Stability in basic self-disturbances and diagnosis in a first treated psychosis: A seven year follow-up study

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Abstract

Background: Basic self-disturbances (BSDs) are considered core features of schizophrenia spectrum disorders, and are present in the prodromal, early psychotic and chronic phases. Considerable levels of BSDs are also present at first treatment in some patients with psychotic disorders outside the schizophrenia spectrum. There is limited knowledge about the stability of self-disturbances over time.

Aim: To explore the stability of BSDs in a seven-year follow-up of first treatment patients, and the association between baseline levels and changes in BSDs and diagnostic changes at follow-up.

Method: Longitudinal study of 56 patients (35 schizophrenia and 21 non-schizophrenia) recruited at their first treatment for a psychotic disorder. BSDs were assessed using the Examination of Anomalous Self-Experience (EASE), while diagnostic categories, clinical symptom severity, and functioning were assessed with standard clinical instruments.

Results: The schizophrenia group had significantly lower levels of BSDs at follow-up compared to baseline. The EASE domain "Cognition and stream of consciousness" was the most stable. There were no diagnostic changes into or out of schizophrenia spectrum. Patients with schizophrenia had significantly higher levels of BSDs both at baseline and at follow up than patients with psychotic disorders outside the schizophrenia spectrum, who showed stable low levels.

Conclusion: We found a decrease and thus less stability in BSDs in schizophrenia than expected. This might indicate that BSDs tent to weaken over time, and that unknown individual characteristics may influence the development of BSDs. Diagnostic stability from baseline to follow-up may be due to long DUP before service entry.

1. Introduction

Basic self-disturbances (BSDs) selectively aggregate in schizophrenia spectrum disorders and are thus considered to be core features of the schizophrenia spectrum (Haug et al., 2012a; Henriksen and

Parnas, 2014; Nordgaard and Parnas, 2014; Sass and Parnas, 2003). BSDs are non-psychotic subtle disturbances of the person's spontaneous experience of him-/herself as a vital subject, naturally immersed in the world. BSDs affect the person's fundamental level of consciousness, the sense of corporeality, stability of self-experience and 'grip' on the world (Parnas and Handest, 2003). Typical descriptions of experiences are statements like "It is almost as I am not thinking my own thoughts", "I have lost something that seems natural for everybody – I have lost the manual for understanding life."

BSDs are in this context not considered as sequelae of psychosis, but instead seen as representing fundamental and potentially generative layers of psychopathology (Nordgaard and Parnas, 2014).

Stimulated by two Scandinavian qualitative studies (Møller and Husby, 2000; Parnas et al., 1998), recent studies have confirmed high levels of BSDs in prodromal/Ultra High Risk (UHR) (Comparelli et al., 2016; Koren et al., 2016; Koren et al., 2013; Koren et al., 2017; Nelson et al., 2012; Parnas et al., 2011; Raballo et al., 2016), early psychotic (Haug et al., 2012b; Nordgaard and Parnas, 2014) and chronic phases of schizophrenia (Raballo et al., 2011). Additional findings of BSDs in a study of children at high risk for schizophrenia support the notion that BSDs are part of a core vulnerability for developing schizophrenia (Parnas et al., 2016). In an Ultra High Risk group, BSDs were primarily seen in the domains "Cognition and stream of consciousness" (Domain 1) and "Self-awareness and presence" (Domain 2). The presence of BSDs in "Cognition and stream of consciousness" were also found to be the most predictive of transition to full-threshold psychosis (Nelson et al., 2012). Studies assessing BSDs in bipolar I disorder (Haug et al., 2012b) and in severe depersonalization (Sass et al., 2013) found both lower levels and a narrower range of BSDs in these disorders than in schizophrenia. Recent additions to the concept of BSDs are theories suggesting that while some BSDs are fundamental and core to schizophrenia (i.e. primary BSDs), others may be more consequential, compensatory or an attempt at coping (e.g, as a response to traumatic environmental circumstances; secondary BSDs**)**.(Borda and Sass, 2015; Sass et al., 2018; Sass and Borda, 2015).

