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The course of negative symptom in first episode psychosis and the relationship with social recovery

Brioney Gee^a, Jo Hodgekins^{a,*}, David Fowler^b, Max Marshall^c, Linda Everard^d, Helen Lester^e, Peter B. Jones^f, Tim Amos^g, Swaran P. Singh^h, Vimal Sharma^{i,j}, Nick Freemantle^k, Max Birchwood^h

^a Norwich Medical School, University of East Anglia, Norwich NR4 7TJ, UK

^b University of Sussex, Brighton BN1 9RH, UK

^c University of Manchester, Oxford Road, Manchester M13 9PL, UK

^d Birmingham and Solihull Mental Health NHS Foundation Trust, UK

^e University of Birmingham, Edgbaston, Birmingham B15 2TT, UK

^f University of Cambridge, Cambridge CB2 1TN, UK

^g University of Bristol, Bristol BS8 1TH, UK

^h University of Warwick, Gibbet Hill Road, Coventry CV4 7AL, UK

ⁱ University of Chester, Parkgate Road, Chester CH1 4BJ, UK

^j Cheshire and Wirral Partnership NHS Foundation Trust, UK

^k University College London, Gower St, London WC1E 6BT, UK

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ABSTRACT

Aims: To investigate trajectories of negative symptoms during the first 12 months of treatment for first episode psychosis (FEP), their predictors and relationship to social recovery.

Method: 1006 participants were followed up for 12 months following acceptance into Early Intervention in Psychosis services. Negative symptom trajectories were modelled using latent class growth analysis (LCGA) and predictors of trajectories examined using multinomial regression. Social recovery trajectories – also modelled using LCGA – of members of each negative symptom trajectory were ascertained and the relationship between negative symptom and social recovery trajectories examined.

Results: Four negative symptom trajectories were identified: Minimal Decreasing (63.9%), Mild Stable (13.5%), High Decreasing (17.1%) and High Stable (5.4%). Male gender and family history of non-affective psychosis predicted stably high negative symptoms. Poor premorbid adolescent adjustment, family history of non-affective psychosis and baseline depression predicted initially high but decreasing negative symptoms. Members of the Mild Stable, High Stable and High Decreasing classes were more likely to experience stably low functioning than the Minimal Decreasing class.

Conclusions: Distinct negative symptom trajectories are evident in FEP. Only a small subgroup present with persistently high levels of negative symptoms. A substantial proportion of FEP patients with elevated negative symptoms at baseline will achieve remission of these symptoms within 12 months. However, elevated negative symptoms at baseline, whether or not they remit, are associated with poor social recovery, suggesting targeted interventions for service users with elevated baseline negative symptoms may help improve functional outcomes.

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1. Introduction

Negative symptoms represent a significant unmet clinical need and the search for effective treatments has received renewed interest in recent years (Kirkpatrick et al., 2006). However, the mechanisms that underpin negative symptoms remain poorly understood. Negative symptoms can be subject to significant fluctuations over time,

particularly in the early course of psychosis (Edwards et al., 1999; Ventura et al., 2004). Individuals vary in the stability of their negative symptoms (Kelley et al., 2008) and those with persistently elevated negative symptoms are at highest risk of poor outcome (Husted et al., 1992; Mäkinen et al., 2008). Increased understanding of variation in negative symptom course might help illuminate the mechanisms which underlie negative symptoms.

The prevalence of persistent negative symptoms in first episode psychosis (FEP) remains unclear due to the use of inconsistent criteria for persistence. Moreover, grouping individuals into those with persistent negative symptoms and those without might mask the true complexity of

* Corresponding author.

E-mail address: j.hodgekins@uea.ac.uk (J. Hodgekins).

individual variation in negative symptom course. [Chen et al. \(2013\)](#) found that variation in negative symptom course in a cohort of schizophrenia patients was best modelled by four distinct trajectory classes, characterised by differing levels of negative symptoms at baseline and a distinctive pattern of longitudinal change. It is not yet known whether multiple negative symptoms trajectories are similarly evident in FEP. This study examines negative symptom trajectories in a large FEP sample using latent class growth analysis (LCGA), a data-driven approach to identifying patterns of longitudinal change within a heterogeneous population. Predictors of the identified trajectories are then investigated.

This study also explores the relationship between negative symptom course and social recovery. Although the association between negative symptoms during FEP and poor functional outcomes is well established ([Evensen et al., 2012](#); [Galderisi et al., 2013](#)), the relationship between the trajectory of an individual's negative symptoms and concurrent change in their functioning has yet to be investigated. Understanding the relationship between negative symptom course and contemporaneous changes in functioning might inform the development of targeted interventions to improve functional outcomes following FEP.

2. Method

2.1. Participants

The sample comprises participants in the National EDEN study: a national evaluation of the impact and cost-effectiveness of Early Intervention in Psychosis (EIP) services in the UK ([Birchwood et al., 2014](#)). All individuals accepted into EIP services in Birmingham, Bristol, Cambridge, Cornwall, Lancashire and Norfolk between August 2005 and April 2009 were invited to take part. The Policy Implementation Guide ([Department of Health, 2001](#)) provides details of the acceptance criteria for these services and the care they offer. In total, 1027 individuals consented to take part: 80% were followed up at 6 months and 77% at 12 months. National EDEN participants assessed with the Positive and Negative Syndrome Scale (PANSS) at one time point or more ($n = 1006$) are included in the current study (see [Table 1](#) for sample characteristics and descriptive statistics).

