



Basic self-disturbances independently predict recovery in psychotic disorders: A seven year follow-up study

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ABSTRACT

Background: Recovery is the ultimate goal of psychosis treatment. Basic self-disturbances (BSDs) are non-psychotic phenomena associated with clinical outcome, present in prodromal, psychotic and residual phases of psychotic disorders.

Aim: To investigate the relationship between BSDs and recovery seven years after first treatment in patients with psychotic disorders.

Method: Prospective longitudinal study of 56 patients recruited during first adequate treatment for schizophrenia (n = 35) and other psychotic disorders (n = 21) (psychotic bipolar disorder, delusional disorder, psychotic disorder NOS). At baseline and follow-up BSDs were assessed using the Examination of Anomalous Self-Experience (EASE) manual, while standard clinical instruments were used to ascertain diagnosis, clinical symptom severity, and functioning. Recovery was defined as absence of psychotic symptoms and regaining of functioning that persisted the last two years before follow-up.

Results: At follow up, 34% achieved recovery (5 (14%) with schizophrenia and 14 (67%) with other psychoses at baseline). Recovery was predicted by an absence of a schizophrenia diagnosis, low baseline level of BSDs and further reductions in BSDs from baseline to follow-up. Change in BSDs was the strongest predictor, also after adjusting for premorbid adjustment and duration of untreated psychosis, and was not confounded by diagnosis.

Conclusion: Low baseline levels of basic self-disturbances and further reductions over time independently predict recovery seven years later in first treated psychosis patients.

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1. Introduction

Full recovery is the optimal goal of any psychiatric treatment. In psychotic disorders, the term “full recovery” has been defined as stable remission of positive, negative and affective symptoms (Andreasen “Remission in Schizophrenia Working Group” (RSWG) criteria), in the context of regained normal functioning (Andreasen

et al., 2005). The rates of recovery in studies of first episode schizophrenia spectrum disorder vary between 10 and 25% of participants, depending on the specific diagnoses included in the study, the length of the follow-up period and the criteria used to define recovery (Austin et al., 2013; Jaaskelainen et al., 2013; Robinson et al., 2004; Torgalsboen et al., 2015). A recent meta-analysis, including 35 studies with a total of 9642 first episode psychosis patients (schizophrenia and affective psychosis), found that 38% were in full recovery after a mean follow-up period of 7.3 years (Lally et al., 2017). In a study of patients with bipolar disorder followed from their first hospitalization for mania, 43% were found to be in full functional recovery at 2–4 years follow-up (Tohen et al., 2003). However, Angst et al. (2009) found that only 16% of patients with bipolar disorder experienced full recovery throughout a five-year

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period (Angst, 2009). The outcome of first episode psychosis is both heterogeneous and difficult to predict on the individual level (Fusar-Poli et al., 2014). Known predictors of poor outcome are poor premorbid adjustment (MacBeth and Gumley, 2008), low age at onset of symptoms (Clemmensen et al., 2012), long duration of untreated psychosis (DUP) (Penttila et al., 2014), depression (Uptegrove et al., 2010), persistent negative symptoms and substance use (Weibell et al., 2017). Some studies also indicate that males have poorer outcome than females (Tandon et al., 2009).

Basic self-disturbances (BSDs) have been established as core features of schizophrenia spectrum disorders (Parnas et al., 2005a; Parnas and Henriksen, 2014). The theory of BSDs is based on Continental phenomenology and psychiatry (Sass and Parnas, 2003) and overlaps with and can be seen as an evolution from the concept of Basic Symptoms (Gross et al., 1998; Klosterkötter et al., 1996; Parnas and Handest, 2003; Schultze-Lutter, 2009). BSDs are characterized by *diminished sense of self-presence* (existing as a vital subject of awareness or agent of actions), *hyperreflexivity* (exaggerated self-consciousness and heightened awareness of normally tacit or implicit aspects of experience), and disturbed 'grip' on the cognitive and/or perceptual field (Sass et al., 2018; Sass and Parnas, 2003). They also have profound implications for interpersonal functioning (Parnas and Handest, 2003). Empirical studies indicate that these phenomena are clearly present before the appearance of frank psychotic symptoms (Moller and Husby, 2000; Parnas et al., 1998) and in high-risk individuals (Davidsen, 2009). Furthermore, studies indicate that the presence of BSDs increases the risk of conversion to psychosis in high-risk groups (Nelson et al., 2012; Parnas et al., 2011). BSDs are present in all stages of psychotic disorders, including in first-episode (Haug et al., 2012a; Nordgaard and Parnas, 2014) and in chronic patients (Raballo et al., 2011). An addition to the BSDs concept, is the view that while some phenomena are fundamental to schizophrenia ("primary BSDs"), others may be particular responses to traumatic environments and could be seen as defensive-compensatory ("secondary BSDs") (Borda and Sass, 2015; Sass et al., 2018; Sass and Borda, 2015).

The presence and degree of BSDs differentiate between schizophrenia spectrum- and affective psychotic disorders (Haug et al., 2012a; Nelson et al., 2013; Nordgaard and Parnas, 2014; Raballo and Parnas, 2012). In the current study sample, we found that BSDs were present at start of first treatment (Haug et al., 2012a) and that this baseline level was significantly associated with long duration of untreated psychosis (DUP) (Haug et al., 2017), low self-esteem, high levels of depression and suicidal behavior (Haug et al., 2016), reduced social functioning (Haug et al., 2014), impaired verbal memory (Haug et al., 2012c), and presence of childhood trauma (in females) (Haug et al., 2015).

