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Subclinical psychosis and depression: Co-occurring phenomena that do not predict each other over time

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ABSTRACT

Background: The path from subclinical psychotic experiences to clinical disorder is thought to be mediated by the persistence of subclinical psychotic experiences. One of the factors that is likely associated with this persistence is depression. Although commonly viewed as interrelated concepts, the exact relationship between subclinical psychosis and depression is not clear.
Methods: Cross-lagged path modeling was used to explore the relationship between subclinical psychosis and depression across and over time in an adolescent population seeking assistance for non-psychotic disorders (N = 138), measured at four occasions over a two-year period.
Results: Subclinical psychosis and depression were related to each other at every cross-sectional measurement, but did not predict each other over time. Subclinical psychotic experiences and depressive symptom levels were highest at baseline, when participants presented to the clinical service for help. In addition, the relationship between them was also strongest at baseline and decreased significantly over time.
Conclusion: The results suggest that psychosis and depression are interrelated phenomena that strongly co-occur in time, but longitudinally, one does not predict change in the other. Both psychopathological dimensions should be addressed when treatment is provided to adolescent help-seekers.

1. Introduction

The extended psychosis phenotype is assumed to exist on a continuum, with many individuals endorsing psychotic experiences below clinical significance (van Os et al., 2009; Yung et al., 2009; Nuevo et al., 2010). This view posits that psychotic experiences do not inevitably result in psychotic disorder. However, for some individuals with subclinical psychotic phenomena, disorder may develop depending on additional factors, such as secondary distress or intrusiveness, psychopathological comorbidities or environmental influences. These may cause subclinical psychotic experiences to become persistent with subsequent impairment and need for care, consistent with the proneness–persistence–impairment model of psychosis (Cougnard et al., 2007).

One of the factors that may play a role in the process of shifting along the psychosis continuum may be depression (Yung, 2007; van Rossum et al., 2009). Depression and positive psychosis are considered separate but interrelated dimensions of psychotic disorder (van Os and Kapur, 2009) and are closely related on all levels of the continuum. Clinically, this is reflected by diagnoses such as schizoaffective or mood disorders with psychotic features, in which depressive and psychotic symptoms co-occur. Furthermore, comorbidity between schizophrenia and depression is very high; up to 50% of schizophrenia patients experience comorbid depression (Buckley et al., 2009). In the earlier phases of psychotic illness, depression is a commonly reported symptom in the prodrome (Häfner et al., 2005; Iyer et al., 2008) and has been shown to predict transition from ultra-high risk status to frank psychosis (Yung et al., 1998, 2003, 2004). Further down the psychosis continuum, subclinical psychotic symptoms and depression are associated in adolescent (Armando et al., 2010; Mackie et al., 2011; Yung et al., 2006; Wigman et al., in press) and adult (Krabbendam et al., 2005a) general population samples. From a longitudinal perspective, data from general population samples show that the

Abbreviations: CAPE, Community Assessment of Psychic Experiences; CES-D, Centre for Epidemiologic Studies Depression Scale; ML, Maximum Likelihood; CFI, Comparative Fix Index; RMSEA, Root Mean Square Error of Approximation.

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developmental patterns of subclinical experiences mirror depressive symptoms in a dose–response fashion over time (Yung, 2007; Wigman et al., in press). Additionally, the presence of depressive symptoms in combination with hallucinatory experiences increases the risk for a later diagnosis of clinical psychosis (Krabbendam et al., 2005b).

Although psychosis and depression often co-occur at clinical and subclinical levels, the exact nature of their relationship is unclear. Depression could directly impact psychotic symptoms (van Rossum et al., 2009) by inducing negative appraisal of external stimuli, subsequently increasing psychotic symptoms (Freeman et al., 2001) and risk for clinical disorder (Yung et al., 2004). Conversely, experiencing psychotic symptoms may induce feelings of fear, hopelessness and depression (Krabbendam et al., 2005a). Other theories suggest that psychosis and depression exist on the same continuum, in that both may result from shared liability (Verdoux et al., 1999). More research is needed to elucidate this complex relationship further.

