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#### Prevalence of item level negative symptoms in first episode psychosis diagnoses

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#### ABSTRACT

The relevance of negative symptoms across the diagnostic spectrum of the psychoses remains uncertain. The purpose of this study was to report on prevalence of item and subscale level negative symptoms across the first episode psychosis (FEP) diagnostic spectrum in an epidemiological sample, and to ascertain whether items and subscales were more prevalent in a schizophrenia spectrum diagnoses group compared to an 'all other psychotic diagnoses' group. We measured negative symptoms in 330 patients presenting with FEP using the Scale for Assessment of Negative Symptoms (SANS), and ascertained diagnosis using the Structured Clinical Interview for DSM IV. Prevalence of SANS items and subscales were tabulated across all psychotic diagnoses, and logistic regression analysis determined which items and subscales were predictive of schizophrenia spectrum diagnoses. SANS items were most prevalent in schizophrenia spectrum conditions but frequently presented in other FEP diagnoses, particularly substance induced psychotic disorder and Major Depressive Disorder. Brief psychotic disorder and bipolar disorders had low levels of negative symptoms. SANS items and subscales which significantly predicted schizophrenia spectrum diagnoses, were also frequently present in some of the other psychotic diagnoses. Conclusions: SANS items have high prevalence in FEP, and while commonest in schizophrenia spectrum conditions are not restricted to this diagnostic subgroup.

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#### 1. Introduction

While negative symptoms are a long established feature of schizophrenia spectrum conditions (Kraepelin, 1919; Bleuler, 1950), our understanding of their relevance across the diagnostic spectrum of psychosis is limited (Andreasen et al., 1995; Kirkpatrick et al., 2006). In spite of this, research has recognised that negative symptoms do not occur exclusively in schizophrenia spectrum diagnoses, and that further investigation of this topic is vital to gain a clear picture of their significance in psychotic illness (Andreasen, 1987; Toomey et al., 1998).

Previous study of negative symptoms across diagnoses has focused on comparisons between schizophrenia and major depression, which have generally indicated that negative symptoms are a feature of both disorders but are overall more prevalent in schizophrenia (Andreasen,

1987; Sax et al., 1996; Herbener and Harrow, 2001; Bottlender et al., 2003). However, as prevalence of negative symptoms in the several other psychotic diagnoses has not been investigated, it is unclear whether negative symptoms are specific to schizophrenia spectrum diagnoses, or whether they are more specific to psychosis, regardless of diagnosis. In particular, there is insufficient literature pertaining to prevalence of negative symptoms in less common diagnoses, such as substance induced psychotic disorder, delusional disorder and brief psychotic disorder.

Estimates of negative symptom prevalence in schizophrenia vary considerably (35–90%), possibly due to research in heterogenous populations, the use of differing measurement instruments, and measurement during different phases of illness (Makinen et al., 2008; Bobes et al., 2010). While it has been reported that negative symptoms can feature in psychotic presentations other than schizophrenia, there are few reports of negative symptom prevalence at the item level, either in schizophrenia or in other psychotic diagnoses (Peralta and Cuesta, 1999). An item level investigation may distinguish more clearly than subscale or global scores which aspects of negative symptoms differ across diagnoses. The argument for item level research is further strengthened by previous authors suggesting there is no evidence that Scale for Assessment of Negative Symptoms (SANS) subscale scores are better measures of negative symptoms than individual item scores (Kibel et al., 1993).

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In this study we address the gap in knowledge in relation to prevalence of negative symptoms across the full psychosis diagnostic spectrum, and we present item level data in a first episode psychosis (FEP) population using the SANS instrument (Andreasen, 1982). No previous study has reported on prevalence of negative symptoms at a homogenous phase of illness presentation across all psychotic diagnoses.

The principle aim of this study was to report item and subscale level prevalence of negative symptoms in a large FEP cohort, across all psychotic diagnoses using the SANS instrument. A second aim was to investigate whether SANS items and subscales were significantly commoner in schizophrenia spectrum diagnoses compared to an 'all other psychotic diagnoses' group in FEP.

#### 2. Methods

#### 2.1. Study setting

The study was based in the Dublin and East Treatment and Early Care Team (DETECT), an early intervention in psychosis project, located in the Dublin Mid-Leinster region of Ireland between February 2005 and February 2010. DETECT assesses all cases of FEP within a defined catchment area. Three geographically defined services, encompassing a population of 390,000, as well as a private in-patient psychiatric facility located in the catchment area participated in the study.

#### 2.2. Participants

The study included consecutive inpatient and outpatient presentations to the catchment area service, aged 16–65 years, with less than 30 days antipsychotic treatment. Informed consent was obtained from all study participants, and Ethics Committee approval was granted from the three participating mental health services prior to the study.