A recent study indicates an association between high level of BSDs in the early phase of illness and poor long-term outcome in the form of more negative symptoms five years later (Nordgaard et al., 2017; Raballo and Preti, 2018). We have recently reported a modest reduction in BSDs in patients with schizophrenia seven years after first treatment (Svendsen et al., 2018). The aim of the current study was to investigate the relationship between BSDs at baseline, change in BSDs over time, and clinical outcome in the seven-year follow-up study, with a specific focus on recovery. Our hypothesis thus is that low levels of BSDs at baseline would be associated with recovery.

2. Materials and method

2.1. Participants

The present study is a part of the Norwegian "Thematically Organized Psychosis" (TOP) study and is a seven year follow up of first-treatment psychosis patients (Haug et al., 2012a). At baseline, participants were recruited from two Norwegian counties with a combined population of 375,000. All patients between 18 and

65 years receiving their first treatment for schizophrenia, schizophreniform disorder and schizoaffective disorder (henceforth: "Schizophrenia"), psychotic bipolar disorder I and NOS, delusional disorder and psychosis NOS (henceforth: "other psychosis"). Exclusion criteria were substance-induced psychosis and having an IQ < 70. Ninety patients were included at baseline, 57 (63%) with schizophrenia and 33 (37%) with other psychosis. In the seven years between baseline and follow-up, patients were offered and mostly received treatment as usual in the local services, including regular appointments with a doctor, psychiatrist, psychologist or a social worker providing mental health support, in addition to medications (antipsychotics and/or mood stabilizers). Twenty patients (36%) also received psychoeducation and/or cognitive behavioral therapy. A total of 56 patients (62% of the baseline cohort) participated in the seven year follow-up. All 90 previous participants were still alive, but 15 (16%) had changed residence and were impossible to reach, and 19 (21%) declined participation. The baseline demographic and clinical characteristics between those who not participated and those who did participate in the follow-up, demonstrate no significant difference. At both time-points, all participants gave informed, voluntary, written consent to participate. Regional Committee for Medical Research Ethics and the Norwegian Data Inspectorate approved the study.

2.2. Assessments

The same clinical assessment battery was used at baseline and at follow up. Only the instruments relevant for this report are presented.

2.2.1. Assessment of basic self-disturbances at baseline and follow-up

BSDs were assessed with the Examination of Anomalous Self Experience (EASE) manual (Parnas et al., 2005b). The interrater reliability (IRR) for EASE assessments has been found to be very good (Moller et al., 2011; Nelson et al., 2012; Raballo and Parnas, 2012). At baseline, the interviews were done by an experienced psychiatrist (EH). A clinically experienced psychiatric nurse (IHS) assessed the EASE at follow-up. She was trained by two certified EASE instructors (EH and PM). Videotaped EASE interviews were used for pre-study training. The interviews were rated by IHS, EH, and PM, and IRR showed an average Cohen's kappa of 0.71 which is considered to be good. The first seven EASE interviews at follow-up (EH and IHS) were also IRR tested and showed a Cohen's kappa of 0.78.

The EASE is grouped into 5 domains: (1) Cognition and stream of consciousness, (2) Self-awareness and presence, (3) Bodily experiences, (4) Demarcation/transitivity, and (5) Existential reorientation. These five domains comprise 57 main items BSDs are not considered to be single and independent phenomena but highly overlapping and interwoven aspects of a gestalt (Nordgaard and Parnas, 2014; Raballo and Parnas, 2012). The items are scored using a 5-point scale (0–4), 0 = absent; 1 = questionably present; 2 = definitely present, mild; 3 = definitely present, moderate; 4 = definitely present, severe. As described in previous publications, the scores were dichotomized into 0 (absent and questionably present) and 1 (definitely present, all severity levels). Item 2.13 (anxiety) does not represent a self-disturbance per se, but serves as a contrast to the item ontological anxiety (Parnas et al., 2005b), and item 2.13. was not included in the analyses at baseline and follow-up. At baseline, we registered life-time experience of BSDs, but at follow-up we registered the presence of BSDs during the previous two years to be able to examine change over time (Svendsen et al., 2018).

2.2.2. Other assessments at baseline and follow-up

At baseline, duration of untreated psychosis (DUP) was ascertained, and Premorbid Adjustment Scale (PAS) was applied (Canon-Spoor et al., 1982). At baseline and follow-up, diagnoses were ascertained using the Structured Clinical Interview for DSM-IV Axis I disorders (SCID module I, chapter A-E) (First et al., 1996). In

addition to personal interviews, information from medical charts was used to aid the assessments. Eight participants had no updated charts available at follow-up because they had no treatment contact with the public health system. At baseline, two experienced psychiatrists determined diagnoses using the SCID-I. At follow-up, SCID-I diagnoses were determined by independent, trained medical doctors or clinical psychologists blind to EASE scores.

To measure present symptom severity, The Global Assessment Functioning scale, split version (GAF–S), (Endicott et al., 1976; Pedersen et al., 2007), the Structured Clinical Interview for Positive and Negative Syndrome Scale (SCI-PANSS) (Kay et al., 1987), and Calgary Depression Scale for Schizophrenia (CDSS) (Addington et al., 1990) were used. Social functioning was assessed using the Social Function Scale (SFS) (Birchwood et al., 2018), and substance use was assessed with the use of the self-report questionnaires Alcohol Use Disorder Identification Test (AUDIT) (Saunders et al., 1993) and the Drug Use Disorder Identification Test (DUDIT) (Berman et al., 2005). Information about childhood trauma was collected using the Norwegian version of the Childhood Trauma Questionnaire, short form (CTQ-SF) (Bernstein et al., 2003) and self-esteem at baseline was measured using the Rosenberg Self-Esteem Scale (RSES) (Rosenberg, 1989).

