [80].

To our knowledge, no studies have prospectively investigated the persistence of BSD phenomena in CHR, and how BSD trajectories and BSD levels at follow-up may be related to symptoms, other clinical characteristics and functioning at baseline and follow-up. This is of importance because it may help us identify CHR subjects at the highest risk of adverse clinical and functional outcomes, and to derive a more nuanced picture of the stability of BSD in CHR.

In this exploratory study, our aims were to address the following questions in a one-year follow-up of a CHR sample:

1) To what extent are clinical characteristics and functioning at baseline associated with the severity of BSD at one-year follow-up?
2) To what extent is the severity of BSD at one-year follow-up associated with clinical characteristics and functioning at follow-up?
3) How stable is BSD from baseline to one-year follow-up?
4) Are different BSD trajectories associated with differences in clinical and functional characteristics at baseline, and with changes in these characteristics from baseline to follow-up?

2. Methods

2.1 Setting and participants

The present study was a one-year follow-up of patients from child/adolescent and adult outpatient units in Oslo and adjacent catchment areas (Oslo University Hospital, Diakonhjemmet Hospital, Vestre Viken Hospital Trust and Akershus University Hospital). Patients were referred to the study if they were clinically suspected by their treating clinicians to be at increased risk of psychosis, and were consecutively recruited and assessed at baseline from June 2012 to December 2015. All participants gave written informed consent. For those below 18 years, parents consented as well. The study was part of the Norwegian Thematically Organized Psychosis (TOP) study, and was approved by the Regional Committee for Medical Research Ethics in Norway (permission number 2011/1070 D).

Inclusion criteria were age between 15 and 30 years, and meeting CHR criteria for one or more of the following UHR syndromes: the Attenuated Positive Symptom Syndrome (APSS), the Brief Intermittent Psychotic Symptoms (BIPS) syndrome or the Genetic Risk and Deterioration (GRD) syndrome, as outlined in the Structured Interview for Prodromal Syndromes (SIPS) [29], Norwegian version 3.1 (see Table 1). An APSS syndrome in this SIPS version does not require social/occupational dysfunction, as in the CAARMS attenuated psychosis group [20], or distress/disability, as in the DSM-5 APS syndrome [1, 61].

In addition, we did not exclude patients with longstanding, non-progressive attenuated psychotic symptoms. They met criteria for an APSS syndrome [29], except the recent onset/progression criteria. We termed these subjects the ‘non-progressive symptoms group’. They would possibly have met the criteria for an APSS syndrome with the ‘current status specifier’ ‘persistence’ in the current version of the SIPS (version 5.6) [81]. Subjects with persistent risk symptoms may be at risk of a range of adverse clinical and functional

outcomes, although the risk for conversion to psychosis is lower than in CHR subjects with progressive symptoms [3, 18, 68, 81]. All subjects were also assessed with respect to cognitive basic symptoms high-risk criteria (COGDIS) during the following baseline assessments. See Table 1 for detailed descriptions of the UHR, COGDIS and non-progressive symptoms group criteria [70].

Table 1 in here

We excluded subjects who met one or more of the following criteria: current or past psychotic disorder (DSM-IV Axis 1 criteria), being treated with antipsychotics currently or for ≥ 4 weeks lifetime (dose equivalent to ≥ 5 mg Olanzapine per day), clearly drug-induced CHR symptoms, neurological disorders or severe medical conditions, intellectual disability (IQ < 70), and incapacity to speak/comprehend Norwegian.

The original baseline sample comprised 38 participants, including seven in the non-progressive symptoms group. Six subjects (5 CHR, 1 non-progressive) did not take part in the assessments at follow-up, i.e. a drop-out rate of 15.8%. Hence, 32 subjects took part in the current follow-up study, including six in the non-progressive symptoms group. There were no significant differences in baseline demographic or clinical characteristics between these 32 and the six drop-outs (supplementary material S1. The original baseline sample is also described in a previous study [77]).

2.2 Measures and procedure

2.2.1 Baseline assessments

Baseline assessments included socio-demographic data and the Structured Interview for Prodromal Syndromes/Scale of Prodromal Symptoms (SIPS/SOPS) [29, 30], Norwegian version 3.1, Jan 2005. The SIPS/SOPS was used for assessing UHR criteria and non-

progressive symptoms criteria, and the last month severity of positive, negative, disorganization and general symptoms (ranging each symptom on the SOPS from 0 = absent to 6 = psychotic/extreme) [31]. Interrater reliability regarding SOPS scores and prodromal/psychosis-risk syndrome diagnostic agreement have been found to be excellent in early studies and in a more recent review [29, 30, 82]. Studies are sparse, but also find the predictive and construct validity of the SIPS/SOPS to be satisfactory [82]. The non-progressive symptoms criteria were not tested for validity and reliability. Considering the overlap with criteria for the CHR "persistence" syndrome, it could be noted that this new CHR classification system has shown promising validity [81].

BSD phenomena were assessed with the Examination of Anomalous Self-Experiences (EASE) (life-time experiences). The EASE comprises 57 main items organized in five domains: (1) Cognition and stream of consciousness, (2) Self-Awareness and presence, (3) Bodily experiences, (4) Demarcation/Transitivism, and (5) Existential reorientation (supplementary material S2) [49]. All EASE items were scored on a 0-4 severity Likert scale, but following other similar studies [24, 39, 54] we subsequently converted these scores into dichotomous 0-1 scores, indicating that the symptom had been absent or questionably present (0), or definitively present (1). The EASE has been found to have good to excellent internal consistency and interrater reliability [33, 37, 41, 55]. SIPS and EASE interviews were videotaped at baseline and follow-up. Based on retrospective inspection of the baseline EASE interviews, we did an additional baseline scoring of all the EASE items (0-1 scores), reflecting present or last year experiences. COGDIS criteria were assessed according to descriptions in the Schizophrenia Proneness Instrument – Adult version (SPI-A) [70], using all available information including the EASE and SIPS interviews. There is considerable overlap between the descriptions of the COGDIS symptoms in the SPI-A and certain EASE

items [49, 70]. The SPI-A has demonstrated good inter-rater reliability [71], and the predictive validity of the COGDIS criteria is comparable to the UHR criteria [60, 72].

Clinical DSM-IV Axis I diagnoses were allocated after an assessment with a full version of the SCID-I [16]. A checklist included in the SIPS for the DSM-IV criteria for Schizotypal Personality Disorder (SPD) was used for assessment of this disorder. We categorized SPD as schizophrenia spectrum disorder, in line with DSM-5 and the understanding of SPD among experts in the field [1, 15, 48, 73]. Present (last week) global functioning was assessed with a split version of the Global Assessment of Functioning scale (S-GAF). S-GAF is divided into a symptom score and a functioning score, ranging in severity from 0 (extreme dysfunction) to 100 (superior function) [51]. Only the functioning scores (GAF-F) are reported here. Childhood (0-11 years) and early adolescent (12-15 years) functioning were assessed with the Premorbid Adjustment Scale (PAS) [9], and adverse childhood experiences with the self-report inventory Childhood Trauma Questionnaire – short form (CTQ-SF) [6]. CTQ-SF include 28 items and categorize experiences in five domains: physical abuse, sexual abuse, emotional abuse, emotional neglect and physical neglect [5].

2.2.2 Follow-up assessments

At follow-up, we did a reassessment with the SIPS/SOPS (based on last month), the EASE (covering last year, since baseline) and GAF-F (based on last week). In line with a recent recommendation from clinical and research experts in the field [52], we used a combined symptomatic and functional measure of remission. This was defined as a score of ≤ 2 on all SOPS positive symptom items, in combination with a score of $\geq$70 points or $\geq$10 points improvement on GAF-F (corresponding, but not identical, to the measure suggested by Polari et al. [52]). In the case of transition to psychosis between baseline and follow-up (reported from treating clinicians), this was evaluated according to the criteria for a psychotic syndrome in the SIPS [29, 30], followed by a differential diagnostic assessment with the SCID-I,

module 1, A-E chapters [16]. Non-transitioning subjects were not reassessed with the SCID-I, but all participants were reassessed at follow-up with the SPD checklist in the SIPS.