2.2. Measures

2.2.1. Positive and Negative Syndrome Scale (PANSS; [Kay et al., 1987](#))

Participants were assessed using the PANSS following acceptance into EIP (baseline) and 6 and 12 months later. The PANSS is a 30-item instrument designed to measure the severity of symptoms associated with schizophrenia. Symptom severity over the previous seven days is assessed by a trained rater following a semi-structured interview with the participant. Each symptom is rated on a 7-point scale from 1 (absent) to 7 (extreme).

2.2.2. Time Use Survey (TUS; [Fowler et al., 2009](#); [Short, 2003](#))

Time spent in 'structured activity' at baseline, 6 and 12 months, as measured by the Time Use Survey (TUS), was used as an index of social recovery. The TUS is a semi-structured interview designed to assess time spent participating in structured activity on average over the previous month. Structured activity is defined as time spent in paid employment, voluntary work, education, childcare, housework, sport and structured leisure activities. The number of hours per week spent engaged in structured activity on average over the previous month was the measure of functioning used to model social recovery trajectories. Social and occupational functioning have been deemed among the most important markers of recovery by experts by both professional ([Kane et al., 2003](#)) and lived experience ([Pitt et al., 2007](#)). Unlike many measures of functioning employed in psychosis research, the TUS has limited conceptual overlap with negative symptoms, reducing the risk of confounding.

Table 1
Sample characteristics and descriptive statistics.

	Percentage	Mean (SD)	Median (Q ₁ , Q ₃)
Age at onset	–	20.07 (7.78)	20 (18, 24)
Male gender	69.1	–	–
Ethnicity			
White British	70.3	–	–
Asian	15.5	–	–
Black	6.8	–	–
Mixed	4.2	–	–
Other	3.3	–	–
Family history of non-affective psychosis	8.9	–	–
Initial clinical diagnosis			
Unspecified psychosis	72.0	–	–
Schizophrenia	10.6	–	–
Bipolar	5.2	–	–
Drug induced psychosis	6.7	–	–
Paranoid psychosis	3.7	–	–
Schizoaffective disorder	1.7	–	–
Antipsychotic use at baseline			
Typical	1.6	–	–
Atypical	78.7	–	–
Both typical and atypical	7.9	–	–
No antipsychotic	12.7	–	–
Antipsychotic use at 12 months			
Typical	2.2	–	–
Atypical	76.5	–	–
Both typical and atypical	2.3	–	–
No antipsychotic	18.9	–	–
Baseline PANSS			
Positive subscale	–	15.28 (6.03)	15 (10, 19)
Negative subscale	–	14.80 (6.52)	13 (9, 19)
General subscale	–	32.85 (9.95)	32 (25, 39)
Negative factor item average	–	2.16 (1.00)	1.86 (1.29, 2.86)
PAS social			
Childhood	–	0.20 (0.21)	0.17 (0, 0.33)
Adolescence	–	0.23 (0.19)	0.17 (0.06, 0.33)
PAS academic			
Childhood	–	0.26 (0.21)	0.25 (0.08, 0.42)
Adolescence	–	0.36 (0.24)	0.33 (0.17, 0.50)
Baseline Calgary depression	–	6.30 (5.38)	5 (2, 10)

Note. PANSS = Positive and Negative Syndrome Scale; PAS = Premorbid Adjustment Scale.

2.2.3. Other measures administered at baseline

Variables hypothesised to be associated with negative symptom course were measured at baseline. Self-reported social and academic adjustment in childhood (up to 11 years) and early adolescence (11–15 years) was assessed using the Premorbid Adjustment Scale (PAS; [Cannon-Spoor et al., 1982](#)). Duration of untreated psychosis was assessed retrospectively using the method described by [Larsen et al. \(1996\)](#). DUP was defined as the interval between onset of frank psychosis and commencement of criterion antipsychotic treatment, ascertained using participant report and examination of clinical notes. Continuous data were dichotomised to create a binary DUP variable (long DUP ≥ 9 months) due to the non-linear relationship between DUP and negative symptoms ([Boonstra et al., 2012](#)). The Calgary Depression Scale (CDSS; [Addington et al., 1994](#)) was used to measure depression and the Drug Check ([Kavanagh et al., 1999](#)) to assess illicit substance use. Family history of non-affective psychosis was ascertained through participant report and diagnoses at baseline obtained from clinical notes.

2.3. Analysis plan

Since it is now accepted that the factor structure of the PANSS is not well represented by the three original subscales ([Kay et al., 2000](#); [White et al., 1997](#)), the PANSS items used to measure negative symptoms in this study were determined using Exploratory Structural Equation Modelling (ESEM; [Asparouhov and Muthén, 2009](#)). Whilst much work has been carried out to determine the factor structure of the PANSS in

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