High levels of anomalous self-experience are associated with longer duration of untreated psychosis

Running title: Anomalous self-experience and DUP

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Abstract

Aim

To investigate the relationship between anomalous self-experiences and duration of untreated psychosis in a sample of patients with first episode schizophrenia spectrum disorders.

Methods

Anomalous self-experiences were assessed by means of the Examination of Anomalous Self-Experience manual in 55 patients referred to their first adequate treatment for schizophrenia. Diagnoses, symptom severity, functioning and childhood trauma were assessed using the Structured Clinical Interview for the Positive and Negative Syndrome Scale, Premorbid Adjustment Scale, Social Functioning Scale and Childhood trauma questionnaire. Substance misuse was measured with the Drug Use Disorder Identification Test, and alcohol use was measured with the Alcohol Use Disorder Identification Test. Duration of untreated psychosis was measured in accordance with a standardized procedure.

Results

High levels of anomalous self-experiences are significantly associated with longer duration of untreated psychosis, an association which held after correcting for other variables associated with long duration of untreated psychosis.

Conclusions

The field of early detection in psychosis is in need of additional clinical perspectives to make further progress. Improved understanding and assessment of anomalous self-experiences may help clinicians to detect these important phenomena and provide earlier help, and thus reduce treatment delay.

Key words: Early intervention, Psychotic Disorders, Schizophrenia, Self

Introduction

Long duration of untreated psychosis (DUP) is associated with more severe symptoms at the start of first treatment (1, 2), not just positive symptoms but also avolition and other negative symptoms (2), poor insight (1), poor social integration (1). Long DUP is also associated with poorer treatment response and poorer short- and long-term outcomes (3, 4), while a reduction of DUP has a positive influence on short- and long –term prognosis (5-7). Several factors are associated with or contribute to long DUP, including poor premorbid adjustment (8), the experience of childhood trauma (8) and a more gradual onset of psychosis (8, 9) . To reduce DUP it is necessary to understand the reasons behind long treatment delays, including psychological impediments to early diagnosis and interpersonal factors that can delay help-seeking (10, 11).

Anomalous self-experiences (ASEs) are mental phenomena that most probably cause delay in help-seeking. ASEs are non-psychotic disturbances of the basic sense of self that characterize schizophrenia spectrum disorders (12-15). They refer to fundamental distortions of the first-person perspective, including deficiencies in the sense of being a self-present, single, temporally persistent, bodily, and bounded subject of experience (16). They represent a wide range of experiential deviations, like certain subtle forms of depersonalization, anomalous experiences of cognition and stream of consciousness, self-alienation, pervasive difficulties in grasping familiar and taken-for-granted meanings, deficiency in automatic and un-reflected immersion in the shared social world, unusual bodily feelings, permeability or complete loss of the self-world boundary, as well as existential reorientation as a consequence of alterations

in the sense of reality and existence (12). ASEs often result in profound social withdrawal, a phenomenon associated with long DUP (1). In addition, ASEs may contribute to poor insight and consequently treatment noncompliance (17).

ASEs are typically most overtly present in the prodromal phase, before the emergence of psychotic symptoms (18, 19), and in some individuals already present during childhood or early adolescence (15). They are present in genetically high-risk samples (20, 21) and predict future onset of schizophrenia spectrum disorders in nonpsychotic clinical populations (22) and in patients at ultra high risk for psychosis (23). Many do not experience or perceive their ASEs as symptoms of an illness, but rather as intrinsic and habitual aspects of their existence and identity; in this sense, they may be thought to contribute to a lack of insight into illness (17). The presence of ASEs could thus be a direct impediment to adequate help seeking and treatment delay. Since ASEs often are present already in childhood or early adolescence they could also contribute to poor premorbid adjustment and thus indirectly increase the DUP.

A previous study reported an association between ASEs and the duration of untreated illness, but no association between ASEs and DUP, as a co-incidental finding (14). However, in addition to patients with psychotic disorders, the study included patients with non-psychotic affective disorders, personality disorders and anxiety disorders, in which DUP (i.e. psychosis) is not a relevant feature. Our aim in the present study is to investigate the relationship between ASEs and DUP in a sample of patients with first treated schizophrenia spectrum disorders, with the hypothesis that a high level of ASEs will have an independent association with long DUP even after correcting for other variables associated with long DUP.