1.1. Aims

The current study aimed to investigate the co-occurrence of, and directional relationship between, subclinical psychosis and depression, across and over time. We investigated this association in an adolescent sample seeking help for general, non-psychotic psychopathology. The dynamic adolescent life phase is an interesting period for studying this association, since proneness for both psychosis (Verdoux et al., 1998) and depression (Costello et al., 2003) are at their peak. Subclinical psychotic experiences were assessed with the Community Assessment of Psychic Experiences (CAPE) and depressive symptoms with the Centre for Epidemiologic Studies Depression Scale (CES-D) questionnaires. Cross-lagged path modeling, a statistical method that enables the investigation of the longitudinal and directional nature of associations, was applied in the present study. Based on evidence for a causal relationship in both directions, it was hypothesized that subclinical psychotic experiences and depressive symptoms would predict each other in and across time.

2. Method

2.1. The setting

Orygen Youth Health (OYH) is a public mental health program for young people between 15 and 24 years old. The catchment area of north and west metropolitan Melbourne, Australia, covers approximately 900,000 people, about 200,000 of whom are aged between 15 and 24. The service provided at OYH has three components: EPPIC (Early Psychosis Prevention and Intervention Centre), which is a service for people with first-episode psychotic disorder, the PACE (Personal Assessment and Crisis Evaluation) clinic, which targets individuals at ultra-high risk of psychosis, and Youthscope, a service for non-psychotic individuals.

Referrals to OYH are taken from a range of sources, including general practitioners (GPs) and other primary care services, school and university counseling services, drug and alcohol services, the justice system, and youth accommodation centres, as well as from families and young people themselves. The procedure for entry into OYH is as follows: first, a brief telephone "triage" interview is undertaken with the referrer and the young person. Once basic criteria are met (i.e. age and location), the young person is referred to one of the three clinical teams (EPPIC, PACE, or Youthscope) for a face-to-face interview to determine eligibility and symptom profile. All young people who are recognized as meeting the criteria for EPPIC and PACE at this interview are accepted. However, because of the high prevalence of non-psychotic disorders such as depression, there are many more young people referred to Youthscope than can be accepted. Thus, criteria have been established for acceptance into Youthscope. These are based largely on presence of a diagnosis of a non-psychotic mental disorder, such as depression, anxiety, and/or severe personality disorder. Degree of risk of suicide or self-harm, disability or functional impairment, and previous history of unsuccessful treatment within primary care services are also taken into account by the Youthscope clinician. Many young people not accepted into Youthscope also have high rates of depressive symptoms and poor functioning. Those not accepted also include young people with a primary diagnosis of an uncomplicated substance use disorder or a primary diagnosis of oppositional defiant disorder. The study group for this project was taken from those who were referred to, but not necessarily accepted into, Youthscope.

2.2. Participants

Two hundred and four young people (aged 15–24 years) referred to Youthscope between April and October 2003 were invited to participate. Exclusion criteria were: known organic cause for presentation, known intellectual disability (IQ<70), and inability to speak English. The overall participation rate was 72.5% (56 refusals). At baseline, 138 participants completed both the CAPE and CES-D. This is the sample included in the current analysis. The mean age was 17.7 (SD 2.6); 58% of the sample was female.

A full description of the psychiatric diagnoses of this cohort, assessed with the Structured Clinical Interview for DSM-IV (SCID; First et al., 1997), is described by Godfrey et al. (2005). Briefly, 46% had current major depressive disorder, 63% had an anxiety disorder and 27% had a substance use disorder. The most common comorbidity was mood and anxiety disorders, followed by substance use disorders in combination with other mental disorders, particularly mood and anxiety disorders (Godfrey et al., 2005).

2.3. Procedure

Data were collected at four assessments: at T1 (baseline; N = 138); at T2, (3 months after baseline; N = 116, 84.1% of original cohort); at T3 (6 months after baseline; N = 113, 81.9% of original sample); and at T4 (2 years after baseline; N = 99, 71.7% of original sample). The study was approved by the local Research and Ethics Committee.

2.4. Instruments

The Community Assessment of Psychic Experiences (CAPE) positive experiences subscale (20 self-report items) was used to assess psychotic experiences (Stefanis et al., 2002; Konings et al., 2006). The CAPE is based on the Peters et al. Delusions Inventory (Peters et al., 1999) (PDI), modified to also include hallucinatory experiences. Each item in the CAPE rates (i) frequency and (ii) associated distress on a four-point scale. The frequency items showed good internal consistency at all time points (Cronbach's alpha: 0.86–0.91). The Centre for Epidemiologic Studies Depression Scale (CES-D) (20 self-report items) was used to assess depressive symptomatology in the past week (Radloff, 1977). This measure rates frequency of symptoms on a four-point scale. The CES-D has been validated in an Australian adolescent sample (Rey et al., 2001). The measure showed good internal consistency at all time points (Cronbach's alpha: 0.78–0.98). Sum scores of both questionnaires were used as continuous indicators with higher scores indicate greater psychopathology.