The first author (IHS) conducted all of the assessments at follow-up, except the diagnostic interviews, in order to attempt to maintain blindness to information from the diagnostic interviews concerning both baseline and current diagnoses. She was also blind to information about baseline BSDs.

2.2.3. Remission and recovery

Remission of symptoms and regaining functioning are both necessary for recovery. We used Andreasen's "Remission in Schizophrenia Working Group" (RSWG) criteria (Andreasen et al., 2005). To meet these criteria, the patient must have a PANSS score of 3 or lower for both positive symptoms (item P1, P3, G9), for disorganization symptoms (P2, G5), and for negative symptoms (N1, N4, N6). Since all participants had a psychotic disorder at baseline we only focused on remission of psychotic symptoms, not affective symptoms. Regained function was defined as having an employment level equal to full-time work or studies and social activities equivalent to at least weekly patient-initiated contact with family and/or friends, in line with a definition previously used in the TIPS study (Ten Velden Hegelstad et al., 2013). In this paper, recovery is defined as experiencing the combination of full remission of psychotic symptoms and regained functioning over the last 24 months before follow-up.

2.3. Statistical analyses

All statistical procedures were conducted using the SPSS version 23.0 (SPSS Inc., Chicago, IL, USA). All continuous/ordinal data had an approximately normal distribution with mean and standard deviation reported. The exceptions were DUP, AUDIT and DUDIT, and here median and range is reported. For categorical variables percentages are reported. Group comparisons for normally distributed data were evaluated with parametric tests, group comparisons for skewed data were evaluated with non-parametric tests and group comparisons for dichotomous variables were evaluated with chi-square tests. Several potential predictors of poor outcome, including premorbid functioning, DUP, childhood trauma, depression and self-esteem were associated with the level of BSDs (EASE score) at baseline. The association between recovery and BSDs at baseline, controlling for potential confounding- or mediating variables, was investigated using multiple logistic regression analysis correcting for diagnosis. Childhood trauma, self-esteem and depression were however not differentially distributed across the recovery-based groups, and

were not included in the final analyses. Also, since the assessment of recovery at follow-up was directly based on current symptoms and functioning at follow-up, with the presence of a high correlation between baseline- and follow-up levels for all clinical measures (GAF–F, GAF–S, PANSS, CDSS, and SFS), these were not entered in the multivariate analysis. Because DUP had a markedly skewed distribution, it was transformed to its natural logarithm which were used in the multivariate analyses (LnDUP - since no participants had a DUP of 0 weeks). Since only one hypothesis – that there was an association between BSDs and recovery – was tested, the alpha level was set to 0.05, two-sided.

3. Results

3.1. General outcome

The follow-up period had a median length of 2579 days (7.1 years) (range: 2362–2973 days; 6.5–8.1 years). At follow-up 35 out of 56 (63%) participants had a DSM-IV diagnosis of schizophrenia and 21 (37%) other psychotic disorders (bipolar disorder with psychotic features, delusional disorder or psychosis NOS). Diagnostic changes from baseline to follow-up were limited (See Svendsen et al. (2018) for details). At follow-up, and across diagnostic groups, a total of 33 (59%) were in stable symptomatic remission, and 19 (34%) met the criteria for recovery. Demographic and clinical data at baseline for recovered vs. non-recovered participants are shown in Table 1. Clinical data at follow-up for recovered vs. non-recovered participants are shown in Table 2.

There were statistically significant associations between baseline and follow-up levels of EASE, GAF-F, GAF-S, PANSS (all components), CDSS, SFS, AUDIT, and DUDIT with significant improvements in all parameters except drug use (Table 3).

Fig. 1 (scatterplot) show the distribution of EASE total score at baseline and changes in EASE total score at follow-up, sorted by recovered and not recovered.

3.2. Basic self-disturbances, remission, and recovery

As reported previously (Svendsen et al., 2018), there was a significant association between total EASE scores at baseline and follow-up ($r = 0.54$ $p < 0.01$) with a modest but significant reduction over the follow-up period ($t = -4.01$, $p < 0.01$).

Participants in stable symptomatic remission (15 out of 35 [43%] with schizophrenia and 19 out of 21 [91%] with other psychoses) had significant lower EASE total scores than those not in symptomatic remission, at both baseline and at follow-up (baseline median EASE total score (sympt. remission) 14 (0–40) vs (sympt. non-remission) 24 (7–45); follow-up median EASE total score 7 (0–7) vs 19 (5–38)) (Mann-Whitney U test, all p 's < 0.01).

The participants who met the criteria for recovery (5 [14%] schizophrenia and 14 [67%] other psychoses) also had significantly lower EASE total scores than those who did not (baseline median of EASE total score (recovery) 7 (0–40) vs. (non-recovery) 21 (2–45) - and follow-up median of EASE total score 5 (0–18) vs 14 (2–38)) (both p 's < 0.01 Mann-Whitney U test).

However, recovered participants were more likely to have a diagnosis outside of the schizophrenia spectrum, better premorbid functioning and shorter DUP than those who had not achieved recovery. These characteristics were also significantly associated with lower baseline- and follow-up EASE total scores, and we could initially not rule out that they confounded or mediated the association between EASE total score and recovery. We thus conducted a hierarchical multivariate binary logistic regression analysis with "Recovered" (yes vs no) as the dependent variable. Since baseline and follow-up levels of EASE total score were highly correlated, we could not enter both EASE total score at baseline and at follow-up

Table 1

Demographic and clinical characteristics at baseline, shown for the total sample, and separately for those recovered versus not recovered at follow-up.