Clinical interviews at baseline and follow-up were performed by TGV. He had participated in the TOP study SCID-I reliability and training program, and had been trained in the use of the SIPS and EASE by Norwegian experts in the field, including supervision in the use of EASE by PM, one of the authors and certified instructors of the EASE. Inter-rater reliability was tested on the SIPS and EASE, revealing excellent reliability for the SIPS and moderate reliability for the EASE (for details, see [77]). DSM-IV diagnoses, CHR status and EASE scores were regularly discussed with PM and JIR, both experienced researchers and psychiatrists.

2.3 Statistical analysis

All statistical analyses were performed with SPSS version 25.0. Non-parametric tests were used, and if not otherwise specified, the significance threshold was set at .05. The severity level of BSD was determined by summing up the dichotomous 0-1 scores on all the 57 main EASE items, giving an EASE total score. Likewise, the severity level of positive, negative, disorganization and general symptoms was determined by summing up the scores on the SOPS subscales. All tests of normality of the distribution of scores were conducted with the Kolmogorov-Smirnov statistic, and we inspected skewness and kurtosis values. Group comparisons of categorical variables were conducted with chi-square statistics.

The EASE total scores at follow-up were positively skewed, clustering at the low values. Correlations between EASE total at follow-up and continuous variables at baseline (first research question) and follow-up (second research question) were tested with Spearman's rho (two-tailed). These analyses were Bonferroni-adjusted for multiple comparisons (alpha level $p < .006$ (.05/9 variables) in the first analysis, and $p < .01$ (.05/5 variables) in the second

analysis. In the first analysis, we included the CTQ subscale Emotional neglect, but not the other CTQ subscales, given a stronger association ($p < .05$) with EASE total at baseline [77]. Analyses of whether differences in EASE total at follow-up were associated with categorical variables at baseline or follow-up were conducted with the Mann-Whitney U Test.

To answer the third and fourth research question, we used the Wilcoxon signed rank test to analyze differences in EASE total between baseline and follow-up. Baseline EASE total scores based on current/last year experiences were included in these analysis (thus comparing the presence of anomalous self-experiences from one year to the next year). One outlier with the strongest increase in EASE scores was included in the analyses, as the inclusion of this outlier did not significantly affect the results.

By inspection of the individual EASE trajectories, we did an ad hoc categorization into three groups: 1) subjects with an *increase* (≥1 points) in EASE total, 2) subjects with *0-3 points decline* in EASE total and 3) subjects with *>3 points decline* in EASE total. We chose this approach over statistical clustering approaches due to the small sample size. Four SOPS subscale change variables and a GAF-F change variable were computed (follow-up minus baseline scores). Differences between the three groups in the scores on the baseline variables and the scores on the SOPS change and GAF-F change variables were analyzed with the Kruskal-Wallis test.

3. Results

3.1 Demographics and clinical characteristics at baseline and one-year follow-up

Twenty-six participants were meeting formal CHR criteria, and six were assessed as 'non-progressive', at baseline. A majority (n = 24, 92%) met criteria for an APSS syndrome, either

alone or in combination with COGDIS criteria or a GRD syndrome (only one). In table 2, demographic and clinical characteristics of the sample (n = 32) are shown. The six participants in the non-progressive symptoms group did not differ significantly from the CHR group in clinical or demographic characteristics, except for being approximately five years older and having approximately one more year of education (supplementary material S3). Medication at baseline had no association to clinical variables at baseline.

Insert Table 2 here

The mean follow-up time was 13 months (Sd = 1.7). The participants received treatment as usual at their local health services between baseline and follow-up, including standard medication, psychotherapy and psychosocial interventions (e.g. family support and work/school adjustments). Outcomes at follow-up were not significantly affected by these treatment variables, or by hospitalizations or discontinuation of treatment. Investigations of relationships between demographic characteristics and clinical and functional outcomes at baseline or follow-up did not reveal any significant associations.

Among the four participants who transitioned to psychosis, three were assigned a DSM-IV SSD diagnosis (2 schizophrenia, 1 schizophreniform disorder). The fourth was diagnosed with DSM-IV Psychosis NOS. Nine were diagnosed with SPD at follow-up (increased from five at baseline). We categorized these nine as schizophrenia spectrum subjects, along with the three with schizophrenia and schizophreniform disorder (n = 12, i.e. 37.5 % of the sample).

3.2 Clinical characteristics at baseline were associated with EASE total at follow-up

Correlations between baseline variables and EASE total at follow-up are shown in Table 3. The scores on the SOPS negative, SOPS disorganization and PAS Early Adolescence subscales correlated with EASE total at a significance level of $p < .05$, but after Bonferroni-

correction ($p < .006$), only the association with SOPS negative was statistically significant, with a large effect size ($r = .58$).

Insert Table 3 here

Subjects meeting COGDIS criteria ($n = 12$) had significantly higher follow-up EASE total scores ($Md = 18$) than the other participants ($n = 20$, $Md = 4.5$), $U = 59.5$, $p = .02$, with a medium effect size ($r = .42$). This difference remained significant when EASE items clearly overlapping with COGDIS items (EASE items 1.1, 1.3, 1.4, 1.12, 1.17 and 5.1) were removed from the EASE total score, $U = 64$, $p = .03$. Baseline SPD subjects also had significantly higher EASE total scores at follow-up ($n = 5$, $Md = 21$) than the other subjects ($n = 27$, $Md = 6$), $U = 28.5$, $p = .04$, $r = .36$.

3.3 Clinical characteristics and functioning at follow-up was associated with EASE total at follow-up

All SOPS subscales and GAF-F at follow-up was significantly associated with EASE total at follow-up (Table 4), with large effect sizes ($r > .60$) for all these correlations.

Insert Table 4 here

SSD subjects ($n = 12$, at follow-up) had significantly higher EASE total scores at follow-up ($Md = 16.5$) than subjects with no SSD ($n = 20$, $Md = 4.5$), $U = 194.5$, $p = .003$, $r = .51$ (highest in the three SSDs with psychotic disorders: $Md = 28$, SPD subjects: $Md = 12$). These SSD subjects also scored significantly higher on all the SOPS subscales at follow-up (SOPS positive and SOPS disorganization: $p < .001$, SOPS negative: $p = .004$), except for SOPS general ($p = .08$), and at a significantly lower level of GAF-F ($p = .003$). Among non-remitted subjects ($n = 21$), eleven were diagnosed with SSDs (9 of 11 with SPD) at follow-up. The

non-remitted subjects (n = 21) had significantly higher EASE total scores at follow-up (Md = 14.5) than the fully remitted subjects (n = 11, Md = 1), U = 16.5, p < .001.

3.4 EASE level trajectories, and their associations with clinical and other characteristics from baseline to follow-up

Individual trajectories of EASE scores from baseline to follow-up are illustrated in figure 1. Median EASE total in the full sample decreased from 12 at baseline to 8.5 at follow-up. This was a significant decline (z = -2.47, p =.01), with a moderate effect size (r = .31). There was one outlier with a very strong increase in EASE total (see figure 1). The significant decline in EASE total scores from baseline to follow-up was found in females (z = -2.94, p = .003), but not in males (z = -1.81, p = .07). Males scored nominally higher on EASE total at follow-up (Md = 12, n = 21) than females (Md = 4, n = 11), but this difference was not significant (U = 163.5, p = .06).

Insert Figure 1 here

Breaking the total sample down into three groups, seven subjects (21.9 %) had an ≥1 point increase in EASE total from baseline (Md = 21) to follow-up (Md = 27), twelve subjects (37.5 %) had a 0-3 points decline (baseline: Md = 6, follow-up: Md = 4.5), and thirteen subjects (40.6 %) had a >3 points decline (baseline: Md = 16, follow-up: Md = 8). The mean changes in EASE total scores for the three groups are illustrated in figure 2. Patients diagnosed with SSDs at follow-up (n = 12) did not have a significant decline in EASE total (baseline: Md = 18.5, follow-up: Md = 16.5), z = -0.45, p = .96. However, SSD subjects were found in all three groups: five increased, four declined 0-3 points, and three declined >3 points.