2.5. Analysis

Analyses were conducted with Mplus 5.1 (Muthén and Muthén, 1998–2007) and PASW Statistics 18 (SPSS Inc., Chicago, Illinois, 2010). Drop-out analyses were conducted using ANOVA and odd ratios (OR). Time effects of CAPE and CES-D scores were tested with Repeated Measures ANOVA.

Table 1
Means (SD) of the CAPE and CES-D at all four time points.

	T1	T2	T3	T4
	Baseline	3 months	6 months	24 months
CAPE—positive experiences	31.0 (9.0)	27.1 (7.4)	25.6 (7.5)	26.5 (8.2)
CES-D—depressive symptoms	28.9 (13.7)	23.0 (14.4)	20.2 (13.5)	18.1 (13.1)

Path modeling was used to investigate the relationships between CAPE and CES-D scores over time, using only observed variables. Full Information Maximum Likelihood estimation was used for missing data; furthermore, robust ML (MLR) was used for model estimation because data was not normally distributed. This method estimates mean-adjusted χ^2, robust to non-normality (Brown, 2006). Over time, CAPE scores were regressed on (i) earlier CAPE scores and (ii) earlier CES-D scores and vice versa. CAPE and CES-D scores were allowed to correlate at all time points; correlations were compared with Wald tests. Thus, a cross-lagged path model was established. CAPE and CES-D scores at T1 were controlled for age and gender.

Several fit indices were used for model evaluation (Brown, 2006). For acceptable model fit, chi-square (χ^2) should be low, Comparative Fix Index (*CFI*) should be above 0.90 and Root Mean Square Error of Approximation (*RMSEA*) should be lower than 0.08.

3. Results

3.1. Descriptives

There were no significant differences between participants who completed all study phases and those who dropped out after T1 on age, gender, socio-economic status, or CES-D and CAPE scores at baseline. Table 1 shows mean scores (SD) of the CAPE and CES-D at the four time points. Both CAPE [$F(3,171) = 14{,}75$; $p < .001$] and CES-D [$F(3,216) = 166{,}66$; $p < .001$) scores decreased significantly over time. Between T1 and T4, CES-D scores decreased by 37.5%, while CAPE scores decreased by 14.5%. The proportion decrease in CES-D scores was significantly greater than that of CAPE scores (OR = 0.29, 95% CI = 0.081–0.995, $p = 0.049$).

3.2. Model development

The model is depicted in Fig. 1. A model with all paths fit the data reasonably: $\chi^2(24) = 51.58$; $p < .0001$; $CFI = 0.903$ and $RMSEA = 0.089$. When non-significant paths were removed, model fit improved and both *CFI* and *RMSEA* were acceptable ($\chi^2(30) = 55.487$; $p < .003$; $CFI = 0.910$; $RMSEA = 0.075$).

CES-D and CAPE scores were significantly and substantially correlated at all assessments ($p < .001$). The correlation decreased significantly between T1 and T2 ($F(1) = 6.06$; $p < .01$), but not between other assessments. CAPE scores were significantly predicted by earlier CAPE scores (β 0.61–0.73). CES-D scores were significantly predicted by earlier CES-D scores (β 0.47–0.62). CAPE scores were never predicted by earlier CES-D scores, nor predicted CES-D scores over time. Effect sizes are reported in beta's, with a beta < 0.10 representing a small effect, a beta of 0.10–0.30 a moderate effect and a beta > 0.50 a large effect.

4. Discussion

The present study investigated the direction and nature of the relationship between subclinical psychotic experiences and depressive symptoms across and over time in an adolescent population which were help-seeking for general, non-psychotic psychopathology. Subclinical psychosis and depression were closely related at every assessment, but did not predict each other over time. The relationship was strongest at baseline, when participants presented to the service, and decreased significantly over time.

These results do not support the hypothesized longitudinal bidirectional relationship between subclinical psychosis and depression (van Rossum et al., 2009; Krabbendam et al., 2005a). Rather, results suggest that subclinical psychotic experiences and depression are interwoven phenomena that co-occur, but do not predict one another over time. However, this does not rule out the possibility of concurrent causation; that is, the notion that subclinical psychotic experiences and depression may exist as expressions of interrelated, yet distinguishable aspects of the same underlying factor.