Methods

Design and sample

The current study is part of the Norwegian Thematically Organized Psychosis (TOP) study (24). The study involved all treatment facilities in two neighbouring Norwegian counties (Hedmark and Oppland) with a county-wide population of 375.000 people. Inclusion criteria were being between 18 to 65 years, and being consecutive in- or outpatient referred to first adequate treatment for a DSM-IV diagnosis of schizophrenia (schizophrenia, schizophreniform disorder and schizoaffective disorder). Exclusion criteria were the presence of brain injury, neurodegenerative disorder, or mental retardation. Patients with concurrent substance use disorders were included, but had to demonstrate at least one month without substance use, or clear signs that the psychotic disorder had started before the onset of significant substance use (i.e. did not meet the criteria for substance induced psychotic disorder).

During 2008 and 2009 a total of 55 patients with schizophrenia spectrum disorders coming to their first adequate treatment (i.e. not having previously received adequate antipsychotic medication in adequate doses for 12 weeks, or until remission); some had not initiated treatment at first evaluation. The sample includes all consecutively identified first episode patients from all participating health services in the two counties. For the purpose of the current analyses we additionally included 11 patients enrolled in a related study of young patients with psychosis born in 1985/86 (25, 26). They were in the early phases of treatment and met the same inclusion and exclusion criteria, except for the strict definition of first treatment.

All participants gave written, informed consent to participate. The study was approved by the Regional Committee for Medical Research Ethics and the Norwegian Data Inspectorate.

Clinical assessments

Diagnoses were ascertained by two researchers who were also experienced psychiatrists (EH and UB) using the Structural Clinical Interview for the Diagnostic and Statistical Manual of Mental Disorders, fourth edition (SCID-IV)(27). Symptom severity were assessed using the Structured Clinical Interview for the Positive and Negative Syndrome Scale (SCI-PANSS) (28). DUP was measured as time in weeks from onset of psychosis (i.e. first week with a score of four or more on one of the of the PANSS subscale items: delusions, hallucinatory behaviour, grandiosity, suspiciousness/persecution or unusual thought content) and until the start of adequate treatment (29).

Both researchers (EH and UB) completed the TOP study group's training and reliability program with SCID training based on- and supervised by the UCLA training program (30). For DSM-IV diagnostics, mean overall kappa for the standard diagnosis of training videos for the study as a whole was 0.77, and mean overall kappa for a randomly drawn subset of study patients was also 0.77 (95% CI 0.60-0.94). Intra Class Coefficients (ICC 1.1) for the other scales were: PANSS positive subscale 0.82 (95% CI 0.66-0.94), PANSS negative subscale 0.76 (95% CI 0.58-0.93) and PANSS general subscale 0.73 (95% CI 0.54-0.90)

ASEs were assessed using the Examination of Anomalous Self-Experience (EASE) manual (12), a 30-90 minutes interview comprising five domains: (1) Cognition and stream of consciousness. (2) Self-awareness and presence. (3) Bodily experiences. (4) Demarcation/transitivism. (5) Existential reorientation. This represents a wide variety of anomalous self-experiences condensed into 57 main items and scored on a 5-point Likert scale (0-4), in which 0=absent; 1=questionably present; 2=definitely present, mild; 3=definitely present, moderate; 4=definitely present, severe. For the purpose of the analyses, the resulting scores were dichotomized into 0 (absent or questionably present) and 1

(definitely present, all severity levels). Theoretically, ASEs are not considered to be discrete symptoms but to present parts of gestalt- like phenomenon. There are thus considerable overlap between single items and domains, and both items and domains are statistically highly inter-correlated. We have thus used the total EASE score in the analyses. The questions about ASEs in the EASE are not focused on a specific time period but captures reports of life-time experiences of ASEs. EH was trained by one of the authors of the EASE (PM), and conducted all the interviews. The inter-rater reliability (IRR) of the EASE, including in the current study, has been found to be very good (23, 31, 32).

Data on childhood trauma were collected using the Norwegian version of the Childhood Trauma Questionnaire (CTQ) (33). Data on childhood adjustment were collected using the Premorbid Adjustment Scale (PAS)(34). For the purpose of this study it was divided into two domains; Academic and Social. For each domain we used the initial (i.e. childhood) mean scores and subsequent change scores till the last premorbid period within each domain (35, 36). Social withdrawal was assessed with the Social Functioning Scale (37), subscale 1, social withdrawal (time spent alone, initiation of conversation, social avoidance).