Insert Figure 2 here

Analyses revealed a statistically significant difference in baseline EASE levels between the three groups, χ^2 (2, n = 32) = 14.06, p =.001. Post hoc comparison tests (Mann Whitney U) revealed that the median EASE total score for the 'EASE 0-3 points decline group' (*Md* = 6) was significantly lower than the median score in both the 'EASE increase group' (*Md* = 21, p = .007) and the 'EASE >3 points decline group' (*Md* = 16, p = .003). Further analyses showed no other significant differences in baseline characteristics between the three groups.

Analyses of differences between the three trajectory groups revealed significant differences in SOPS positive change (χ^2 (2, n = 32) = 11.25 , p = .004) and in GAF-F change (χ^2 (2, n = 32) = = 9.11, p = .01), but not in the other three SOPS change variables. Mean change scores for the three groups are illustrated in table 5. As can be seen, there was a nominal *increase* in positive symptoms and a decreased functioning in the EASE increase group. This contrasted significantly with the *decrease* in positive symptoms and the increased functioning at follow-up in the two other groups.

Insert table 5 here

4. Discussion

4.1 Baseline characteristics and EASE total at follow-up

The strong, positive correlation between baseline negative symptoms and BSD levels at one-year follow-up was in line with the strong association between negative symptoms and BSD levels at baseline found in a previous study of this sample (also including the six drop-outs) [77]. This may imply that a higher severity of negative symptoms in CHR may be associated with a higher probability of sustained or recurring high BSD levels as future outcomes. However, this of course does not necessarily mean that negative symptoms *cause* BSD, or vice versa. Phenomenologically oriented theories suggest that negative symptoms (along with

other clinical manifestations) are meaningful, intimately interconnected aspects of an underlying psychopathological ”Gestalt”, characterized by disturbances in the structure of subjectivity, i.e. BSD [42, 64, 67]. Basic symptoms may also constitute such aspects [43-45], thus possibly explaining that subjects meeting COGDIS criteria at baseline had higher levels of BSD at follow-up than the other participants (also when removing EASE items from the analyses clearly overlapping with the COGDIS items). The significantly higher BSD levels at follow-up, as well as at baseline [77], in subjects assessed with SPD at baseline, were in line with other studies demonstrating that SPD and ICD-10 schizotypal disorder are associated with BSD levels markedly higher than in conditions outside of the schizophrenia spectrum [22, 40, 55, 57].

The results indicated better outcomes in females than males with respect to future BSD levels (a significant decline). Studies have found more severe negative symptoms and poorer social functioning in CHR males [2, 59], which are characteristics associated with poorer clinical and functional prognosis in several studies, e.g. [4, 10, 25, 68]. Considering that BSD levels and negative symptoms were strongly associated in this study, the better outcome in females seems not surprising. However, the severity of negative symptoms was only nominally higher in males at both time points. Gender differences are underexplored as a research topic in CHR studies, and have been found to be rather small [28]. Hence, the differences found in the current and other studies should be investigated in larger samples.

We can only speculate about the lack of a significant effect of medication and other aspects of treatment on EASE total and other clinical variables at baseline and follow-up. The small sample size may have diminished the probability of finding such effects. The effect of medication on BSD is another underexplored field, and for the majority of subjects prescribed antipsychotics, daily doses were considerably below what is considered having an antipsychotic effect.

4.2 EASE total at follow-up vs. other characteristics at follow-up

The strong associations at follow-up between high BSD levels, lower level of global functioning and higher severity of symptoms on all SOPS subscales, point to a consolidation of a psychopathological Gestalt with BSD as a core feature, accruing as time has passed. The more severe clinical pattern found in SSD subjects fits well with the BSD/ipseity disturbance model [36, 42, 48, 65, 67]. An alternative hypothesis is that BSD may be a marker of elevated (severe) levels of a "general psychopathology" (*p*) factor crossing symptomatic domains and diagnostic boundaries [11], increasing the risk of the psychopathological expressions typically found in the SSDs.

Our results contrast to some extent with the findings in a 5-year follow-up study, investigating associations between BSD levels, positive and negative symptoms, and functioning in schizophrenia spectrum patients [39]. In this study, only positive symptoms at follow-up correlated with BSD levels at follow-up. In addition, significant correlations were found between baseline BSD and global symptom levels at baseline and follow-up [39]. It is likely that the difference between these two studies is due to stronger diagnostic homogeneity and higher severity of the sample in the 5-year follow-up study, in comparison with the heterogeneous CHR sample in the current study.

A possible explanation for the weaker correlations between baseline SOPS subscale and GAF-F variables and BSD levels at follow-up, compared to the correlations only including follow-up equivalents of these variables, could be that the symptoms measured by SOPS and GAF are affected by many other factors than BSD in early CHR conditions. Attenuated psychotic symptoms are not uncommon in youth with mental health concerns and functional decline [12, 76, 79], and not even in the general population [23, 26]. These attenuated symptoms may constitute quite non-specific reactions to stressful conditions, rather than be driven by BSD [32]. Hence, they may also be of a transient or fluctuating nature in many

CHR subjects. In addition, weaker correlations at baseline between BSD and positive symptoms may reflect a more restricted range of positive symptoms at baseline, due to the inclusion criteria. Dysfunction in CHR may also vary and improve as time unfolds [68], though it may also have a non-remitting or even deteriorating course in these conditions [38, 68].

4.3 Changes in EASE total and associations with other characteristics

Median BSD levels decreased in the total sample, but individual BSD trajectories varied considerably. This might indicate that BSD is not unconditionally trait-like and stable in CHR conditions. According to a recent update of the self-disorder model [7, 62, 66], some BSD phenomena may have a 'secondary', reactive, state-like quality, due to the interaction between adverse environmental circumstances and individual vulnerabilities. These are assumed to occur in SSDs, but also in dissociative and anxiety conditions [27, 63, 78]. Possibly, they are also frequent in CHR conditions. Other BSD phenomena may be more 'primary', 'automatic', stable features, possibly resulting from early neurodevelopmental disturbances [53]. These may be more specific to SSDs and prodromal schizophrenia. Individual differences in the predominance of primary versus secondary BSD phenomena could possibly manifest in different BSD trajectories.

As a group, subjects with SSD diagnoses at follow-up did not show a significant decline in BSD levels, but some had and increase while others were quite stable or had a marked decline. The EASE increase group (5 of 7 with SSDs) was characterized by a more severe clinical pattern, including higher baseline levels of BSD, and symptomatic and functional non-remission at follow-up. Svendsen et al. [75] also found increasing, stable and decreasing BSD levels in patients with schizophrenia. As suggested by these authors, BSD levels may be more influenced by individual characteristics, including response to treatment, than previously thought [8, 46]. In the current study, subjects with a 0-3 points decline in EASE

total had significantly lower BSD levels at baseline than the other participants. Given the low levels at baseline, which implies a good prognostic sign, it is not surprising that these levels were still low and stable at follow-up.

The updated BSD model remains to be properly tested. This would require prospective studies in larger samples than the current study, investigating the presence and stability of BSD in patients from different diagnostic groups, and addressing both intra-individual patterns and inter-individual differences. It should also be noted that changes in EASE scores may not necessarily reflect more or less anomalous self-experiences, but may also be due to variations in the "availability" (mental awareness) of experiences for the person, and the ability to communicate them [34, 49].

5. Limitations

The firmness of the conclusions is restricted due to the small sample size, which also included the 'non-progressive symptoms group'. We partly controlled for this limitation by doing all analyses with and without the 'non-progressive' subjects, and this did not affect the results. Analyses comparing the small sub-groups in the sample may have increased the risk of type 1 and type II errors. Including a larger control group of help-seeking non-CHR subjects with no positive symptom inclusion criterion, would have been appropriate to avoid the problem of the restricted range of positive symptoms at baseline. This would also have increased the possibility of doing comparative analyses, and thus the generalizability of the results. The ad hoc approach to the categorization of BSD trajectories in three groups is another limitation. Finally, the rater doing the follow-up assessments should have been blind to the baseline findings. On the other hand, this is to our knowledge the first CHR study investigating with the full EASE scale at two time points. In light of the small sample, findings are primarily of interest in order to generate hypotheses well worth investigating in larger samples.