	Baseline	Not recovered follow-up	Recovered follow-up	t-test/ Chi-Square Analysis/ Mann Whitney U for recovered vs not recovered participants (baseline data)	
	(N = 56)	(n = 37)	(n = 19)	t/ χ^2 /U	P
Male (N/%)	28/50	20/54	8/42	$\chi^2 = 0.31$	0.57
Age (mean/median/SD)	25.2/22/7.5	25.3/23/7.4	24.5/22/8.0	U = 309	0.46
DUP ^a in weeks (median/range)	86/1–1041	105/1–1041	9/1–675	U = 169.5	<0.01
EASE ^b total (mean/SD)	17.2/11.7	19.2/10.9	10.1/12.5	t = 2.49	=0.02
GAF-S ^c (mean/SD)	37.6/11.3	34.2/8.25	44.2/13.6	t = -2.96	<0.01
GAF-F ^d (mean/SD)	38.9/9.3	35.7/5.7	45/11.8	t = 3.21	<0.01
PANSS ^e positive component (mean/SD)	16.9/4.9	18.3/4.4	13.9/4.6	t = -2.96	<0.01
PANSS ^e negative component (mean/SD)	16.6/7.4	17.7/8.1	14.2/5.2	t = 1.74	0.09
PANSS ^e general component (mean/SD)	37.8/9.2	40.3/8.3	32.8/8.9	t = 3.14	<0.01
SFS ^f total score (mean/SD)	103.2/8.4	101.7/7.5	106.7/9.7	t = 2.07	0.04
CDSS ^g (mean/SD)	8.4/5.7	9/5.6	7.2/5.6	t = 1.16	0.25
AUDIT ^h (median/range)	7/0–38	7/0–38	8/1–19	U = 340.5	0.85
DUDIT ⁱ (median/range)	0/0–44	0/0–44	0/0–20	U = 321	0.46
PAS ^j -social function, childhood (median/range)	1/0–6	1.5/0–5	0.5/0–3.5	U = 216	<0.01
PAS ^j -academic function, childhood (median/range)	1.25/0–5	1.5/0–6	0/0–6	U = 203.5	<0.01
RSES ^k (mean/SD)	21.9/6.9	20.8/5.4	24.2/9	t = -1.45	0.16
CTQ-SF ^l (median/range)	41/25–117	41/25–117	41/27–54	U = 221.0	0.54

P-values in bold are statistically significant.

^a DUP; Duration of Untreated Psychosis.^b EASE; Examination of Anomalous Self-Experiences.^c GAF-S; Global Assessment Functioning Scale split version – Symptom.^d GAF-F; Global Assessment Functioning Scale split version – Function.^e PANSS; Positive and Negative Syndrome Scale.^f SFS; Social Function Scale.^g CDSS; Calgary Depression Scale for Schizophrenia.^h AUDIT; Alcohol Use Identification test.ⁱ DUDIT; Drug Use Disorder Identification Test.^j PAS; Premorbid Adjustment Scale.^k RSES; Rosenberg Self-esteem Scale.^l CTQ-SF; Childhood Trauma Questionnaire – Short Form.

into the equation. Instead we used the change in the EASE total score from baseline until follow-up as an expression of the EASE total score at follow up (Fig. 1). EASE total score baseline and EASE

change were entered into the regression as separate variables. At the final step, only EASE total score at baseline and change in EASE total score had statistically significant contributions (Table 4).

Table 2

Clinical characteristics at follow-up, shown for the total sample, and separately for those recovered versus not recovered at follow-up.

	Follow-up	Not recovered follow-up	Recovered follow-up	T-test/ Chi-Square Analysis/ Mann Whitney U for recovered vs not recovered participants (follow-up data)	
	(N = 56)	(n = 37)	(n = 19)	t/ χ^2 /U	P
EASE ^a total (mean/SD)	11.7/8.9	14.5/8.7	5.0/5.1	t = 3.60	<0.01
GAF-S ^b (mean/SD)	57.2/16.8	48.2/10.8	74.6/12.0	t = -8.33	<0.01
GAF-F ^c (mean/SD)	60.4/16.9	51.5/11.9	77.7/10.3	t = -8.18	<0.01
PANSS ^d positive component (mean/SD)	11.8/4.3	13.6/4.4	8.2/2	t = 5.06	<0.01
PANSS ^d negative component (mean/SD)	13/5.3	15.2/5.1	8.8/2.3	t = 6.37	<0.01
PANSS ^d general component (mean/SD)	25.8/6.3	28.7/5.5	20.7/4.8	t = 5.33	<0.01
SFS ^e total score (mean/SD)	108.3/10.5	103.2/7.8	117.6/8.2	t = -6.33	<0.01
CDSS ^f total score (mean/SD)	4.3/4.3	5.3/4.1	2.4/3.7	t = 2.45	0.02
RSES ^g	21.9/6.9	21.5/5.9	23.2/9.8	t = -0.73	0.47
AUDIT ^h (median/range)	5/0–28	5/0–28	3/0–15	U = 169	0.06
DUDIT ⁱ (median/range)	0/0–42	0/0–42	0/0–4	U = 237	0.52

P-values in bold are statistically significant.

