Positive and negative subclinical symptoms and MCCB performance in non-psychiatric controls

C. Korponay
G. C. Nitzburg
Anil Malhotra
P. DeRosse

Follow this and additional works at: https://academicworks.medicine.hofstra.edu/articles

Part of the Medical Molecular Biology Commons, and the Psychiatry Commons

Recommended Citation
POSITIVE AND NEGATIVE SUBCLINICAL SYMPTOMS AND MCCB PERFORMANCE IN NON-PSYCHIATRIC CONTROLS

Cole Korponay¹, George C. Nitzburg, PhD², Anil K. Malhotra, M.D.²,³,⁴,⁵, and Pamela DeRosse, PhD²,³

¹University of Pennsylvania, Philadelphia, PA 19104
²Center for Translational Psychiatry, The Feinstein Institute for Medical Research, Manhasset, NY, USA
³Division of Psychiatry Research, The Zucker Hillside Hospital, Division of the North Shore–Long Island Jewish Health System, Glen Oaks, NY 11004
⁴Department of Psychiatry and Behavioral Science, Albert Einstein College of Medicine, Yeshiva University, Bronx, NY 10461
⁵Hofstra North Shore – LIJ School of Medicine, Departments of Psychiatry and Molecular Medicine, Hempstead, NY 11550

Abstract

Considerable data support the phenomenological and temporal continuity between subclinical psychosis and psychotic disorders. In recent years, neurocognitive deficits have increasingly been recognized as a core feature of psychotic illness but there are few data seeking to elucidate the relationship between subclinical psychosis and neurocognitive deficits in non-clinical samples. The goal of the present study was to examine the relationship between subclinical positive and negative symptoms, as measured by the Community Assessment of Psychic Experiences (CAPE) and performance on the MATRICS Consensus Cognitive Battery (MCCB) in a large (n=303) and demographically diverse non-clinical sample. We found that compared to participants with low levels of subclinical positive symptoms, participants with high levels of subclinical positive symptoms performed significantly better in the domains of working memory (p<.001), verbal learning (p=.007) and visual learning (p=.014). Although comparison of participants with high and low levels of subclinical negative symptoms revealed no differences in MCCB performance, we found that individuals with high levels of subclinical negative symptoms performed significantly
better on a measure of estimated IQ (WRAT-3 Reading subtest; p=.02) than those with low levels of subclinical negative symptoms. These results are at odds with prior reports that have generally shown a negative relationship between neurocognitive functioning and severity of subclinical psychotic symptoms, and suggest some potential discontinuities between clinically significant psychotic symptoms and sub-syndromal manifestations of psychosis.

Keywords
subclinical psychosis; cognition; MCCB

1. INTRODUCTION
Considerable data support the phenomenological and temporal continuity between psychotic disorders and subclinical manifestations of psychotic symptoms. Subclinical psychotic symptoms are common in the general population with an estimated prevalence of 7.2% and an annual incidence of 2.5% (Linscott & van Os 2013). The continuity between subclinical psychosis and psychotic disorders is supported by longitudinal studies demonstrating that high levels of subclinical psychotic symptoms predate the onset of psychotic illness (Chapman et al 1994; Poulton et al 2000; Cannon et al 2002; Hanssen et al 2005; Wellham et al 2009; Fisher et al 2013) as well as studies demonstrating substantial overlap in genetic predisposition for clinical and subclinical levels of psychotic symptoms (Schulsinger 1976; Kendler et al 1993; Tienari et al 2003). Moreover, a recent review and meta-analysis of the literature on subclinical psychosis spanning over 2 decades (Linscott & van Os 2013) found that nearly all of the demographic and experiential risk factors for psychotic disorders predicted greater risk of subclinical psychosis.

Over the last several decades, deficits across a range of cognitive skills have increasingly been recognized as a core feature of psychotic illness (e.g. Barch & Ceaser 2012) but to date, only a limited number of studies have examined whether similar deficits are associated with subclinical psychosis in non-clinical samples. Data derived from studies of patients with schizotypal personality disorder (SPD), however, have reported considerable overlap in the neurocognitive deficits observed in SPD relative to schizophrenia (SZ) (Siever & Davis 2004 for a review). Because SPD is believed to represent an underlying predisposition for SZ or “psychosis-proneness” (Claridge et al 1996), these data suggest that neurocognitive deficits may be present across the lower ends of the psychosis continuum.

