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

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

---

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 3.1, Jan. 2005). 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 ≥70) or improved functioning (≥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
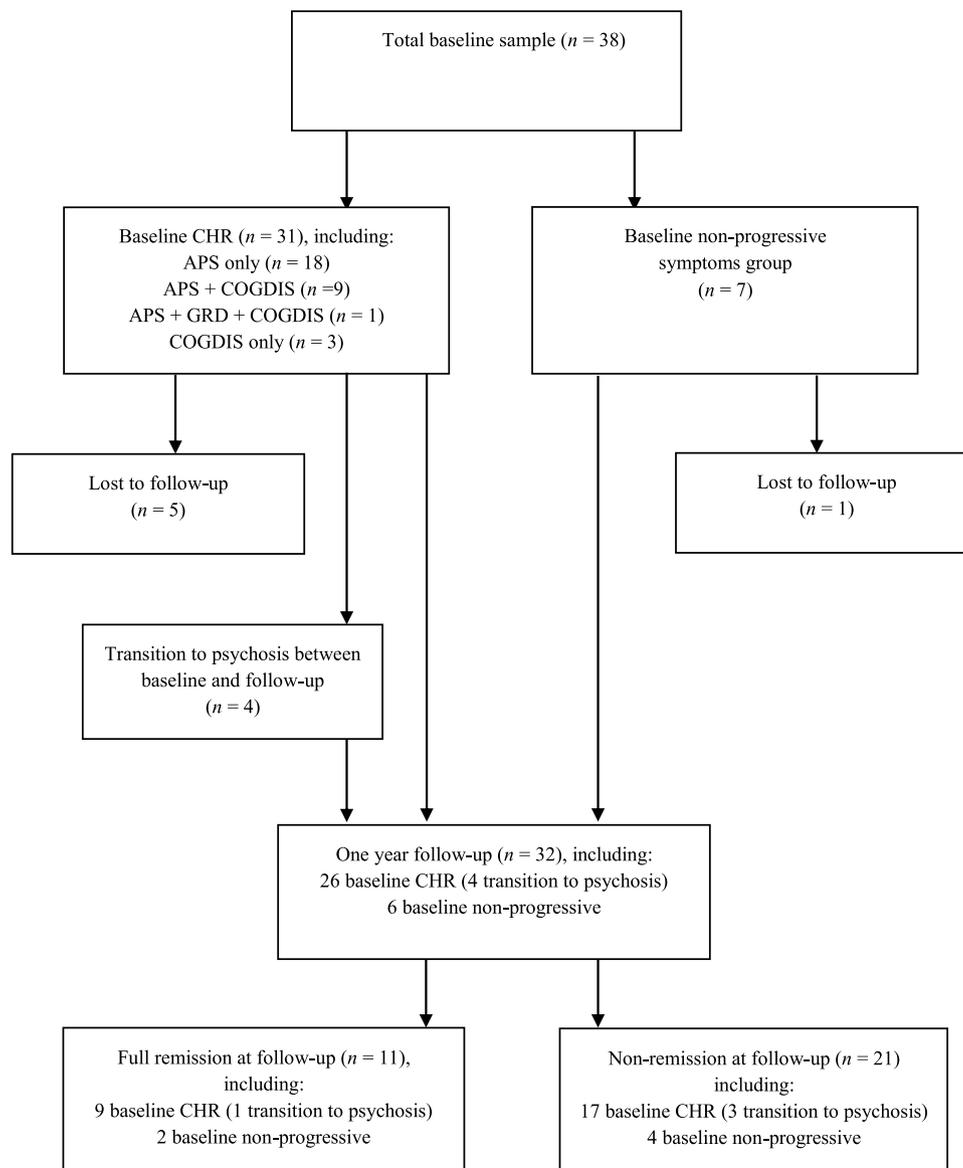

Fig. 1.. Flow chart showing CHR status at baseline, sample attrition, transition to a psychotic episode, and remission status at 1-year follow-up

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 change | SOPS Neg change | SOPS Dis change | SOPS Gen change | GAF-F change |
	SOPS Pos	SOPS Neg	SOPS Dis	SOPS Gen	GAF-F					
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] = Pearson two-tailed, [b] = Spearmans rho 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).

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

Baseline demographics and clinical characteristics	Remitters, N= 11 (34.4%)	Non-remitters, N = 21 (66.6%)	Difference between remitters/non-remitters: 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

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	R²	% 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

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. Psychiatry 168 (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: preliminary evidence of 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., 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.