^a EASE; Examination of Anomalous Self-Experiences.^b GAF-S; Global Assessment Functioning Scale split version – Symptom.^c GAF-F; Global Assessment Functioning Scale split version – Function.^d PANSS; Positive and Negative Syndrome Scale.^e SFS; Social Function Scale.^f CDSS; Calgary Depression Scale for Schizophrenia.^g RSES; Rosenberg Self-esteem Scale.^h AUDIT; Alcohol Use Identification test.ⁱ DUDIT; Drug Use Disorder Identification Test.

Table 3
Bivariate correlation, paired samples *t*-test, and Wilcoxon signed rank test between baseline and follow-up scores.

	Correlations		Paired samples <i>t</i> -test				t-value	P-value	
	r-value	P-value	Paired differences		Std. Err. Mean	99% CI			
			Mean	SD					
						Lower	Upper		
EASE total score	0.541	<0.01	-5.50	10.20	1.36	9.14	1.86	4.04	<0.01
GAF function	0.509	<0.01	21.52	14.55	1.94	16.33	26.71	11.07	<0.01
GAF symptom	0.400	<0.01	19.61	16.09	2.15	13.87	25.34	9.12	<0.01
PANSS positive	0.440	<0.01	-5.04	5.00	0.67	6.82	3.25	7.53	<0.01
PANSS negative	0.426	<0.01	-3.50	7.02	0.94	6.00	1.00	3.73	<0.01
PANSS general	0.344	<0.01	-11.79	9.22	1.23	15.07	8.50	9.57	<0.01
CDS total score	0.447	<0.01	-4.04	5.39	0.72	5.96	2.11	5.60	<0.01
SFS total score	0.500	<0.01	4.37	9.62	1.35	0.76	7.97	3.24	<0.01
RSES score	0.455	<0.01	-4.02	6.75	0.96	-5.96	-2.08	-4.17	<0.01

	Rho	P-value	Median	Min	Max	Wilcoxon signed rank test	P-value
AUDIT total score ^a	0.607	<0.01	-1.00	-17.0	11.0		=0.01
DUDIT total score ^a	0.447	=0.01	0.00	-5.0	23.0		0.92

^a Nonparametric tests are used for AUDIT and DUDIT because of a skew distribution.

4. Discussion

4.1. General discussion

Consistent with recent reviews, as many as one third of all participants in the present study achieved recovery at follow-up (Lally et al., 2017). We found that a lower EASE total score at baseline and reduction of EASE total score from baseline to follow-up increased the chance of recovery seven years later, also after adjustment for other characteristics previously found to influence the outcome (diagnosis, DUP, premorbid functioning). These characteristics had statistically significant bivariate associations with recovery in the current study but had less explanatory power than the EASE level when entered together in multi-variate analyses. Most notably, the findings were not confounded by diagnosis

The considerable impact of high levels of BSDs on mental state and functioning is in many ways self-evident. The weakening or loss of ownership of one's own thoughts, feelings, sensations, body,

movements, or personal history will influence life markedly. Even though these phenomena pertain to the person's inner world and are not visible to others, they regularly lead to compromised engagement with the outer world (Nelson et al., 2009), reduced capacity to interact with other people, to work, to study or to maintain self-care. This is in line with studies showing associations between BSDs and self-esteem, depression (Haug et al., 2016), suicidality (Haug et al., 2012b; Skodlar and Parnas, 2010), social function (Haug et al., 2014), verbal memory (Haug et al., 2012c), and negative symptoms (Nordgaard et al., 2018). According to the ipseity disturbance model (Nelson et al., 2014; Sass and Parnas, 2003) BSDs serve as precursors or vulnerability factor for developing psychotic symptoms, also indicating that changes in the level of BSDs may lead to changes in symptomatology and functioning.

Based on the notion that BSDs are core features in schizophrenia, it has been presumed that they are reasonably stable over time. Although there is considerable support for this view (Nordgaard et al., 2017; Nordgaard et al., 2018), a previous report has

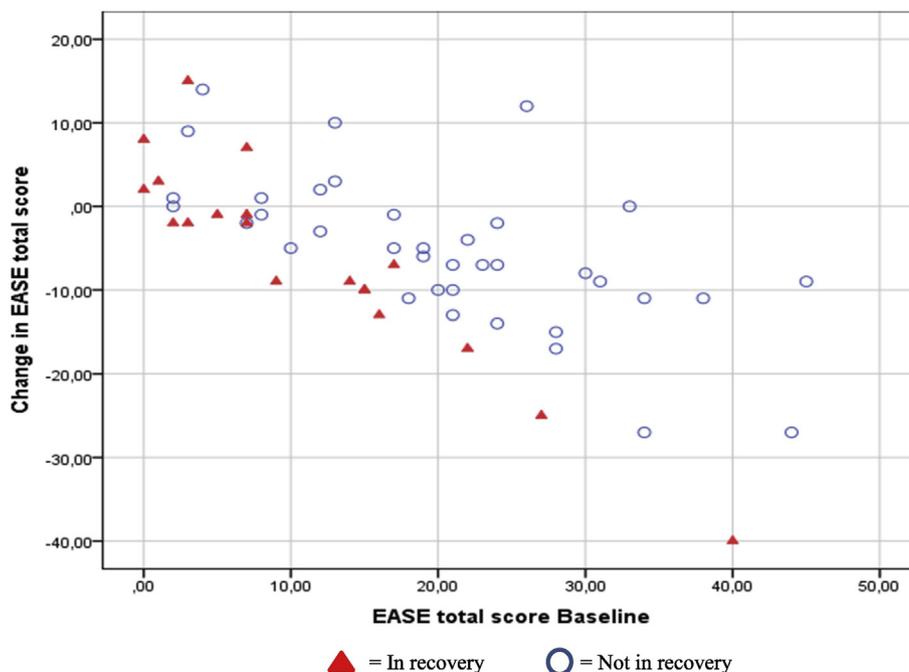


Fig. 1. Scatterplot of EASE total score at baseline by change in EASE total score over the follow up period.