Insight was measured at baseline with the PANSS item G12 (insight) and Birchwood Insight Scale (38), which is a self-report with 8 questions addressing 3 components of insight (need for treatment, awareness of illness, and relabeling of symptoms). We have used the G12 in our regression analyses because this showed a stronger correlation with DUP than Birchwood Insight Scale.

Substance misuse was measured with the Drug Use Disorder Identification Test (DUDIT) (39), and alcohol use was measured with the Alcohol Use Disorder Identification Test (AUDIT) (40).

Statistical analysis

All analyses were performed with the statistical package SPSS, version 18.0. Mean and standard deviations are reported for continuous variables and percentages for categorical variables. Since DUP had a markedly skewed distribution (Table 1), it was transformed to its natural logarithm (LnDUP) and the transformed variable was used in all subsequent analyses. We first examined the bivariate associations between LnDUP and demographic- and clinical characteristics putatively associated with DUP. A multivariate linear regression analysis with LnDUP as the dependent variable was then conducted including variables that had a correlation coefficient > 0.1 with LnDUP in the bivariate analyses, before entering ASEs (EASE total score) at the last step. Only variables with a $p < 0.1$ were kept in the final model.

Results

Table 1 presents the demographic and clinical characteristics of the sample. The mean EASE total score was 25.5 ($\pm$ 9.7), indicating high levels of ASEs in the current sample with half of the items scored as present. The median DUP was 122 weeks (range 4-2040), indicating an unusually long DUP. There were no statistically significant differences between the group of strict first treatment patients and the 11 patients from the birth cohort study for gender, age, DUP, ASEs, childhood trauma, premorbid adjustment, symptom severity (PANSS subscales), insight, social withdrawal or substance misuse (data not shown).

Table 1 Demographic and clinical characteristics

Number of patients	55
Demographics	
Male gender, n (%)	28 (51)
Age years, mean (SD)	25.2 (7.3)
DUP weeks, median (range)	122 (4-2040)

Anomalous Self-Experiences	
EASE total score , mean (SD)	25.5 (9.7)
Childhood trauma	
CTQ total score, mean (SD)	47.2 (18.8)
Premorbid adjustment	
PAS, mean (SD)	
Premorbid /childhood social function	1.7 (1.7)
Premorbid /childhood academic function	2.1 (1.6)
Change in premorbid social function	0.5 (1.9)
Change in premorbid academic function	0.8 (1.5)
Symptom severity	
PANSS, mean (SD)	
PANSS positive score	18.7 (4.6)
PANSS negative score	18.2 (7.1)
PANSS general score	40.0 (8.0)
Substance misuse	
AUDIT, mean (SD)	9.1 (8.8)
DUDIT, mean (SD)	2.9 (7.8)
Insight	
PANSS G12, mean (SD)	2.5 (1.4)
Birchwood insight, mean (SD)	7.8 (2.2)

In the bivariate analyses we found significant, positive correlations between ASEs (EASE total score) and DUP (LnDUP) (r=.320, p=.017), and between childhood trauma (CTQ total score) and DUP (Table 2). We did not find any significant correlations between DUP and

gender, negative symptoms, insight, social withdrawal, substance misuse, or premorbid adjustment (Table 2). Nor did we find any significant association between EASE total score and gender, negative symptoms, insight, childhood trauma, social withdrawal, substance misuse, or premorbid adjustment (Table 2). When combined in a multiple linear regression analysis we found that the association between ASEs and DUP remained statistically significant while the association between childhood trauma and DUP only reached a trend level for statistical significance, indicating a possibly mediating effect of ASEs on the association between childhood trauma and DUP (Table 3). Based on our a priori hypothesis regarding premorbid adjustment we also conducted a follow-up multiple linear regression analysis including the full range of premorbid adjustment data, but this had no influence on the results (data not shown).

Table 2 Correlations between DUP, ASEs and other variables.