6. Conclusions

This study found that CHR subjects characterized by more severe negative symptoms, cognitive disturbances and higher BSD levels at baseline were particularly vulnerable for a consolidation of a comprehensive psychopathological Gestalt as time passed, with BSD as a core feature. In line with the BSD model, this consolidation was more common in subjects with SSDs (9 of 12 with SPD) at follow-up. The general decrease in BSD levels, together with the individual variations in BSD trajectories, indicated that BSD phenomena in CHR conditions may vary with respect to having a state-like or a trait-like character, in line with the updated self-disorder model [62]. Increasing BSD levels may constitute a marker of a non-remitting or even progressively worsening symptomatic and functional course. Taken together, the results demonstrated that longitudinal investigations of BSD are helpful in identifying CHR subjects at particularly high risk for adverse symptomatic and functional outcomes, even in non-converting to psychosis cases. If replicated in prospective CHR studies with larger samples, these findings may contribute considerably to the clinical identification of such particularly vulnerable CHR subjects.

Declaration of interests

The authors declare that they have no conflicts of interest concerning this article.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Ethical standards

All participants gave written informed consent. For those below 18 years, parents consented as well. The study was approved by the Regional Committee for Medical Research Ethics (REC South-East) in Norway (permission number 2011/1070 D), and was conducted in accordance with the 1964 Declaration of Helsinki.

References

1. American Psychiatric A (2013) Diagnostic and statistical manual of mental disorders, fifth edition (dsm-5®). American Psychiatric Publishing, Washington, D.C.
2. Barajas A, Ochoa S, Obiols JE, Lalucat-Jo L (2015) Gender differences in individuals at high-risk of psychosis: A comprehensive literature review. TheScientificWorldJournal 2015:430735
3. Beck K, Andreou C, Studerus E, Heitz U, Ittig S, Leanza L, Riecher-Rossler A (2019) Clinical and functional long-term outcome of patients at clinical high risk (chr) for psychosis without transition to psychosis: A systematic review. Schizophr Res
4. Beck K, Studerus E, Andreou C, Egloff L, Leanza L, Simon AE, Borgwardt S, Riecher-Rössler A (2019) Clinical and functional ultra-long-term outcome of patients with a clinical high risk (chr) for psychosis. Eur Psychiatry 62:30-37
5. Bernstein DP, Ahluvalia T, Pogge D, Handelsman L (1997) Validity of the childhood trauma questionnaire in an adolescent psychiatric population. Journal of the American Academy of Child & Adolescent Psychiatry 36:340-348
6. Bernstein DP, Stein JA, Newcomb MD, Walker E, Pogge D, Ahluvalia T, Stokes J, Handelsman L, Medrano M, Desmond D, Zule W (2003) Development and validation of a brief screening version of the childhood trauma questionnaire. Child Abuse Negl 27:169-190
7. Borda JP, Sass LA (2015) Phenomenology and neurobiology of self disorder in schizophrenia: Primary factors. Schizophr Res 169:464-473
8. Bovet P, Parnas J (1993) Schizophrenic delusions: A phenomenological approach. SchizophrBull 19:579-597
9. Cannon-Spoor HE, Potkin SG, Wyatt RJ (1982) Measurement of premorbid adjustment in chronic schizophrenia. Schizophr Bull 8:470-484
10. Carrion RE, Demmin D, Auther AM, McLaughlin D, Olsen R, Lencz T, Correll CU, Cornblatt BA (2016) Duration of attenuated positive and negative symptoms in individuals at clinical high risk: Associations with risk of conversion to psychosis and functional outcome. J Psychiatr Res 81:95-101
11. Caspi A, Moffitt TE (2018) All for one and one for all: Mental disorders in one dimension. Am J Psychiatry 175:831-844
12. Clarke S, Hanna D, Davidson S, Shannon C, Mulholland C (2020) The association between sleep quality and attenuated psychotic symptoms. Early Interv Psychiatry
13. Comparelli A, Corigliano V, De Carolis A, Pucci D, Angelone M, Di Pietro S, Kotzalidis GD, Terzariol L, Manni L, Trisolini A, Girardi P (2016) Anomalous self-experiences and their relationship with symptoms, neuro-cognition, and functioning in at-risk adolescents and young adults. Compr Psychiatry 65:44-49
14. Davidsen KA (2009) Anomalous self-experience in adolescents at risk of psychosis. Clinical and conceptual elucidation. Psychopathology 42:361-369

15. Ettinger U, Meyhofer I, Steffens M, Wagner M, Koutsouleris N (2014) Genetics, cognition, and neurobiology of schizotypal personality: A review of the overlap with schizophrenia. Frontiers in psychiatry 5:18
16. First MB (1997) Structured clinical interview for dsm-iv axis i disorders (scid-i) : Clinician version : User's guide for the structured clinical interview for dsm-iv axis i disorders. American Psychiatric Press, Washington, D.C
17. Fuchs T (2015) From self-disorders to ego disorders. Psychopathology 48:324-331
18. Fusar-Poli P, Bonoldi I, Yung AR, Borgwardt S, Kempton MJ, Valmaggia L, Barale F, Caverzasi E, McGuire P (2012) Predicting psychosis: Meta-analysis of transition outcomes in individuals at high clinical risk. Archives of general psychiatry 69:220
19. Fusar-Poli P, Borgwardt S, Bechdolf A, Addington J, Riecher-Rossler A, Schultze-Lutter F, Keshavan M, Wood S, Ruhrmann S, Seidman LJ, Valmaggia L, Cannon T, Velthorst E, De Haan L, Cornblatt B, Bonoldi I, Birchwood M, McGlashan T, Carpenter W, McGorry P, Klosterkotter J, McGuire P, Yung A (2013) The psychosis high-risk state: A comprehensive state-of-the-art review. JAMA psychiatry 70:107-120
20. Fusar-Poli P, Cappucciati M, Rutigliano G, Lee TY, Beverly Q, Bonoldi I, Lelli J, Kaar SJ, Gago E, Rocchetti M, Patel R, Bhavsar V, Tognin S, Badger S, Calem M, Lim K, Kwon JS, Perez J, McGuire P (2016) Towards a standard psychometric diagnostic interview for subjects at ultra high risk of psychosis: Caarms versus sips. Psychiatry journal 2016:7146341
21. Fusar-Poli P, Salazar de Pablo G, Correll CU, Meyer-Lindenberg A, Millan MJ, Borgwardt S, Galderisi S, Bechdolf A, Pfennig A, Kessing LV, van Amelsvoort T, Nieman DH, Domschke K, Krebs MO, Koutsouleris N, McGuire P, Do KQ, Arango C (2020) Prevention of psychosis: Advances in detection, prognosis, and intervention. JAMA psychiatry
22. Handest P, Parnas J (2005) Clinical characteristics of first-admitted patients with icd-10 schizotypal disorder. BrJPsychiatry Suppl 187:s49-s54
23. Kelleher I, Connor D, Clarke MC, Devlin N, Harley M, Cannon M (2012) Prevalence of psychotic symptoms in childhood and adolescence: A systematic review and meta-analysis of population-based studies. Psychol Med 42:1857-1863
24. Koren D, Tzivoni Y, Schalit L, Adres M, Reznik N, Apter A, Parnas J (2019) Basic self-disorders in adolescence predict schizophrenia spectrum disorders in young adulthood: A 7-year follow-up study among non-psychotic help-seeking adolescents. Schizophr Res
25. Koutsouleris N, Kambeitz-Ilankovic L, Ruhrmann S, Rosen M, Ruef A, Dwyer DB, Paolini M, Chisholm K, Kambeitz J, Haidl T, Schmidt A, Gillam J, Schultze-Lutter F, Falkai P, Reiser M, Riecher-Rössler A, Upthegrove R, Hietala J, Salokangas RKR, Pantelis C, Meisenzahl E, Wood SJ, Beque D, Brambilla P, Borgwardt S (2018) Prediction models of functional outcomes for individuals in the clinical high-risk state for psychosis or with recent-onset depression: A multimodal, multisite machine learning analysis. JAMA psychiatry 75:1156-1172
26. Linscott R, van Os J (2013) An updated and conservative systematic review and meta-analysis of epidemiological evidence on psychotic experiences in children and adults: On the pathway from proneness to persistence to dimensional expression across mental disorders. In:Cambridge University Press, Cambridge, p 1133-1149
27. Madeira L, Carmenates S, Costa C, Linhares L, Stanghellini G, Figueira ML, Sass L (2017) Basic self-disturbances beyond schizophrenia: Discrepancies and affinities in panic disorder - an empirical clinical study. Psychopathology 50:157-168
28. Menghini-Müller S, Studerus E, Ittig S, Heitz U, Egloff L, Andreou C, Valmaggia LR, Kempton MJ, van der Gaag M, de Haan L, Nelson B, Barrantes-Vidal N, Nordentoft M, Ruhrmann S, Sachs G, Rutten BP, Os JV, Riecher-Rössler A, McGuire P, Valmaggia LR, Kempton MJ, Calem M, Tognin S, Modinos G, de Haan L, van der Gaag M, Velthorst E, Kraan TC, van Dam DS, Burger N, Nelson B, McGorry P, Amminger GP, Pantelis C, Politis A, Goodall J, Riecher-Rössler A, Borgwardt S, Rapp C, Ittig S, Studerus E, Smieskova R, Bressan R, Gadelha A, Brietzke E, Asevedo G, Asevedo E, Zugman A, Barrantes-Vidal N, Domínguez-Martínez T, Racioppi A, Cristóbal-Narváez P, Kwapil TR, Monsonet M, Kazes M, Daban C, Bourgin J, Gay O, Mam-Lam-