Table 4

Hierarchical logistic regression analysis with recovery as the dependent variable and EASE total score at baseline, EASE total score change, DUP, premorbid academic function, premorbid social function and diagnosis as independent variables.

Dependent variable: Recovery	B	P	95% CI
EASE total score at baseline	−0.31	<0.01	0.62 to 0.87
EASE total score change	−0.26	<0.01	0.65 to 0.90
Dependent variable: Recovery	B	P	95% CI
EASE total score at baseline	−0.32	<0.01	0.60–0.87
EASE total score change	−0.28	<0.01	0.63–0.90
Premorbid academic function	−0.49	0.23	0.26–1.13
Premorbid social function	−0.41	0.12	0.39–1.12
Dependent variable: Recovery	B	P	95% CI
EASE total score at baseline	−0.29	<0.01	0.61–0.91
EASE total score change	−0.29	<0.01	0.62–0.91
Premorbid academic function	−0.47	0.25	0.28–1.40
Premorbid social function	−0.42	0.13	0.38–1.14
LnDUP	−0.63	0.27	0.17–1.65
Dependent variable: Recovery ^a	B	P	95% CI
EASE total score at baseline	−0.20	0.03	0.67–0.98
EASE total score change	−0.26	<0.01	0.60–0.92
Premorbid academic function	−0.55	0.21	0.25–1.36
Premorbid social function	−0.43	0.14	0.37–1.15
LnDUP	−0.48	0.45	0.18–2.12
Diagnosis	2.32	0.06	0.87–118.8

^a Model Nagelkerke R square: 0.67.

shown a modest but statistically significant reduction in BSDs from baseline to follow-up (Svendsen et al., 2018). This support the need to further explore the potential for a changeable and treatment-responsive aspect of some BSDs. Recent ideas suggest that certain BSD phenomena can be triggered by or are reactive to stressors (Sass et al., 2018; Sass and Borda, 2015), and may thus be considered more ‘secondary’, while other phenomena are more foundational or ‘primary’. This might imply that at least some BSDs could remit with the removal of the stressor, or through treatment efforts specifically targeting the relevant BSDs. In the current study, therapists received a report from the baseline EASE interview. Most participants had long-term treatment contact, and the therapists’ knowledge of the presence and type of specific BSD features could possibly have directed the focus of psychosocial interventions. Our follow-up data does however not contain any qualitative information about treatment at this level of detail. Further research is required to study interventions specifically targeting BSDs.

4.2. Strengths and limitation of the study

4.2.1. Strengths

The study had few exclusion criteria, so the sample was broadly recruited through the Norwegian national public mental health system. There are almost no private mental health care in Norway, and the sample thus represents a comprehensive, near-to epidemiological sample of first treated psychosis. To our knowledge, this study has the longest follow-up period of studies using EASE. The study also had a fairly high follow-up rate (62%). The person who conducted the assessments of BSDs at follow-up was blind to baseline data and to the results of the diagnostic interviews at follow-up. The results of this study is found also after adjusting for diagnostic categories.

4.2.2. Limitations

Remission and recovery are both parts of a continuum. While there is a consensus about a cut-off for the term “recovery”, the experience of recovery is also a uniquely personal process and

participants that did not meet these criteria could still have a functional and meaningful life. The definition of recovery was based on psychotic symptoms. Since this definition does not include affective symptoms, we cannot rule out that some in the recovery group experienced depression or elevated mood at follow up. A total of 38% of the patients from the baseline study did not participate in the follow-up study; however, there was no indication that the attrition was biased. The sample size is low, increasing the risk for type II errors and for overestimating the effect sizes of positive findings. Finally, we are highlighting the findings relating to BSDs since they are seen as more basic and stable traits compared to clinical symptoms, but any conclusions regarding causality should be drawn with caution.

4.2.3. Conclusion

Low baseline level of basic self-disturbances in first treated psychotic disorders, and further reduction over time, independently predicted recovery seven years later. These findings strongly support the clinical value of including BSDs as core measures in the routine assessment of psychotic disorders.

Contributions

EH, MØ, PM and IM planned the original study, while EH, MØ, IM, BN and IHS planned the follow-up study. IHS and EH conducted the follow-up. IHS conducted the follow-up interviews, the statistical analyses and wrote the first draft of the paper. All authors made contributions to interpretations and content.

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Declaration of competing interest

The authors report no conflicts of interest.

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References

- Addington, D., Addington, J., Schissel, B., 1990. A depression rating scale for schizophrenics. *Schizophr. Res.* 3 (4), 247–251.
- Andreasen, N.C., Carpenter Jr., W.T., Kane, J.M., Lasser, R.A., Marder, S.R., Weinberger, D.R., 2005. Remission in schizophrenia: proposed criteria and rationale for consensus. *Am. J. Psychiatry* 162 (3), 441–449.
- Angst, J., 2009. Course and prognosis of mood disorders. In: Gelder, M., Andreasen, N.C., Lopez-Ibor, J.J., Geddes, J.R. (Eds.), *New Oxford Textbook of Psychiatry*. Oxford University Press, Oxford, pp. 665–669.
- Austin, S.F., Mors, O., Secher, R.G., Hjorthoj, C.R., Albert, N., Bertelsen, M., Jensen, H., Jeppesen, P., Petersen, L., Randers, L., Thorup, A., Nordentoft, M., 2013. Predictors of recovery in first episode psychosis: the OPUS cohort at 10 year follow-up. *Schizophr. Res.* 150 (1), 163–168.
- 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.
- Bernstein, D.P., Stein, J.A., Newcomb, M.D., 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 (2), 169–190.
- Birchwood, M., Smith, J., Cochrane, R., Wetton, S., Copestake, S., 2018. The social functioning scale the development and validation of a new scale of social adjustment for use in family intervention programmes with schizophrenic