In clinical practice, diagnoses are based on cross-sectionally- and historically reported symptoms. Since the clinical syndromes might not be fully formed at first treatment contact, diagnoses can change over time (Castro-Fornieles et al., 2011; Kim et al., 2011). This change may reflect the natural evolution of the disorder and/or new sources of information regarding the quality and quantity of initial symptoms (Schwartz et al., 2000). A study that examined diagnostic stability in first episode psychosis patients found that 11 out of 42 patients (26%) diagnosed with a mood disorder (major depression, bipolar I and II) with mood incongruent psychotic features in the first weeks of treatment had their diagnoses changed to schizophrenia or schizoaffective disorder over the next one to two years (Haahr et al., 2008). Another five-year follow-up study of first-admission patients found that high baseline levels of BSDs, as measured with a subset of the Bonn Scale for the Assessment of Basic Symptoms (BSABS), predicted subsequent development of schizophrenia spectrum disorders in those initially diagnosed outside of the spectrum. BSDs also predicted diagnostic stability in those within the spectrum (Parnas et al., 2011). That study is to our knowledge the only one until now to examine the association between BSDs and diagnostic stability and change.

Our research group have previously shown that BSDs aggregate in first-treatment patients with schizophrenia (Haug et al., 2012b). While clinical symptoms are unstable and diagnosis might change, BSDs are thought to be a more stable structural aspect of consciousness rather than fluctuating

abnormal mental content (Nordgaard et al., 2017a). There are, however, very few empirical studies investigating to what extent BSDs are stable over time. A recent follow-up study of first admission patients with non-affective psychosis, schizotypal disorder and other mental illnesses, examined the temporal persistence of life-time BSDs (assessed with the BSABS expanded with additional items targeting self-disorders) and found increased levels of BSDs after five years (Nordgaard et al., 2017a). Another study from the same research group investigated the development of BSDs from baseline to five years follow-up in 48 patients with first admission schizophrenia, using the Examination of Anomalous Self-Experiences (EASE) at baseline and during the 18-month period prior to follow up (Nordgaard et al., 2017b). The study found the same level of BSDs at baseline and follow-up. Both studies only included patients within the schizophrenia spectrum and could thus not investigate diagnostic stability for other conditions.

The current study was a seven year follow-up of a first treatment psychosis group (including both schizophrenia spectrum and non-schizophrenia spectrum cases). The aims were to investigate:

1) The stability/change of BSDs, at total and domain level.
2) Whether *baseline* levels of BSDs predicted diagnostic change.
3) Whether *changes* in the levels of BSDs predicted diagnostic change.

Our hypotheses were: (1) Because BSDs are core features of schizophrenia, they may show minor individual fluctuations but are relatively stable at the group level. Based on previous findings we hypothesized that particularly Domains 1 and 2 would show a high degree of stability. (2) High levels of BSDs at start of treatment in patients with psychotic disorder outside of the schizophrenia spectrum predict diagnostic change into schizophrenia seven years later, (3) An increase in BSDs over time in patients with a diagnosis outside the schizophrenia spectrum is associated with diagnostic change into schizophrenia.

2. Material and methods

2.1. Participants

The current study was a seven-year follow up of a cohort of first treatment psychosis patients from the Norwegian "Thematically Organized Psychosis" (TOP) study.

At baseline the study involved all treatment facilities in two neighboring Norwegian counties, with a county-wide population of 375,000 people. The study included all patients entering first adequate treatment for a broadly defined psychotic disorder including schizophrenia, schizophreniform disorder and schizoaffective disorder (hereafter referred to as "schizophrenia"), bipolar psychosis (bipolar disorder I and NOS – all with psychotic symptoms), and other psychotic disorders usually classified outside of the (narrow) schizophrenia spectrum (delusional disorder and psychosis NOS). Inclusion criteria were: Between 18 and 65 years of age and IQ > 70. Patients with concurrent substance use disorders were not excluded, but had to demonstrate at last one month without substance use or clear signs that the psychotic disorder had started before onset of significant substance use. All possible cases at all treatment facilities were screened, and all patients who met the inclusion criteria and agreed to participate were included. The study also included 13 patients enrolled in a closely related and partly overlapping cohort study of young psychosis patients born in 1985/86 (Bratlien et al., 2013). They met the same inclusion and exclusions criteria except the strict definition of first treatment.

Forty-nine from the early treatment group (32 schizophrenia, 9 bipolar, 8 OP) and seven patients from the birth cohort (3 schizophrenia, 4 bipolar) participated in the follow-up study. The 90 people originally included thus represented close to an epidemiological sample. Fifty seven individuals (63%) in the baseline study met the DSM-IV (Diagnostic and Statistical Manual of Mental Disorder, Fourth Edition) (First, 1996) criteria for schizophrenia, twenty (22%) for bipolar disorders and thirteen (14%) for other psychotic disorders. For more detailed description of the baseline study see Haug and colleagues (Haug et al., 2012b).