Studies examining the relationship between subclinical psychosis and neurocognitive functioning in non-clinical samples have yielded inconsistent results and have been limited in terms of the cognitive domains assessed (Giakoumaki 2012). For example, van Os and colleagues (2005) found that in males, but not females, deficits in verbal fluency were associated with severity of overall levels of subclinical psychosis. However, these authors did not assess other domains of cognitive function. Contrary to the sex effect reported by van Os and colleagues (2005), Simons et al. (2007) measured speed of processing and verbal learning in an all female sample and found a significant association between both positive and negative subclinical symptoms and decreased speed of processing. Laurent et al. (2001)
examined only set-shifting with the Wisconsin Card Sorting Test (WCST) and concluded that first-degree relatives of patients with SZ who had high scores of negative schizotypy on the Chapman scales scored significantly worse than relatives who had low scores and worse than healthy controls. Finally, Barnett and colleagues (2013) recently investigated whether childhood cognitive function was associated with adult subclinical psychotic symptoms in a large prospective birth cohort. They found that general cognitive ability (g) assessed at age 8, 11 and 15 was significantly predictive of subclinical psychotic symptoms in middle age. Specifically, lower cognitive scores were associated with a greater likelihood of endorsing subclinical psychotic symptoms. In this study, however, the association between current cognitive function and endorsement of subclinical psychotic symptoms was not assessed.

Several limitations of the aforementioned studies should be noted. First, most of these studies did not examine the effects of subclinical positive and negative symptoms separately. Cross-sectionally, the relationship between symptom severity and cognitive impairment in patients with SZ suggest that negative symptoms are more closely related to cognitive deficits than positive symptoms (Harvey et al 2006). Thus, it is possible that the mixed findings on the relationship between subclinical psychosis and cognitive function are related, in part, to the focus on overall levels of subclinical psychosis. Additionally, the cognitive domains examined have been limited and do not provide a comprehensive assessment of the relation between subclinical psychosis and cognitive function across the full range of domains typically observed to be impaired in SZ.

Thus, the goal of the present study was to examine this relationship in a large and demographically diverse non-clinical sample comprehensively characterized for the presence of subclinical psychotic symptoms and comprehensively assessed for neurocognitive performance. Specifically, we aimed to evaluate whether the presence of high levels of subclinical positive or negative symptoms as measured by the Community Assessment of Psychic Experiences (CAPE) (Stefanis et al 2002) would be associated with differential performance across the 7 neurocognitive domains assessed by the MATRICS Consensus Cognitive Battery (MCCB) (Kern et al. 2008).

2. METHOD

2.1 Participants

The present sample comprised 303 healthy adult volunteers (53.13% female, 60.40% Caucasian, $M_{\text{age}}=38.12\pm14.29$ years, $M_{\text{IQ}}$ (based on WRAT-3 Reading) = $103.14\pm8.43$) recruited from the general population via word of mouth, newspaper and internet advertisements and posted flyers for an NIMH-funded study of subclinical psychosis in the general population (MH086756 to PD). Participants were excluded if they had a past or present affective or psychotic disorder diagnosis, active or recent substance abuse, or if they had a history of CNS trauma, neurological disorder, or previously diagnosed learning disability.
2.2 Diagnostic Assessments

Participants were initially administered the Structured Clinical Interview for the DSM-IV, Non-Patient edition (SCID-I/NP) to rule out a past or present affective or psychotic disorder. Information obtained from the SCID was compiled into a narrative case summary and lifetime diagnosis was determined by two senior members of the ZHH faculty.

2.3 Assessment of Subclinical Psychosis

Participants were administered the Community Assessment of Psychic Experiences (CAPE) (Stefanis et al 2002), a 42-item, self-report questionnaire that measures three dimensions of subclinical psychopathology including positive, negative and depressive symptoms. In the present study, the positive and negative frequency dimensions were examined for relation to neurocognitive functioning. Consistent with prior reports (van Os et al 2009), the positive and negative subscale scores derived from the CAPE were not normally distributed. Indeed, inspection of the data in our sample indicated that the CAPE subscale scores produced a half-normal distribution. Thus, because standard statistical techniques could not be utilized, we chose to dichotomize the subscale scores to facilitate the use of parametric tests. Initially, scores were divided into quartiles for both the negative and positive dimensions of subclinical psychotic symptoms. Any participant with a score at or above the 75th percentile was assigned to the high symptom group while those falling below the 75th percentile were assigned to the low symptom group. Thus, participants with a negative symptom subscale score greater than 20, representing on average, a score 1.23 standard deviations above the sample mean were considered to have high levels of negative symptoms. This score is consistent with participants experiencing several infrequent negative psychotic-like experiences or experiencing 2-3 recurrent experiences. Participants with a raw positive symptom subscale score greater than 24, representing on average, a score 1.10 standard deviations above the sample mean were considered to have high levels of positive symptoms. This score is consistent with participants experiencing several infrequent positive psychotic-like experiences or experiencing 1-2 recurrent experiences. It should also be noted that the CAPE provides a measure of the distress associated with the experience of positive and negative subclinical symptoms. In our data, these distress scores are highly correlated with the frequency scores (rho > .9). Thus, these data were not examined as we believed they were redundant with analyses based on the frequency scores.