Fook C, Krebs MO, Nordholm D, Randers L, Krakauer K, Glenthøj L, Glenthøj B, Nordentoft M, Ruhrmann S, Gebhard D, Arnhold J, Klosterkötter J, Sachs G, Lasser I, Winklbaur B, Delespaul PA, Rutten BP, van Os J (2019) Gender differences of patients at-risk for psychosis regarding symptomatology, drug use, comorbidity and functioning - results from the eu-gei study. Eur Psychiatry 59:52-59
29. Miller TJ, McGlashan TH, Rosen JL, Cadenhead K, Cannon T, Ventura J, McFarlane W, Perkins DO, Pearlson GD, Woods SW (2003) Prodromal assessment with the structured interview for prodromal syndromes and the scale of prodromal symptoms: Predictive validity, interrater reliability, and training to reliability. SchizophrBull 29:703-715
30. Miller TJ, McGlashan TH, Rosen JL, Somjee L, Markovich PJ, Stein K, Woods SW (2002) Prospective diagnosis of the initial prodrome for schizophrenia based on the structured interview for prodromal syndromes: Preliminary evidence of interrater reliability and predictive validity. AmJPsychiatry 159:863-865
31. Miller TJ, McGlashan TH, Woods SW, Stein K, Driesen N, Corcoran CM, Hoffman R, Davidson L (1999) Symptom assessment in schizophrenic prodromal states. PsychiatrQ 70:273-287
32. Millman ZB, Pitts SC, Thompson E, Kline ER, Demro C, Weintraub MJ, DeVylder JE, Mittal VA, Reeves GM, Schiffman J (2018) Perceived social stress and symptom severity among help-seeking adolescents with versus without clinical high-risk for psychosis. Schizophr Res 192:364-370
33. Moller P, Haug E, Raballo A, Parnas J, Melle I (2011) Examination of anomalous self-experience in first-episode psychosis: Interrater reliability. Psychopathology 44:386-390
34. Moller P, Husby R (2000) The initial prodrome in schizophrenia: Searching for naturalistic core dimensions of experience and behavior. SchizophrBull 26:217-232
35. Nelson B, Parnas J, Sass LA (2014) Disturbance of minimal self (ipseity) in schizophrenia: Clarification and current status. Schizophr Bull 40:479-482
36. Nelson B, Raballo A (2015) Basic self-disturbance in the schizophrenia spectrum: Taking stock and moving forward. Psychopathology 48:301-309
37. Nelson B, Thompson A, Yung AR (2012) Basic self-disturbance predicts psychosis onset in the ultra high risk for psychosis "prodromal" population. Schizophr Bull 38:1277-1287
38. Niendam TA, Bearden CE, Zinberg J, Johnson JK, O'Brien M, Cannon TD (2007) The course of neurocognition and social functioning in individuals at ultra high risk for psychosis. SchizophrBull 33:772-781
39. Nordgaard J, Nilsson LS, Saebye D, Parnas J (2017) Self-disorders in schizophrenia-spectrum disorders: A 5-year follow-up study. Eur Arch Psychiatry Clin Neurosci
40. Nordgaard J, Parnas J (2014) Self-disorders and the schizophrenia spectrum: A study of 100 first hospital admissions. Schizophr Bull 40:1300-1307
41. Norgaard J, Parnas J (2012) A semi structured, phenomenologically-oriented psychiatric interview: Descriptive congruence in assessing anomalous subjective experience and mental status. Clinical neuropsychiatry 9:123
42. Parnas J (2011) A disappearing heritage: The clinical core of schizophrenia. SchizophrBull 37:1121-1130
43. Parnas J, Handest P (2003) Phenomenology of anomalous self-experience in early schizophrenia. ComprPsychiatry 44:121-134
44. Parnas J, Handest P, Jansson L, Saebye D (2005) Anomalous subjective experience among first-admitted schizophrenia spectrum patients: Empirical investigation. Psychopathology 38:259-267
45. Parnas J, Handest P, Saebye D, Jansson L (2003) Anomalies of subjective experience in schizophrenia and psychotic bipolar illness. Acta PsychiatrScand 108:126-133
46. Parnas J, Henriksen MG (2014) Disordered self in the schizophrenia spectrum: A clinical and research perspective. Harv Rev Psychiatry 22:251-265

47. Parnas J, Jansson L, Sass LA, Handest P (1998) Self-experience in the prodromal phases of schizophrenia: A pilot study of first-admissions. Neurology Psychiatry and Brain Research 6:97-106
48. Parnas J, Jansson LB (2015) Self-disorders: Clinical and conceptual implications for the diagnostic concept of schizophrenia. Psychopathology 48:332-338
49. Parnas J, Moller P, Kircher T, Thalbitzer J, Jansson L, Handest P, Zahavi D (2005) Ease: Examination of anomalous self-experience. Psychopathology 38:236-258
50. Parnas J, Raballo A, Handest P, Jansson L, Vollmer-Larsen A, Saebye D (2011) Self-experience in the early phases of schizophrenia: 5-year follow-up of the copenhagen prodromal study. World Psychiatry 10:200-204
51. Pedersen G, Hagtvet KA, Karterud S (2007) Generalizability studies of the global assessment of functioning-split version. Compr Psychiatry 48:88-94
52. Polari A, Lavoie S, Yuen HP, Amminger P, Berger G, Chen E, deHaan L, Hartmann J, Markulev C, Melville F, Nieman D, Nordentoft M, Riecher-Rossler A, Smesny S, Stratford J, Verma S, Yung A, McGorry P, Nelson B (2018) Clinical trajectories in the ultra-high risk for psychosis population. Schizophr Res 197:550-556
53. Postmes L, Sno HN, Goedhart S, van der Stel J, Heering HD, de Haan L (2014) Schizophrenia as a self-disorder due to perceptual incoherence. Schizophr Res 152:41-50
54. Raballo A, Pappagallo E, Dell' Erba A, Lo Cascio N, Patane M, Gebhardt E, Boldrini T, Terzariol L, Angelone M, Trisolini A, Girardi P, Fiori Nastro P (2016) Self-disorders and clinical high risk for psychosis: An empirical study in help-seeking youth attending community mental health facilities. Schizophr Bull 42:926-932
55. Raballo A, Parnas J (2012) Examination of anomalous self-experience: Initial study of the structure of self-disorders in schizophrenia spectrum. J Nerv Ment Dis 200:577-583
56. Raballo A, Parnas J (2010) The silent side of the spectrum: Schizotypy and the schizotaxic self. SchizophrBull
57. Raballo A, Poletti M, Preti A, Parnas J (2021) The self in the spectrum: A meta-analysis of the evidence linking basic self-disorders and schizophrenia. Schizophr Bull
58. Raballo A, Saebye D, Parnas J (2009) Looking at the schizophrenia spectrum through the prism of self-disorders: An empirical study. SchizophrBull
59. Rietschel L, Lambert M, Karow A, Zink M, Müller H, Heinz A, de Millas W, Janssen B, Gaebel W, Schneider F, Naber D, Juckel G, Krüger-Özgürdal S, Wobrock T, Wagner M, Maier W, Klosterkötter J, Bechdolf A (2017) Clinical high risk for psychosis: Gender differences in symptoms and social functioning. Early Interv Psychiatry 11:306-313
60. Ruhrmann S, Schultze-Lutter F, Salokangas RK, Heinimaa M, Linszen D, Dingemans P, Birchwood M, Patterson P, Juckel G, Heinz A, Morrison A, Lewis S, von Reventlow HG, Klosterkötter J (2010) Prediction of psychosis in adolescents and young adults at high risk: Results from the prospective european prediction of psychosis study. Arch Gen Psychiatry 67:241-251
61. Salazar de Pablo G, Catalan A, Fusar-Poli P (2019) Clinical validity of dsm-5 attenuated psychosis syndrome: Advances in diagnosis, prognosis, and treatment. JAMA psychiatry
62. Sass L, Borda JP, Madeira L, Pienkos E, Nelson B (2018) Varieties of self disorder: A bio-pheno-social model of schizophrenia. Schizophr Bull 44:720-727
63. Sass L, Pienkos E, Nelson B, Medford N (2013) Anomalous self-experience in depersonalization and schizophrenia: A comparative investigation. Conscious Cogn 22:430-441
64. Sass LA (2003) "Negative symptoms", schizophrenia, and the self. [references]. International Journal of Psychology & Psychological Therapy:153-180
65. Sass LA (2014) Self-disturbance and schizophrenia: Structure, specificity, pathogenesis (current issues, new directions). Schizophr Res 152:5-11
66. Sass LA, Borda JP (2015) Phenomenology and neurobiology of self disorder in schizophrenia: Secondary factors. Schizophr Res 169:474-482