During the follow-up period, the patients received treatment as usual in their local health services. This treatment comprised regular supportive appointments with a therapist and psychopharmacological medication. A few also received psycho-educative sessions and/or cognitive behavioral therapy. Of the 90 patients included, 56 patients (62%) agreed to participate in the follow-up study: Forty-nine from the early treatment group (32 schizophrenia, 9 bipolar, 8 OP) and seven patients from the birth cohort (3 schizophrenia, 4 bipolar). All of the 34 patients who were not part of the follow-up were alive, however 15 had moved and were impossible to reach, and 19 did not want to participate. There were no significant differences in the baseline demographic and clinical characteristics between those who participated and who did not participate in the follow-up.

All participants provided informed consent to participate at both time-points. The study was approved by the Regional Committee for Medical Research Ethics and the Norwegian Data Inspectorate.

2.2. Assessments

All patients were evaluated with an extensive clinical assessment battery at baseline, and reevaluated with the same battery seven years later. Only the instruments relevant for this part of the study are presented here.

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

At baseline, BSDs were assessed with the Examination of Anomalous Self Experience (EASE) manual (Parnas et al., 2005) by an experienced psychiatrist (EH). The inter-rater reliability (IRR) for the EASE assessments, including the baseline study, has been found to be very good (Moller et al., 2011; Nelson et al., 2012; Raballo and Parnas, 2012). At follow-up the EASE was assessed by a clinically experienced psychiatric nurse (IHS) after comprehensive EASE training with two experienced psychiatrists and certified EASE instructors (EH and PM). For training, videotaped EASE interviews were used and rated by IHS, EH and PM. The training IRR demonstrated an average Cohen's kappa of 0.71 which is considered to be good. IRR testing of the first seven follow-up EASE interviews (EH and IHS) showed Cohen's kappa of 0.78.

The EASE manual usually aims to capture life-time experiences of BSDs, but this can be adjusted according to the study aim. At baseline we registered only life-time experiences. Since we aimed to measure change in BSDs between baseline and follow-up, we rated BSDs that the patients had at the interview time or could recall as an experience over the last two years before follow-up, and used this information in the current analyses.

The EASE comprises 57 main items organized in five domains: (1) Cognition and stream of consciousness, (2) Self-awareness and presence, (3) Bodily experiences, (4) Demarcation/transitivism, and (5) Existential reorientation. BSDs are not considered to be discrete symptoms but highly overlapping and interconnected aspects of a gestalt. There are thus

considerable overlap between single items and domains, and both items and domains are statistically highly inter-correlated (Nordgaard and Parnas, 2014; Raballo and Parnas, 2012). The items are scored using a 5-point Likert scale (0-4), 0=absent; 1= questionably present; 2= definitely present, mild; 3= definitely present, moderate; 4= definitively present, severe. To be able to compare to previous publications these were dichotomized into 0 (for absent and questionably present) and 1 (for definitely present, all severity levels). Item 2.13 (anxiety) was not included in these analyses, neither at baseline nor at follow-up, because that item is not a BSD per se but serves to enrich the data and as a contrast to the next item, ontological anxiety (item 2.14)(Parnas et al., 2005). The EASE has demonstrated high internal consistency (Moller et al., 2011; Nordgaard and Parnas, 2014).

2.2.2. Clinical assessments at follow-up

Diagnoses at follow-up were ascertained by trained clinical psychologists or medical doctors using Structured Clinical Interview for DSM-IV Axis I disorders (SCID module I, chapter A-E) (First, 1996), with additional information from medical charts. Eight of the patients were not in treatment contact with the public health system and were thus without available updated charts. They were still diagnosed based on SCID and available information.

Present symptom severity and functional status were measured with the Global Assessment of Functioning scale, split version - symptom (GAF-S) and, function (GAF-F) (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 the Calgary Depression Scale (CDSS) (Addington et al., 1990).

All assessments except the diagnostic interviews were conducted by the first author (IHS), who was blind both to baseline and current diagnoses and to baseline BSDs assessments to avoid assessment bias.

2.3. Statistical analyses

SPSS version 23.0 (SPSS inc., Chicago, IL, USA) was used to perform all statistical analyses. Mean and standard deviation are reported for continuous variables and percentages for categorical variables. Correlations were assessed using Pearson r and Spearman's *rho*. Since BSDs are considered to be a core feature of schizophrenia and not of other psychotic disorders, we *a priori* decided to combine patients with bipolar psychotic disorders and other psychotic disorders into one group, the "non-schizophrenia group". There were no significant differences between the bipolar group and the other psychosis group (psychotic disorder, NOS and delusional disorder) in the EASE total score or any EASE domain scores neither at baseline or at follow-up. Group comparisons for dichotomous variables were done using chi-square statistics, while group comparisons for continuous variables were evaluated with independent sample t-test for normally distributed data and Mann-Whitney test for data without normal distribution. The EASE scores were significantly skewed and were analyzed using nonparametric tests. We used Wilcoxon sign rank test to test the changes between baseline and follow-up for the dichotomized EASE scores. The level of significance was set to p=0.05, two-sided.