2.4 Neurocognitive Assessment: the MCCB

To assess neurocognitive functioning, The MATRICS Consensus Cognitive Battery (MCCB) was administered to all participants. The MCCB is comprised of 10 standardized cognitive measures that collectively capture functioning within seven cognitive domains that are reliably impaired in schizophrenia (Nuechterlein et al 2004) including: Speed of Processing, Attention/Vigilance, Working Memory, Verbal Learning, Visual Learning, Reasoning/Problem-solving, and Social Cognition. Participants in the current study completed the MCCB in one visit. In the present study, T scores, corrected for age and sex, derived from the MCCB scoring program were utilized as the primary dependent measures. Additionally, we utilized the Wide Range Achievement Test-Third Edition-Reading Subtest.
(WRAT-3) as an estimate of IQ. The WRAT-3 Reading subtest is a test that assesses single word reading skill and is highly correlated with full scale IQ (Kremen et al. 2006).

2.5 Statistical Analyses

We initially sought to rule out differences between participants with high and low levels of symptoms on age, sex, race and estimated IQ (based on WRAT-3 Reading subtest score). Thus, we utilized t-tests or chi square tests, as appropriate, to examine the distributions of these variables in those characterized as having high levels of positive symptoms vs. those with low levels of positive symptoms and in those characterized as having high levels of negative symptom vs. those with low levels of negative symptoms. Following these analyses, we carried out two multivariate analysis of covariance (MANCOVA) comparing the high and low positive symptom groups and the high and low negative symptoms groups on all 7 MCCB domains. Because both race and general intelligence level have been shown to influence performance on the tests comprising the MCCB (Nitzburg et al. 2014; Rushton and Jensen 2005; Diaz-Asper et al. 2004), racial group (white and non-white) and WRAT-3 Reading subtest standard score were included as covariates in these analyses. We did not include age and sex as covariates in these analyses because the MCCB T scores used as the dependent measures were corrected for these demographic variables a priori using the MCCB scoring program.

3. RESULTS

Comparison of the high and low positive symptom groups revealed no differences in age, sex, race or estimated IQ (all p’s>0.19). These data are shown in Table 1. The MANCOVA comparing the high and low positive symptom group revealed a significant overall effect (F(7,260)=4.68; p<0.001) with post hoc tests indicating that participants with high levels of positive symptoms scored significantly higher than participants with low levels of positive symptoms on working memory (F(1,266)=16.47; p<0.001), verbal learning (F(1,266)=7.40; p=0.007) and visual learning (F(1,266)=6.11; p=0.014). These data are show in Figure 1.

It should be noted that some of our participants (N=42) were still within the age range of risk for conversion to a psychotic disorder (i.e. < 30 years old), which could have implications for cognitive functioning. Thus, to ensure that these results were not driven by a subset of participants who could potentially transition to a psychotic disorder, we removed participants under that age of 30 and re-ran the MANCOVA. The results of this analysis were identical to the results obtained in the full sample. Additionally, because negative symptoms are generally highly correlated with positive symptoms in both clinical and non-clinical samples (Linscott & van Os 2013), we followed up this analysis by examining 1) the relation between positive and negative symptoms subscale scores and 2) the effect of including the negative symptom subscale score as a covariate in the original MANCOVA comparing the high and low positive symptom groups. In these analyses, the positive symptom and negative symptom subscales were highly correlated (rho=.59; p<0.001). Moreover, although the MANCOVA remained significant (F(7,259)=2.45; p=0.02), the post hoc tests indicated that the difference between groups was no longer significant in the visual learning domain. The differences in working memory and verbal learning however,
remained significant (p=0.004 and p=0.03, respectively). Finally, to confirm that these findings were not an artifact of the method we used to dichotomize our sample, we also examined the correlations between the raw CAPE positive symptom subscale score and T scores for the working memory and verbal learning domain. These analyses indicated the CAPE positive symptom subscale was positively correlated with both working memory (rho=0.14; p=0.02) and verbal learning (rho=0.12; p=0.04).