67. Sass LA, Parnas J (2003) Schizophrenia, consciousness, and the self. SchizophrBull 29:427-444
68. Schlosser DA, Jacobson S, Chen Q, Sugar CA, Niendam TA, Li G, Bearden CE, Cannon TD (2012) Recovery from an at-risk state: Clinical and functional outcomes of putatively prodromal youth who do not develop psychosis. Schizophrenia bulletin 38:1225-1233
69. Schmidt SJ, Schultze-Lutter F, Schimmelmann BG, Maric NP, Salokangas RK, Riecher-Rossler A, van der Gaag M, Meneghelli A, Nordentoft M, Marshall M, Morrison A, Raballo A, Klosterkotter J, Ruhrmann S (2015) Epa guidance on the early intervention in clinical high risk states of psychoses. Eur Psychiatry 30:388-404
70. Schultze-Lutter F, Addington J, Ruhrmann S, Klosterkotter J (2007) Schizophrenia proneness instrument: Adult version (spi-a). Giovanni Fioriti Editore, Roma
71. Schultze-Lutter F, Klosterkötter J, Picker H, Steinmeyer E-M, Ruhrmann S (2007) Predicting first-episode psychosis by basic symptom criteria. Clinical neuropsychiatry 4:11-22
72. Schultze-Lutter F, Michel C, Schmidt SJ, Schimmelmann BG, Maric NP, Salokangas RK, Riecher-Rossler A, van der Gaag M, Nordentoft M, Raballo A, Meneghelli A, Marshall M, Morrison A, Ruhrmann S, Klosterkotter J (2015) Epa guidance on the early detection of clinical high risk states of psychoses. Eur Psychiatry 30:405-416
73. Schultze-Lutter F, Nenadic I, Grant P (2019) Psychosis and schizophrenia-spectrum personality disorders require early detection on different symptom dimensions. Frontiers in psychiatry 10:476
74. Stanghellini G (2000) Vulnerability to schizophrenia and lack of common sense. SchizophrBull 26:775-787
75. Svendsen IH, Oie MG, Moller P, Nelson B, Melle I, Haug E (2018) Stability in basic self-disturbances and diagnosis in a first treated psychosis: A seven year follow-up study. Schizophr Res
76. Thompson E, Kline E, Ellman LM, Mittal V, Reeves GM, Schiffman J (2015) Emotional and behavioral symptomatology reported by help-seeking youth at clinical high-risk for psychosis. Schizophr Res 162:79-85
77. Vaernes TG, Rossberg JI, Moller P (2019) Anomalous self-experiences are strongly associated with negative symptoms in a clinical high-risk for psychosis sample. Compr Psychiatry 93:65-72
78. Vaernes TG, Rossberg JI, Moller P (2018) Anomalous self-experiences: Markers of schizophrenia vulnerability or symptoms of depersonalization disorder? A phenomenological investigation of two cases. Psychopathology:1-12
79. van Os J, Guloksuz S (2017) A critique of the "ultra-high risk" and "transition" paradigm. World Psychiatry 16:200-206
80. Værnes TG, Røssberg JI, Melle I, Nelson B, Romm KL, Møller P (2021) Basic self-disturbance in subjects at clinical high risk for psychosis: Relationship with clinical and functional outcomes at one year follow-up. Psychiatry Res 300:113942
81. Woods SW, Walsh BC, Addington J, Cadenhead KS, Cannon TD, Cornblatt BA, Heinssen R, Perkins DO, Seidman LJ, Tarbox SI, Tsuang MT, Walker EF, McGlashan TH (2014) Current status specifiers for patients at clinical high risk for psychosis. Schizophr Res 158:69-75
82. Woods SW, Walsh BC, Powers AR, McGlashan TH (2019) Reliability, validity, epidemiology, and cultural variation of the structured interview for psychosis-risk syndromes (sips) and the scale of psychosis-risk symptoms (sops). In:Cham: Springer International Publishing, Cham, p 85-113

Table1 UHR/COPS[1], non-progressive symptoms criteria, and COGDIS[2] criteria

Prodromal syndromes	**Criteria of Prodromal Syndromes (COPS)**
Attenuated Positive Symptom syndrome (APSS)[3] Scale of Prodromal Symptoms (SOPS), positive subscale, include: unusual thought content/delusional ideas, suspiciousness/persecutory ideas, grandiosity, perceptual abnormalities/hallucinations and disorganized communication	One or more of the 5 SOPS positive items scoring in the prodromal range (rating of 3-5) AND Symptoms beginning within the past year or currently rate at least one scale point higher than it would if rated 12 months ago AND Symptoms occurring at least once per week for last month
Brief Intermittent Psychotic Symptom (BIPS) syndrome	One or more of the 5 SOPS positive items in the psychotic range (rating of 6) AND Symptoms beginning in the past 3 months AND Symptoms occurring currently at least several minutes per day at least once per month
Genetic Risk and Deterioration (GRD) syndrome	First degree relative with history of any psychotic disorder OR Criteria for schizotypal personality disorder met in patient AND GAF drop of at least 30% over the last month vs 1 year ago
Non-progressive symptoms group	**Criteria for the non-progressive symptoms group**
	One or more of the 5 SOPS positive items scoring in the prodromal range (rating of 3-5) AND Symptoms occurring at least once per week for last month
COGDIS items	**COGDIS criteria**
Inability to divide attention, thought interference, thought pressure, thought blockages, disturbance of receptive speech, disturbance of expressive speech, unstable ideas of reference, disturbances of abstract thinking, captivation of attention by details of the visual field	Presence of ≥ 2 of the 9 basic symptoms with a SPI-A score of ≥ 3 within the last 3 months

[1]Descriptions are from the SIPS version 3.1 (McGlashan, Miller TJ, Woods SW et al 2001), translated to Norwegian in 2005

[2]The listed COGDIS items and criteria are obtained from: Schultze-Lutter F, Addington J, Ruhrmann S, Klosterkötter J (2007) Schizophrenia Proneness Instrument – Adult version (SPI-A). Giovanni Fiori Editore, Roma

Table 2 Demographics and clinical characteristics at baseline and one-year follow-up