3. Results

The median follow-up period was 2579 days/7.5 years (range: 2362 - 2973 days). Baseline and follow-up socio-demographic and clinical features for each diagnostic group are reported in Table 1. There were significant clinical improvements, i.e. increase in functioning and a decrease in symptoms over time, with a clear effect of diagnostic groups and no time x group interactions (Table 1). There

was a statistically significant association between baseline total EASE scores and baseline clinical characteristics, ranging from -0.60 for GAF symptoms to 0.28 for PANSS negative symptoms and between follow-up total EASE score and follow-up clinical characteristics ranging from -0.72 for GAF symptoms to 0.32 for PANSS negative symptoms (for full correlational matrix see supplementary Tables 2 and 3).

The significant differences in baseline EASE total score between diagnostic groups were reproduced also for the follow-up subsample: The baseline median score was 22 (range 4 – 45) for the schizophrenia group and 7 (range 0 – 31) for the non-schizophrenia group (Mann Whitney U test z-score -5.23, $p< 0.01$). While 80 % of the patients with schizophrenia had an EASE total score $\geq$ 15 at baseline, there was only four patients (19%) who had an EASE total score of $\geq$15 in the non-schizophrenia group. At follow-up the median score was 14 (range 0-38) for the schizophrenia group and five (range 0-22) for the non-schizophrenia group (Mann Whitney U test z-score -3.51, $p<0.01$). The significant differences between the two diagnostic groups in EASE total at follow-up were mainly based on differences in Domain 1 (Cognition and stream of consciousness), with lower differences, but still statistically significant, for Domains 2 (Self-awareness and presence) and 3 (Bodily experiences) and no differences for Domains 4 (Demarcation/transitivism), and 5 (Existential reorientation). However, Domain 1 scores were also the highest in the non-schizophrenia group.

Figure 1 illustrates the correlation matrix of EASE domain scores at baseline and follow-up in the two diagnostic groups, and show increases as well as decreases in EASE scores for individual patients. A Wilcoxon Signed Rank Test confirmed significant reduction from baseline to follow-up in total EASE score in the schizophrenia group ($z=-3.81$, $p < 0.001$) but not in the no-schizophrenia group ($z=-0.66$, ns)). The least changes were seen in domains 1 (Cognition and stream of consciousness) and 4 (Demarcation/transitivism) (supplementary table 1). Because these tests were based on the sum of reported items within each domain, it is not given that the same items were reported at both baseline and at follow-up (supplementary table 2). For patients in the non-schizophrenia group, there were no significant EASE changes over time, probably based in the very low scores with limited variation at both time-points creating low statistical power and a ceiling effect for change.

There were limited diagnostic changes over the follow-up period *within* the diagnostic main groups, and no change *between* the diagnostic groups (Figure 2). The four patients in the non-schizophrenia group with high baseline EASE total scores (more than 15; range 15-31) retained their baseline diagnosis at follow-up. Two of these four patients were diagnosed with bipolar disorder (baseline EASE total score 15 and 17) and two patients were diagnosed with psychotic disorder NOS (baseline EASE total score 15 and 31). At follow-up these four patients' EASE scores were reported as 10, 5, 5 and 22 respectively. A total of six (29%) non-schizophrenia patients also reported one or more new EASE items at follow-up that they did not report at baseline (see supplementary Table 2). None of these however had high EASE total scores (i.e. ≥15).

4. Discussion

4.1 General discussion

As expected, we found significantly higher levels of BSDs in the schizophrenia compared to the non-schizophrenia group also at follow-up, particularly for Domain 1 (Cognition and stream of consciousness). We also hypothesized that BSDs would show limited individual changes and be relatively stable at the group level, but the results did not support this hypothesis: We found significantly lower level of reported BSDs for the last two years before follow-up for the schizophrenia group, with an all-over stability of low levels for the non-schizophrenia group.