Comparison of the high and low negative symptom groups revealed no differences in age, sex or race (all p's>0.38). Comparison of the high and low negative symptom groups on our measure of estimated IQ, however, indicated that participants with high levels of negative symptoms had significantly better WRAT-3 Reading subtest standard scores than those participants who had low levels of negative symptoms (t=2.38, p=0.02). These data are shown in Table 1. The MANCOVA comparing the high and low negative symptom groups across the 7 MCCB domains revealed no significant overall effect. These data are shown in Figure 2.

In the present sample of 303 participants 47 participants were classified as high in both positive and negative subclinical symptoms. Comparison of these participants to those characterized as low in both symptom domains (N=150) using a MANCOVA identical to the primary analyses, revealed that those with high levels of both subclinical positive and negative symptoms performed significantly better in the domains of working memory (p<0.001) and visual learning (p=0.036) and trended toward better performance in the verbal learning domain (p=0.053).

Finally, to demonstrate that those in the high symptom groups were exhibiting symptoms that could be considered clinically relevant, we assessed a sample of stable outpatients with schizophrenia or schizoaffective disorder (N=184) recruited to an NIMH-funded study of functional disability using the CAPE. We have previously demonstrated that scores obtained on the CAPE in patient samples are valid and converge with those derived from clinician-administered assessment scales (DeRosse et al 2014). Using this sample, which is well matched in age and sex to the control sample in the present study, we compared the raw CAPE scores in 1) our high positive symptom group to patients scoring within the lower half of the distribution on the raw CAPE positive symptom score and 2) our high negative symptom group to patients with scoring within the lower half of the distribution on the raw CAPE negative symptom score. In the positive symptom analysis, the mean rank of the controls was significantly higher than the mean rank of the patients (mean rank controls=121.89 vs. mean rank patients=75.22; p<0.001). Similarly, in the negative symptom analysis, the mean rank of the controls was significantly higher than the mean rank of the patients (mean rank controls=119.58 vs. mean rank patients=50.00; p<0.001). These data suggest that the symptom levels experienced by participants characterized as having “high” subclinical symptoms are very similar to the mild symptoms observed in patients with psychotic disorders.
4. DISCUSSION

The present findings suggest that high levels of positive subclinical symptoms in participants with no history of an axis I psychotic or affective disorder is associated with significantly better performance on measures of working memory, verbal learning, and visual learning as measured by the MCCB. Moreover, although no effect of high negative symptoms were noted on MCCB performance, ancillary findings indicated that those who scored high on negative symptoms evidenced significantly better performance on a measure of estimated IQ (WRAT-3 Reading subtest). These results are at odds with several prior reports that have generally shown a negative relationship between neurocognitive functioning and severity of subclinical psychotic symptoms (Laurent et al 2001; van Os et al 2005; Jabben et al 2007; Simons et al 2007).

Our findings suggest some potential discontinuities between clinically significant psychotic symptoms and sub-syndromal manifestations of psychosis. Specifically, if subclinical psychosis represents a milder manifestation of the psychotic symptoms observed in disorders such as SZ, we might expect to see cognitive impairment in the individuals exhibiting high levels of subclinical psychotic symptoms similar to, albeit less severe than, those observed in SZ. Indeed, it has generally been found that cognitive deficits consistently accompany clinically significant psychotic symptoms (Bora, Yucel & Pentelis 2010; Simonsen et al 2011; Lewandowski et al 2011). Contrary to this expectation, however, we found better cognitive performance in individuals with high levels of subclinical psychosis.

One possible explanation for this discrepancy is that symptom severity bears a correlational, but not causative, relation to neurocognitive capacity. Support for this idea draws from a series of complementary findings that suggest higher cognitive capacities act as a resilience factor against clinically significant psychosis (Green 1996; Green, Kern & Heaton 2004; Morrison et al 2004). First, patients with higher a priori cognitive capacities tend to have better functional outcomes than patients with lower cognitive capacities (Green 1996; Green, Kern & Heaton 2004). Moreover, the risk of transitioning from a prodromal state to a psychotic disorder is significantly associated with impaired neurocognitive function (Keefe et al 2006). Thus, when considering the population of individuals with high levels of subclinical psychosis, those with low a priori cognitive capacities would be expected to transition to clinically significant psychosis at a higher rate while those with higher cognitive capacities would be expected to pool in comparatively larger numbers in the subclinical domain because their high cognitive capacities protect them from transitioning. If this is the mechanism at work, then the results of the present study could be attributed to an inherent sampling bias. This conclusion would also suggest that the cognitive deficits observed in psychotic disorders such as SZ may be independent from the positive and negative symptoms characteristic of the illness. This is consistent with several lines of research suggesting psychotic and cognitive symptoms may be separable and perhaps independent characteristics of SZ (see Harvey et al 2006 for a review).