Characteristics	Baseline	Follow-up
Participants, *n*	32	32
Male, *n* (%)	21 (65.6)	
Age, mean (*SD*)	19.9 (3.8)	21.1 (4.0)
Born in Norway, *n* (%)	29 (90.6)	
Employed or studying, *n* (%)	17 (53.1)	
Years of education, mean (*SD*)	11.7 (1.8)	
CHR positive, *n* (%), including:	26 (81.3)	9 (28.1)[a]
APS only	14 (43.8)	2 (6.2)
APS+COGDIS	9 (28.1)	1 (3.1)
APS+GRD+COGDIS	1 (3.1)	1 (3.1)
COGDIS only	2 (6.2)	5 (15.6)
Non-progressive SOPS pos, *n* (%)	6 (18.8)	4 (66.7)
Transition to psychosis, *n* (%)		4 (12.5)
Symptomatic and functional remission, *n* (%)[b]		11 (34.4)
SOPS (number of items)		
Positive (5), mean (*SD*)	10.41 (3.45)	6.56 (5.58)
Negative (6), mean (*SD*)	12.50 (7.02)	9.94 (7.39)
Disorganization (4), mean (*SD*)	6.91 (3.36)	5.13 (4.32)
General (4), mean (*SD*)	7.59 (3.31)	4.97 (3.49)
EASE total, mean (*SD*)/median		
Baseline: lifetime	15.31 (8.01) /13.50	
Baseline: last year	13.78 (8.06) /12.00	11.09 (10.03)/8.50
GAF-F, mean (*SD*)	56.31 (10.83)	59.80 (15.72)
Diagnoses		
Mood disorders, *n* (%)	13 (40.6)	
Anxiety disorders, *n* (%)	8 (25.0)	
Other Axis 1 disorders, *n* (%)	4 (12.5)	
Schizotypal pers. dis., *n* (%)	5 (15.6)	9 (28.1)
Schizophrenia, *n* (%)		2 (6.2)
Schizophreniform disorder, *n* (%)		1 (3.1)
Psychosis NOS, *n* (%)		1 (3.1)
No DSM-IV diagnosis, *n* (%)	2 (6.3)	
Medication, prescribed[c], *n* (%)		
Antipsychotics	7 (21.9)	8[d] (25.0)
Antidepressants	6 (18.8)	10 (31.3)
Anxiolytic	2 (6.3)	0
Anticonvulsants	1 (3.1)	1 (3.1)
Psychostimulants	1 (3.1)	1 (3.1)
Hospitalization between baseline and follow-up		3 (9.4)
Discontinuation of treatment before follow-up		8 (25)

[a] Meeting full CHR criteria, e.g. worsening of attenuated positive symptoms last year

[b] ≤ 2 on all SOPS positive symptom items, in combination with a score of ≥70 points or ≥10 points improvement on GAF-F. Two of the 11 remitted subjects were from the non-progressive symptoms group

[c] Data in the follow-up column represents prescribed medication *between* baseline and follow-up

[d] 5 of the 8 had "Defined Daily Dose" below the recommended for antipsychotic treatment

Table 3 Correlations between clinical and demographic characteristics at baseline and EASE total at one-year follow-up (n = 32)

Baseline variables →	SOPS Pos	SOPS Neg	SOPS Disorg	SOPS Gen	GAF-F	CTQ total	CTQ Emot. Negl	PAS Child hood	PAS Early adol.
EASE total at 1 year	.17	**.58****	.46*	.20	-.30	.11	.26	.22	.38*

*p < .05, **p < .006 (Bonferroni-adjusted), Spearmans rho, two-tailed

Table 4 Correlations between EASE total and clinical characteristics at follow-up (n = 32)

Measures at f-u →	SOPS pos	SOPS neg	SOPS disorg	SOPS gen	GAF-F
EASE total at f-u	**.75***	**.76***	**.75***	**.64***	**-.79***

*p < .01 (Bonferroni-adjusted), Spearmans rho, two-tailed

Table 5 Changes in SOPS symptoms and GAF-F in three EASE change groups

	SOPS positive change *M (SD)*	SOPS negative change *M (SD)*	SOPS disorg. change *M (SD)*	SOPS general change *M (SD)*	GAF-F change *M (SD)*
EASE increase (≥1 pt)	2.00 (5.69)	-0.86 (6.28)	.71 (4.46)	-1.29 (4.31)	-8.43 (8.60)
EASE 0-3 pt decline	-4.08 (4.91)	-1.33 (4.21)	-1.92 (2.88)	-2.08 (4.38)	7.83 (10.04)
EASE > 3 pt decline	-6.77 (3.30)	-4.62 (3.62)	-3.00 (2.16)	-3.85 (3.74)	5.77 (10.58)
Exact p-value[a]	.004*	.085	.052	.273	.011*

[a]Kruskal Wallis test, *p < .05

Fig. 1 Individual trajectories in mean EASE total scores from baseline to follow-up

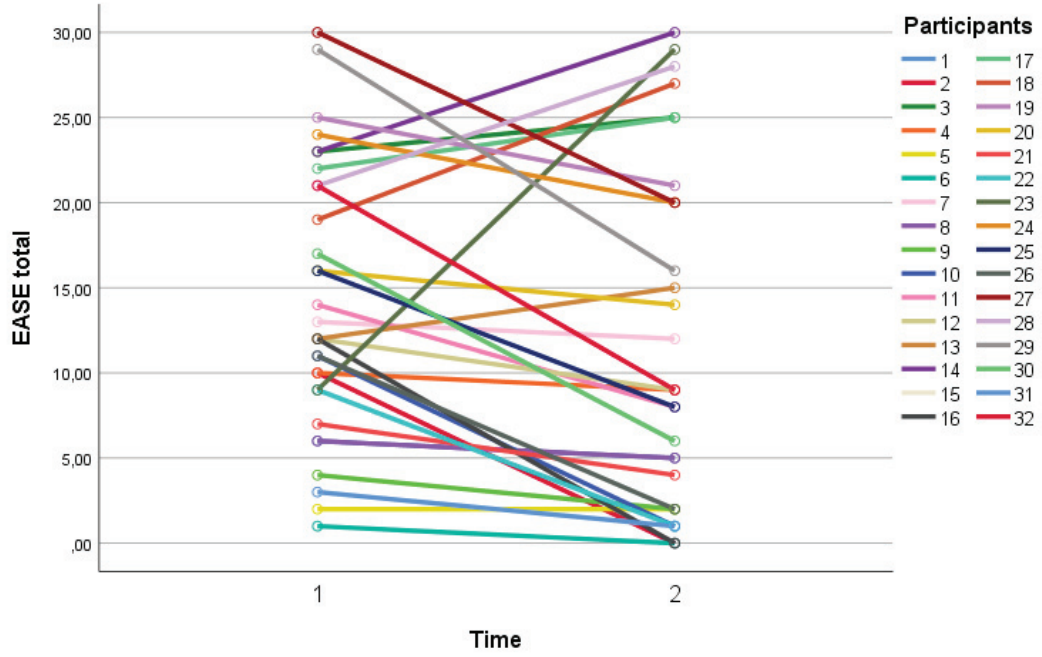
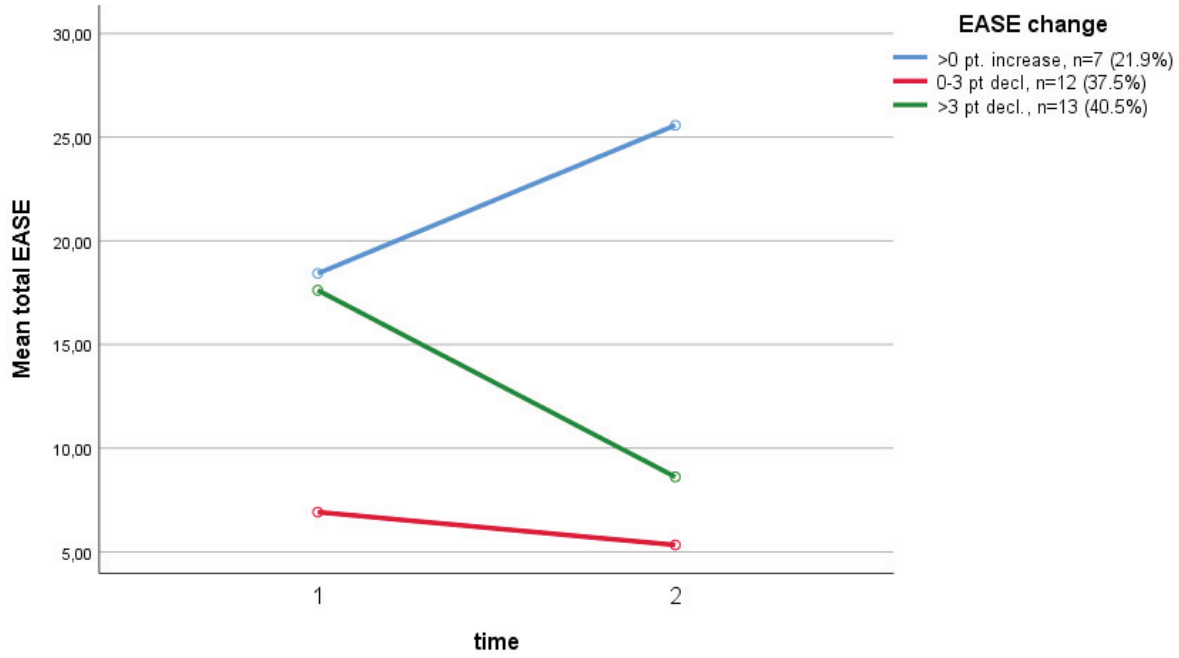