At baseline the BSDs were based on reports of life-time experiences. However, if the same approach had been taken to rating SD at follow up (i.e., lifetime rating, including the baseline time point), only increases in SD could be detected and not decreases. In line with this, Nordgaard et al. who reported *lifetime* levels of BSDs at baseline *and* at follow-up indicated an increase in BSDs over time (Nordgaard et al., 2017a). In the next study from the same group they reported BSDs from the 18 month period prior to follow-up, and here found no changes in BSDs compared to baseline (Nordgaard et al., 2017b). We thus decided to restrict the follow-up to the two-years preceding the interview**.** During the interviews, patients with a decrease in reported BSDs confirmed having experienced BSDs previously. A common answer was, "When I was really sick, I felt that way, but I don't have this feeling now" followed by an example. Thus, the reduction does not appear to be based on recollection bias. However, we cannot know the exact level of BSDs during the two years prior to baseline. Based on the patient's reports of "when I was really sick" we however find it likely that levels were at their highest close to the start of first treatment (i.e. study baseline).

We saw the least changes in Domain 1 (Cognition and stream of consciousness) and 4 (Demarcation/transitivism), controlled for the number of items comprised by the domains. In addition, Domain 1 scores were higher with significantly more items reported at both time points. This was in line with our hypothesis. Distinctive of the items in domain 1 is the experience of a disturbance in the flow of thoughts and in the ownership of one's own thoughts, i.e. the feeling of a gap between the self and the mental content. Domain 1 disturbances have previously been described as some of the first BSDs appearing in the prodromal phase and are also found to be the most predictive of transition to full-threshold psychosis in an treated Ultra High Risk group (Nelson et al., 2012). It is worth considering that there might be a link between Domain 1 as the strongest predictor of transition to psychosis in high risk groups, and for lack of therapeutic response.

We also hypothesized that high levels of BSDs at baseline and/or an increase in BSDs over time in patients with a non-schizophrenia group would predict diagnostic change to the schizophrenia group seven years later. However, we found a very high degree of diagnostic stability with no changes between the two diagnostic main groups during the follow-up period. Previous studies of diagnostic stability (Haahr et al., 2008; Parnas et al., 2011) were both conducted in urban areas, and particularly in the case of the Haahr study, the participants had very short durations of untreated psychosis (DUP). The current study was conducted in rural areas with considerable distances to the specialized psychiatric health services, and consequently with long DUPs. Since the expected diagnostic change usually take place early in the first episode, in this case before the first treatment contact, the observed diagnostic stability could thus be related to sample characteristics. Based on the diagnostic stability we could neither confirm nor reject our hypotheses related to BSDs and diagnostic change. It is however noteworthy that the four patients in the non-schizophrenia group

with high baseline levels of BSDs did not convert to schizophrenia, nor did the six patients in the non-schizophrenia group who reported an appearance of BSDs in new domains at follow-up.

While the main effect was a decrease of BSDs at the group level, some patients had stable levels, some experienced increases while others experienced decreases from baseline to follow-up. Since the two pre-existing studies of longitudinal development of BSDs report either an increase or stability in BSDs as main effects, the nuances in our findings might indicate that as yet unknown individual characteristics may influence the level or severity of BSDs which make them more susceptible to fluctuations than previously thought. At baseline the patients had experienced their first psychotic episode, which is usually associated with stress and emotional arousal, while at follow up most patients were in a more advanced and stable phase. This may explain some of the decreases in BSDs seen at follow-up in this study, as also indicated in the guidelines for the EASE interview (Parnas et al. 2005, p.239). As indicated by others, it is also possible that some BSDs fluctuate on top of stable trait disturbance while acute "episodes "of BSDs are trigged by or exacerbated as a response to traumatic environmental circumstances (secondary BSDs) (Koren et al., 2017; Sass et al., 2018; Sass and Borda, 2015).

The patients' treatment units received general information about BSDs and, when the patient agreed, the clinician also received a report including information about BSDs for the particular patient at baseline. Receiving a report detailing aspects of BSDs may have influenced the content of treatment. At follow-up, a majority of the patients had regular contact with a specialist or a general practitioner, over a third was using anti-psychotic medication and nearly thirty percent used medication for mood-disorders. To what extent treatment directly or indirectly influences fluctuations in BSDs is not known at this stage. Our results however suggest that this should be a focus for future studies.

4.2 Strengths and limitation of the study

4.2.1. Strengths

The patient sample was broadly recruited with few exclusions criteria and represents a comprehensive, near to epidemiological sample. The follow-up period was seven and a half year and is to our knowledge the longest follow-up study of BSDs using the EASE instrument at both baseline and follow-up.

4.2.2. Limitations

There was some attrition of the original sample, but without signs that attrition was biased. After standard training, the IRR testing of the follow-up EASE assessments comprised the first seven (12.5 %) out of 56 interviews. We used a standard life-time measure of BSDs at baseline but chose to measure over the last two years at follow-up. We do not know if the life-time report is fully representative of the level of BSDs in the two-year period preceding baseline.

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