- patients. *Br. J. Psychiatry* 157 (06), 853–859.
- Borda, J.P., Sass, L.A., 2015. Phenomenology and neurobiology of self disorder in schizophrenia: primary factors. *Schizophr. Res.* 169 (1–3), 464–473.
- Cannon-Sporer, H.E., Potkin, S.G., Wyatt, R.J., 1982. Measurement of premorbid adjustment in chronic schizophrenia. *Schizophr. Bull.* 8 (3), 470–484.
- Clemmensen, L., Vernal, D.L., Steinhilber, H.C., 2012. A systematic review of the long-term outcome of early onset schizophrenia. *BMC Psychiatry* 12 (1), 150.
- Davidson, K.A., 2009. Anomalous self-experience in adolescents at risk of psychosis. *Psychopathology* 42 (6), 361–369.
- Endicott, J., Spitzer, R.L., Fleiss, J.L., Cohen, J., 1976. The global assessment scale: a procedure for measuring overall severity of psychiatric disturbance. *Arch. Gen. Psychiatry* 33 (6), 766–771.
- First, M., Spitzer, R.L., Gibbon, M., Williams, J.B.W., 1996. Structured Clinical Interview for DSM-IV Axis I Disorders, Clinician Version (SCID-CV). American Psychiatric Press.
- 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.
- Gross, G., Huber, G., Klosterkötter, J., 1998. The early phase of schizophrenia and prediction of outcome. *Int. Clin. Psychopharmacol.* 13 (Suppl. 1), S13–S22.
- 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.
- Haug, E., Melle, I., Andreassen, O.A., Raballo, A., Bratlien, U., Oie, M., Lien, L., Moller, P., 2012. The association between anomalous self-experience and suicidality in first-episode schizophrenia seems mediated by depression. *Compr. Psychiatry* 53 (5), 456–460.
- Haug, E., Oie, M., Melle, I., Andreassen, O.A., Raballo, A., Bratlien, U., Lien, L., Moller, P., 2012. The association between self-disorders and neurocognitive dysfunction in schizophrenia. *Schizophr. Res.* 135 (1–3), 79–83.
- Haug, E., Oie, M., Andreassen, O.A., Bratlien, U., Raballo, A., Nelson, B., Moller, P., Melle, I., 2014. Anomalous self-experiences contribute independently to social dysfunction in the early phases of schizophrenia and psychotic bipolar disorder. *Compr. Psychiatry* 55 (3), 475–482.
- Haug, E., Oie, M., Andreassen, O.A., Bratlien, U., Nelson, B., Aas, M., Moller, P., Melle, I., 2015. Anomalous self-experience and childhood trauma in first-episode schizophrenia. *Compr. Psychiatry* 56, 35–41.
- Haug, E., Øie, M.G., Andreassen, O.A., Bratlien, U., Romm, K.L., Møller, P., Melle, I., 2016. The association between anomalous self-experiences, self-esteem and depressive symptoms in first episode schizophrenia. *Front. Hum. Neurosci.* 10.
- Haug, E., Oie, M., Andreassen, O.A., Bratlien, U., Nelson, B., Melle, I., Moller, P., 2017. High levels of anomalous self-experience are associated with longer duration of untreated psychosis. *Early Interv Psychiatry* 11 (2), 133–138.
- Jaaskelainen, E., Juola, P., Hirvonen, N., McGrath, J.J., Saha, S., Isohanni, M., Veijola, J., Miettunen, J., 2013. A systematic review and meta-analysis of recovery in schizophrenia. *Schizophr. Bull.* 39 (6), 1296–1306.
- Kay, S.R., Fiszbein, A., Opler, L.A., 1987. The positive and negative syndrome scale (PANSS) for schizophrenia. *Schizophr. Bull.* 13 (2), 261–276.
- Klosterkötter, J., Ebel, H., Schultze-Lutter, F., Steinmeyer, E.M., 1996. Diagnostic validity of basic symptoms. *Eur. Arch. Psychiatry Clin. Neurosci.* 246 (3), 147–154.
- Lally, J., Ajnakina, O., Stubbs, B., Cullinane, M., Murphy, K.C., Gaughran, F., Murray, R.M., 2017. Remission and recovery from first-episode psychosis in adults: systematic review and meta-analysis of long-term outcome studies. *Br. J. Psychiatry* 211 (6), 350–358.
- MacBeth, A., Gumley, A., 2008. Premorbid adjustment, symptom development and quality of life in first episode psychosis: a systematic review and critical reappraisal. *Acta Psychiatr. Scand.* 117 (2), 85–99.
- 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.
- 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.
- Nelson, B., Sass, L.A., Thompson, A., Yung, A.R., Francey, S.M., Amminger, G.P., McGorry, P.D., 2009. Does disturbance of self underlie social cognition deficits in schizophrenia and other psychotic disorders? *Early Interv Psychiatry* 3 (2), 83–93.
- 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., Thompson, A., Yung, A.R., 2013. Not all first-episode psychosis is the same: preliminary evidence of greater basic self-disturbance in schizophrenia spectrum cases. *Early Interv Psychiatry* 7 (2), 200–204.
- Nelson, B., Parnas, J., Sass, L.A., 2014. Disturbance of minimal self (ipseity) in schizophrenia: clarification and current status. *Schizophr. Bull.* 40, 479–482.