Fig. 2 Mean changes in EASE total scores for the three EASE trajectories groups



S1 Comparison of demographics and clinical characteristics at baseline in the follow-up study sample and in the drop-outs

Demographic and characteristics at baseline	Sample in follow-up study *N* = 32	Drop-outs *N* = 6	*P*-value
Male, *n* (%)	21 (65.6)	3 (50.0)	NS[a]
Age, mean (*SD*)	19.9 (3.83)	19.2 (2.64)	.86[b]
Years of education, mean (*SD*	11.3 (1.03)	11.7 (1.81)	.74[b]
Employed or studying, *n* (%)	17 (53.1)	3 (50.0)	NS[a]
Born in Norway, *n* (%)	29 (90.6)	5 (83.3)	NS[a]
CHR positive, *n* (%)	26 (81.3)	5 (83.3)	NS[a]
EASE total (lifetime), mean (*SD*)	15.31 (8.13)	16.17 (10.03)	.86[b]
EASE total (last year), mean (*SD*)	13.78 (8.06)	14.83 (10.42)	.89[b]
SOPS positive, mean (*SD*)	10.41 (3.45)	8.67 (3.72)	.36[b]
SOPS negative, mean (*SD*)	12.50 (7.02)	15.33 (6.88)	.36[b]
SOPS disorganization, mean (*SD*)	6.91 (3.36)	7.00 (2.97)	.86[b]
SOPS general, mean (*SD*)	7.59 (3.31)	10.17 (3.82)	.21[b]
GAF-F, mean (*SD*)	56.31 (10.83)	52.83 (12.67)	.54[b]

**P* < .05. [a]Non-significant, but Chi Square test is not valid due to expected count <5 in several cells, [b]Mann Whitney U[b]

S2 Examination of Anomalous Self-Experience (EASE) domain and items

Domain 1 Cognition and stream of consciousness
Thought interference 1.1
Loss of thought ipseity 1.2
Thought pressure 1.3
Thought block 1.4
Silent thought echo 1.5
Ruminations-obsessions 1.6
Perceptualization of inner speech or thought 1.7
Spatialization of experience 1.8
Ambivalence 1.9
Inability to discriminate modalities of intentionality 1.10
Disturbance of thought initiative/intentionality 1.11
Attentional disturbances 1.12
Disorder of short-term memory 1.13
Disturbance of time experience 1.14
Discontinuous awareness of own action 1.15
Discordance between expression and expressed 1.16
Disturbance of expressive language function 1.17

Domain 2 Self-awareness and presence
Diminished sense of basic self 2.1
Distorted first-person perspective 2.2
Psychic depersonalization (self-alienation) 2.3
Diminished presence 2.4
Derealization 2.5

Hyperreflectivity (increased reflectivity) 2.6
I-split (‘‘Ich-Spaltung’’) 2.7
Dissociative depersonalization 2.8
Identity confusion 2.9
Sense of change in relation to chronological age 2.10
Sense of change in relation to gender 2.11
Loss of common sense, perplexity, lack of natural evidence 2.12
Anxiety 2.13
Ontological anxiety 2.14
Diminished transparency of consciousness 2.15
Diminished initiative 2.16
Hypohedonia 2.17
Diminished vitality 2.18

Domain 3 Bodily experiences
Morphological change 3.1
Mirror-related phenomena 3.2
Somatic depersonalization (bodily estrangement) 3.3
Psychophysical misfit and psychophysical split 3.4
Bodily disintegration 3.5
Spatialization (objectification) of bodily experiences 3.6
Cenesthetic experiences 3.7
Motor disturbances 3.8
Mimetic experience (resonance between own movement and others’ movements) 3.9

Domain 4 Demarcation/transitivism
Confusion with the other 4.1
Confusion with one’s own specular image 4.2
Threatening bodily contact and feelings of fusion with another 4.3
Passivity mood 4.4
Other transitivistic phenomena 4.5

Domain 5 Existential reorientation
Primary self-reference phenomena 5.1
Feeling of centrality 5.2
Feeling as if the subject’s experiential field is the only extant reality 5.3
‘‘As if ’’ feelings of extraordinary creative power or extraordinary insight into hidden dimensions of reality 5.4
‘‘As if ’’ feeling that the experienced world is not truly real, as if it was only somehow apparent, illusory or deceptive 5.5
Magical ideas linked to the subject’s way of experiencing 5.6
Existential or intellectual change 5.7
Solipsistic grandiosity 5.8

Definitions of domains, items and subtypes (subtypes not included in S2) are outlined in:

Parnas, J., et al. (2005). "EASE: Examination of Anomalous Self-Experience." Psychopathology **38**(5): 236-258.

S3 Demographic and clinical characteristics at baseline and follow-up in the CHR and in the non-progressive symptoms group

Characteristics	CHR *N* = 26	Non-progressive symptoms group *N* = 6	*P*-value
Male, n (%)	15 (58.0)	6 (100)	*NS*[a]
Age, mean (SD)	19.0 (3.4)	24.2 (2.8)	.002[b]*
Years of education, mean (SD)	11.4 (1.8)	12.8 (1.2)	.03[b]*
Employed or studying, n (%)	15 (58.0)	2 (33.3)	*NS*[a]
Born in Norway, n (%)	23 (88.5)	6 (100)	*NS*[a]
EASE total baseline (lifetime), mean (SD)	15.19 (8.81)	15.83 (4.54)	.72[b]
EASE total baseline (last year), mean (SD)	13.77 (8.73)	13.83 (4.62)	.83[b]
EASE total follow-up, mean (SD)	11.27 (10.40)	10.33 (9.03)	.94[b]
SOPS positive, baseline, mean (SD)	10.77 (3.63)	8.83 (2.04)	.16[b]
SOPS negative, baseline, mean (SD)	12.38 (6.95)	13.00 (7.95)	.91[b]
SOPS disorg., baseline, mean (SD)	6.81 (3.49)	7.33 (3.01)	.69[b]
SOPS general, baseline, mean (SD)	7.81 (3.11)	6.67 (4.27)	.52[b]
SOPS positive, follow-up , mean (SD)	6.38 (5.94)	7.33 (3.93)	.44[b]
SOPS negative, follow-up, mean (SD)	9.38 (6.81)	12.33 (9.81)	.44[b]
SOPS disorg., follow-up, mean (SD)	4.96 (4.53)	5.83 (3.54)	.49[b]
SOPS general, follow-up, mean (SD)	5.12 (3.54)	4.33 (3.50)	.72[b]
GAF-F, baseline, mean (SD)	56.42 (10.63)	55.83 (12.70)	.76[b]
GAF-F, follow-up, mean (SD)	60.46 (15.55)	56.67 (17.87)	.62[b]
Transition to psychosis, n (%)	4 (15.4)	0	
Full remission, n (%)	9 (34.6)	2 (33.3)	*NS*[a]
SPD baseline, n (%)	4 (15.4)	1 (16.7)	*NS*[a]
SPD follow-up, n (%)	6 (23.1)	3 (50.0)	*NS*[a]

*$P < .05$. [a]Non-significant, but Chi Square test is not valid due to expected count <5 in several cells, [b]Mann Whitney U Test [b]