		† DUP	‡ ASEs
Gender	Pearson Correlation	-.092	.175
	Sig. (2-tailed)	.502	.200
§ Negative symptoms	Pearson Correlation	.003	-.217
	Sig. (2-tailed)	.981	.112
¶ Insight (G12)	Pearson Correlation	.101	.028
	Sig. (2-tailed)	.461	.838
¶ ¶ Insight (Birchwood)	Pearson Correlation	.077	-.117
	Sig. (2-tailed)	.574	.394
¥ Childhood trauma	Pearson Correlation	.323*	.207
	Sig. (2-tailed)	.024	.154
¥ Social withdrawal	Pearson Correlation	-.112	-.156
	Sig. (2-tailed)	.417	.257
Premorbid /childhood social function	Pearson Correlation	-.005	.147
	Sig. (2-tailed)	.970	.289
Premorbid /childhood academic function	Pearson Correlation	.039	-.016
	Sig. (2-tailed)	.782	.908
Change in premorbid social function	Pearson Correlation	.042	.040
	Sig. (2-tailed)	.766	.781
Change in premorbid academic function	Pearson Correlation	.119	.076
	Sig. (2-tailed)	.405	.596
¤ AUDIT	Pearson Correlation	.162	-.109
	Sig. (2-tailed)	.237	.427
¤¤ DUDIT	Pearson Correlation	.127	.238
	Sig. (2-tailed)	.356	.080

*Correlation is significant at the 0.05 level (2-tailed).

† LnDUP

‡EASE total score

§ PANSS negative score

¶ PANSS general item 12

¶ ¶ Birchwood Insight Scale

¥CTQ total score

¥SFS subscale 1, social withdrawal

¤Alcohol Use Disorder Identification Test

¤¤Drug Use Disorder Identification Test

Table 3 Multiple linear regression analysis with DUP as the dependent variable, and Childhood trauma and ASEs as independent variables.

Discussion

Our main finding was that high levels of ASEs are associated with longer DUP in a first episode schizophrenia sample even after correcting for other variables associated with long DUP. ASEs are by nature for the majority of patients confusing, scaring and very difficult to describe and communicate to others, even family members (18). People with a high level of ASEs often report that they feel alienated and detached from their surroundings; some even report that they sometimes feel that they are not human beings, or that neither they nor other people exist at all. As a result, patients with high levels of ASEs often feel that nobody is able to understand them. As a consequence, it is likely that they hesitate or decide not to seek help or tell other people about their distressing experiences, even if they may have some insight into having a severe mental disorder. The distortion of basic self-experience tends to occur gradually rather than abruptly, and ASEs are not necessarily experienced by the person as symptoms of an illness, even though they experience a fundamental change (18, 19). This may delay help seeking too (17). Further, clinicians may have a tendency to focus on conventional psychotic symptoms and not these non-psychotic early phenomena, which are not included in standard contemporary diagnostic systems (41). This could certainly contribute to a delay in diagnosis and adequate treatment, even in help-seeking patients. Since ASEs can be present very early in the development of schizophrenia, they are often considered as stable or trait-like phenomena. Still, we cannot rule out that ASEs might increase over time in untreated patients and that high levels of ASEs are induced by a long DUP, and not the other way around.

The only previous study reporting on the relationship between ASEs and DUP did not find any statistically significant association (14).The finding was however coincidental, and the study included non-psychotic patients and did not report on the length of DUP or how it was

measured. The exceptionally long DUP and wide range of measures in the current study may have increased the statistical power to detect associations. One probable reason for the long DUP could be that this was the first early psychosis study in the two counties, which covered a very large and sparsely populated geographical area, with several small general psychiatric treatment units in charge of treating patients with schizophrenia, thus clearly limiting clinicians' experience with assessing and recognizing first episode patients.

Limitations

In a cross-sectional design it is difficult to distinguish the causes from the consequences of DUP. However, even though they may fluctuate to some extent, researchers and clinicians today see ASEs as mainly trait-like disturbances that are present before the occurrence of frank psychotic symptoms and that do not increase during persistent psychosis (23, 42, 43). T hus it is likely that ASEs are causally related to rather than a consequence of long DUP. We do not have reliability calculations for the DUP measures in the current study. The very long DUP cases were however made as all-information consensus scores between the two researchers (EH and UB) and the last author.

Implications

More focus on and knowledge about ASEs in patients at high risk for psychosis and also in nonpsychotic clinical populations may help clinicians to detect these phenomena, even before the emergence of frank psychotic symptoms, and thus avoid treatment delay once psychotic symptoms emerge.

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