- Nordgaard, J., Parnas, J., 2014. Self-disorders and the schizophrenia spectrum: a study of 100 first hospital admissions. *Schizophr. Bull.* 40 (6), 1300–1307.
- Nordgaard, J., Handest, P., Vollmer-Larsen, A., Saebye, D., Pedersen, J.T., Parnas, J., 2017. Temporal persistence of anomalous self-experience: a 5-year follow-up. *Schizophr. Res.* 179, 36–40.
- Nordgaard, J., Nilsson, L.S., Saebye, D., Parnas, J., 2018. Self-disorders in schizophrenia-spectrum disorders: a 5-year follow-up study. *Eur. Arch. Psychiatry Clin. Neurosci.* 268 (7), 713–718.
- Parnas, J., Handest, P., 2003. Phenomenology of anomalous self-experience in early schizophrenia. *Compr. Psychiatry* 44 (2), 121–134.
- Parnas, J., Henriksen, M.G., 2014. Disordered self in the schizophrenia spectrum: a clinical and research perspective. *Harv Rev Psychiatry* 22 (5), 251–265.
- Parnas, J., Jansson, L., Sass, L., Handest, P., 1998. Self-experience in the prodromal phases of schizophrenia: a pilot study of first-admissions. *Neurol. Psychiatry Brain Res.* 6 (2), 97–106.
- 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.
- 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.
- 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. *Compr. Psychiatry* 48 (1), 88–94.
- Penttilä, M., Jaaskelainen, E., Hirvonen, N., Isohanni, M., Miettunen, J., 2014. Duration of untreated psychosis as predictor of long-term outcome in schizophrenia: systematic review and meta-analysis. *Br. J. Psychiatry* 205 (2), 88–94.
- 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., Preti, A., 2018. The self in the spectrum: a closer look at the temporal stability of self-disorders in schizophrenia. *Psychopathology* 1–5.
- Raballo, A., Saebye, D., Parnas, J., 2011. Looking at the schizophrenia spectrum through the prism of self-disorders: an empirical study. *Schizophr. Bull.* 37 (2), 344–351.
- Robinson, D.G., Woerner, M.G., McMeniman, M., Mendelowitz, A., Bilder, R.M., 2004. Symptomatic and functional recovery from a first episode of schizophrenia or schizoaffective disorder. *Am. J. Psychiatry* 161 (3), 473.
- Rosenberg, M., 1989. Society and the Adolescent Self-image. Rev. ed. Wesleyan University Press, Middletown, Conn.
- 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.
- 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.
- Saunders, J.B., Aasland, O.G., Babor, T.F., de la Fuente, J.R., Grant, M., 1993. Development of the alcohol use disorders identification test (AUDIT): WHO collaborative project on early detection of persons with harmful alcohol consumption—II. *Addiction* 88 (6), 791–804.
- Schultze-Lutter, F., 2009. Subjective symptoms of schizophrenia in research and the clinic: the basic symptom concept. *Schizophr. Bull.* 35 (1), 5–8.
- Skodlar, B., Parnas, J., 2010. Self-disorder and subjective dimensions of suicidality in schizophrenia. *Compr. Psychiatry* 51 (4), 363–366.
- 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.* <https://doi.org/10.1016/j.schres.2018.1007.1011>.
- Tandon, R., Nasrallah, H.A., Keshavan, M.S., 2009. Schizophrenia, "just the facts" 4. Clinical features and conceptualization. *Schizophr. Res.* 110 (1–3), 1–23.
- Ten Velden Hegelstad, W., Haahr, U., Larsen, T.K., Auestad, B., Barder, H., Evensen, J., Joa, I., Johannessen, J.O., Langeveld, J., Melle, I., Opjordsmoen, S., Rossberg, J.I., Rund, B.R., Simonsen, E., Vaglum, P., McGlashan, T., Friis, S., 2013. Early detection, early symptom progression and symptomatic remission after ten years in a first episode of psychosis study. *Schizophr. Res.* 143 (2–3), 337–343.
- Tohen, M., Zarate Jr., C.A., Hennen, J., Khalsa, H.M., Strakowski, S.M., Gebre-Medhin, P., Salvatore, P., Baldessarini, R.J., 2003. The McLean-Harvard First-episode mania study: prediction of recovery and first recurrence. *Am. J. Psychiatry* 160 (12), 2099–2107.
- Torgalsboen, A.K., Mohn, C., Czajkowski, N., Rund, B.R., 2015. Relationship between neurocognition and functional recovery in first-episode schizophrenia: results from the second year of the Oslo multi-follow-up study. *Psychiatry Res.* 227 (2–3), 185–191.
- Uphthegrove, R., Birchwood, M., Ross, K., Brunett, K., McCollum, R., Jones, L., 2010. The evolution of depression and suicidality in first episode psychosis. *Acta Psychiatr. Scand.* 122 (3), 211–218.
- Weibell, M.A., Hegelstad, W.T.V., Auestad, B., Bramness, J., Evensen, J., Haahr, U., Joa, I., Johannessen, J.O., Larsen, T.K., Melle, I., Opjordsmoen, S., Rund, B.R., Simonsen, E., Vaglum, P., McGlashan, T., McGorry, P., Friis, S., 2017. The effect of substance use on 10-year outcome in first-episode psychosis. *Schizophr. Bull.* 43 (4), 843–851.