It is also possible, however, that there is a direct causative link between subclinical psychosis and increased cognitive function. Several studies seeking to elucidate why psychosis continues to persist despite the substantial decrements in reproductive fitness...
associated with it, have proposed that genetic variants associated with subclinical psychosis may be beneficial in some way. Several studies have suggested that some of the risk variants may be associated with heightened creativity or other intellectual abilities (Karlsson 1970; Keefe & Magaro 1980; Green & Williams 1999; Burch et al 2006; Miller et al 2007; Batey et al 2008; Claridge et al 2009; Keri 2009). For example, Karlsson (1970) found that patient relatives, but not the patients themselves, had a significantly higher probability of being persons of eminence than people in the general population, and Green and Williams (1999) reported that individuals with higher scores on a test of schizotypy produced the most creative responses on a divergent thinking battery.

Several limitations of the present study should be noted. First, because the scores obtained on the positive and negative symptom subscales of the CAPE were not normally distributed, we opted to use an extreme groups analysis (Preacher et al. 2005), which has some inherent limitations. This approach may have limited our ability to detect more nuanced relationships between the level of subclinical psychotic symptoms and neurocognitive performance. Moreover, because participants in the overall sample were only excluded if they met criteria for a psychotic or mood disorder 16 participants met criteria for another axis I disorder (4 anxiety disorder NOS, 12 past substance abuse). However, to rule out the effects of these diagnoses on our findings we re-ran both of the primary MANCOVA. The results of these analyses were identical to what was found in the larger sample suggesting that the observed differences were not driven by participants who met criteria for an axis I disorder. Despite these limitations, however, the present findings contribute to a growing literature seeking to elucidate the relationship between subclinical psychosis and neurocognitive functioning in otherwise healthy adults. Additional studies in larger samples are warranted.

Acknowledgements

None

Role of Funding Source: Funding for this work was supported in part by grants from the National Institute of Mental Health to Dr. DeRosse (MH086756) and Dr. Malhotra (MH079800), the NSLIJ Research Institute General Clinical Research Center (M01 RR018535), Advanced Center for Intervention and Services Research (P30 MH090590) and a Center for Intervention Development and Applied Research (P50 MH080173). The NIMH had no further role in study design; in the collection, analysis and interpretation of data; in the writing of the report; and in the decision to submit the paper for publication.

REFERENCES


Linscott RJ, Van Os J. An updated and conservative systematic review and meta-analysis of epidemiological evidence on psychotic experiences in children and adults: on the pathway from
Figure 1.
Comparison of participants classified as high vs. low on subclinical positive psychotic symptoms across all 7 MCCB Domains. Mean T scores have been adjusted for race and WRAT-3 performance. Significant differences are indicated by an asterisk (*).
Figure 2.
Comparison of participants classified as high vs. low on subclinical negative psychotic symptoms across all 7 MCCB Domains. Mean T scores have been adjusted for race and WRAT-3 performance. No significant differences were found for any of the MCCB domains.
Table 1

Participant demographics

<table>
<thead>
<tr>
<th>Symptom Domain</th>
<th>% Minority</th>
<th>Age (SD)</th>
<th>% Female</th>
<th>WRAT-3 (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Positive Symptoms</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High (N=103)</td>
<td>44.66%</td>
<td>37.91 (14.27)</td>
<td>48.54%</td>
<td>104.02(8.48)</td>
</tr>
<tr>
<td>Low (N=200)</td>
<td>37.00%</td>
<td>38.53(14.40)</td>
<td>55.5%</td>
<td>102.68 (8.39)</td>
</tr>
<tr>
<td><strong>Negative Symptoms</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High (N=92)</td>
<td>35.87%</td>
<td>38.91 (14.08)</td>
<td>53.26%</td>
<td>104.88 (7.41) **</td>
</tr>
<tr>
<td>Low (N=211)</td>
<td>41.23%</td>
<td>37.77 (14.81)</td>
<td>53.08%</td>
<td>102.38 (8.74)</td>
</tr>
</tbody>
</table>

Note: Scores for the Wide Range Achievement Test-Third Edition-Reading Subtest (WRAT-3) are presented as standard scores.

** Participants classified as high on subclinical negative symptoms score significantly higher on the WRAT-3 than those classified as low on negative symptoms (t (300)=2.38; p = .02).