The finding is consistent with suggestions that levels of depression mirror, almost exactly, levels of subclinical psychotic experiences in the general population (Yung et al., 2009; Wigman et al., in press). Van Os and Kapur (2009) suggest that psychosis consists of multiple domains (positive, negative, cognitive and affective symptoms). The present findings support this by demonstrating that depression and psychosis exist as parallel and comorbid phenomena, but changing relatively distinguishably of one another. Other researchers have posited that psychosis and depression share a common liability (Verdoux et al., 1999) or common risk factors (Stefanis et al., 2002). These hypotheses are supported by previous findings in the general population. Using both self-report (Stefanis et al., 2002) and clinical interview data (Krabbendam et al., 2004), subclinical psychosis and depression have been shown to exist as separate but correlated dimensions.

In the current study, depressive symptoms decreased more strongly over time than subclinical positive psychotic experiences. This may be explained by the fact that participants were referred to Youthscope for non-psychotic disorders (e.g., depression and anxiety). Treatment is likely to have been focused on reducing mood-related symptoms rather than subclinical psychotic experiences, leading depressive symptoms to improve more. The highest correlation between subclinical psychosis

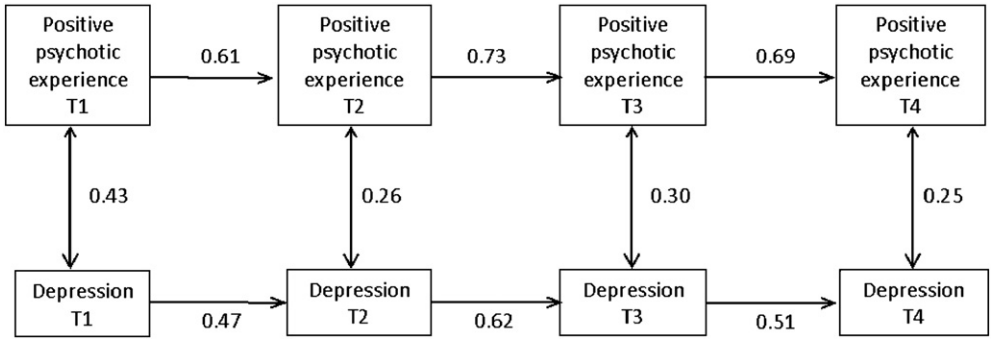

Fig. 1. Path model of subclinical positive psychotic experiences and depressive symptoms. *Note:* only significant paths are depicted. Model was controlled for age and gender. Effect sizes are given in beta's.

and depression was at presentation to the service. Over time, the relationship decreased, although the two are always significantly correlated. This decrease cannot be ascribed as inherent to the path model (i.e. that correlations at later time points are lower because these associations are more strongly controlled for), since the individual correlations also decreased over time (data not shown). This is a classic example of Berkson's bias; the phenomenon that two psychopathological dimensions are more highly correlated in clinical samples than at the general population level (Boccia et al., 2007).

The present findings should be interpreted in light of the strengths and weaknesses of the study. These results are important because they suggest that, over time, changes in one of these dimensions do not appear to lead to changes in the other, at least at this subclinical stage of the psychosis continuum. Self-report questionnaires were used for collecting data. This method may lead to data loss compared to clinical interviews, but several studies have shown that it is a reliable method to assess subclinical psychotic experiences (Allardyce et al., 2007; Kelleher et al., 2011). The fact that the sample is help-seeking can be either an advantage or a disadvantage. The interesting finding that the relationship between subclinical psychosis and depression was strongest at the moment of presentation and decreased over time would have been impossible to find in a general population sample. However, because of the nature of this sample, the results may not be generalizable to psychotic, UHR or general population samples. Future research should aim at replicating the findings in different samples to fully understand the complex relations between these two concepts, since the dynamics between psychosis and depression may differ along the psychosis phenotype. It is also necessary to better understand other factors that may mediate the relationship.

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Contributors

JW and AL undertook data analysis, interpreted the data and co-wrote the manuscript. JvO, WV and BN reviewed the manuscript. GB collected the data. QR assisted with data analysis. AY designed the protocol and assisted in interpreting data and writing the manuscript. All authors contributed to and have approved the final manuscript.

Conflicts of interest

Dr. van Os is/has been an unrestricted research grant holder with, or has received financial compensation as an independent symposium speaker from Eli Lilly, BMS, Lundbeck, Organon, Janssen-Cilag, GSK, AstraZeneca, Pfizer and Servier, companies that have an interest in the treatment of psychosis. All other authors have no conflict of interests.

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