#### 2.3. Assessments

The SANS is recognised as a high quality tool for assessment of negative symptoms (Kirkpatrick et al., 2006), with sound psychometric properties, such as interrater reliability, internal consistency, and predictive validity (Andreasen, 1982; Andreasen, 1990). The scale is divided into 19 item ratings, and five global factor ratings (affective flattening, alogia, avolition-apathy, anhedonia-asociality and attention). Each item and subscale is scored on a 6 point scale (0–5). Structured Clinical Interview for DSM IV (SCID) was used to obtain diagnoses for all individuals (First et al., 2002). Scale for Assessment of Positive Symptoms (SAPS) ascertained positive symptom scores (Andreasen, 1984), and the Calgary Depression Scale for Schizophrenia (CDSS) was used to measure depressive symptoms (Addington et al., 1993).

Assessments began within 30 days of commencing antipsychotic medication for all participants. Data were collected as part of a larger study of outcomes in FEP, and the same rater collected all data for each participant. Twelve clinical assessors collected data for this study, each receiving comprehensive training prior to commencement as data collectors. Reliability data were gathered by persons sitting in on the same interview for at least five subjects, and using videos for a further three interviews. Concordance of SCID diagnosis ranged between 93 and 100%. Pearson correlation coefficients for SANS global total ranged between 0.61 and 0.99, with all but one inter-rater pair being above 0.7. Pearson correlation coefficients for SAPS global total ranged between 0.66 and 0.99, and for CDSS total between 0.71 and 0.99. Collected information was discussed at weekly team meetings where a consensus diagnosis was agreed upon.

#### 2.4. Statistical analysis

We tabulated SANS items and subscale totals across all SCID psychotic diagnoses defining the presence or absence of a negative symptom as a SANS item or subscale score of three or greater. This definition has been used by other authors (Malla et al., 2002; Emmerson et al., 2009), and a score of less than three has also been used for remission criteria purposes (Andreasen et al., 2005). We used exact chi-square testing to ascertain which SANS items were significantly different between a schizophrenia spectrum diagnoses group and other diagnostic subgroups, including an 'all other psychotic diagnoses' group. This latter group included all non-schizophrenia spectrum diagnoses, which was chosen as negative symptoms are not currently considered in diagnostic criteria for these diagnoses (First et al., 2002).

Only SANS items significantly different between the schizophrenia spectrum diagnoses group and the 'all other psychotic diagnoses' group were included in a forced entry binary logistic regression model which ascertained which SANS items were significantly associated with schizophrenia spectrum diagnoses. The binary dependent variable consisted of a schizophrenia spectrum diagnoses group versus an 'all other psychotic diagnoses' group. We did not have sufficient participants in each diagnostic group to analyse each individual diagnosis using regression modelling. We repeated both regression models adding CDSS total and SAPS global total to control for potential confounding of other symptomatology. We also repeated the regression analysis replacing items with subscale totals. All analyses were conducted using Predictive Analytics SoftWare (PASW) Statistics Version 18.0.

#### 3. Results

SANS data was available for 86.4% of subjects (330/382) referred with FEP within the defined catchment area (44 subjects refused to participate, and SANS data was not collected for eight other subjects). There were no significant differences in age, sex and marital status between those included in the study (n=330), and non-participants (n=52). For individuals included in the study 216/330 (65.4%) were inpatients at assessment.

Patient characteristics are outlined in Table 1. This table reads across from the left in order of prevalence of presence of any SANS item (Table 2). There were six cases of schizoaffective disorder, which we included with schizophrenia and schizophreniform disorder in the schizophrenia spectrum diagnoses group. Twenty six of the 330 subjects had diagnoses in groupings too small for consideration (Substance Induced Mood Disorder, n=5; Psychotic Disorder due to GMC, n=6; Psychotic Disorder NOS, n=15), and were excluded from the tables presented, however they were included in the 'all other psychotic diagnoses' group.

The low prevalence of females presenting with Major Depressive Disorder with psychotic features (MDD) was unexpected at just 39%, however an explanation for this could be the small sample size. The low prevalence of 41.2% of cannabis abuse in the last month in the substance induced psychotic disorder group can be explained by the relatively high proportion of alcohol induced psychoses in this population (41.2% of the substance induced psychotic disorder group had a diagnosis of alcohol abuse or dependence in the last month).

Table 2 gives descriptive results for prevalence of a score of three or greater for each SANS item and subscale total across each diagnosis. Percentage prevalence in this table was rounded to the nearest whole number. SANS items and subscales were particularly common in schizophrenia spectrum diagnoses, but were also often present in substance induced psychotic disorder and MDD. A score of three or greater on at least one SANS item had a high prevalence both in the schizophrenia spectrum diagnoses group (87%) and in the 'all other

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