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Interrelationships between depressive symptoms and positive and negative symptoms of recent onset schizophrenia spectrum disorders: A network analytical approach

Sarah E. Herniman^{a,b,c,*}, Lisa J. Phillips^c, Stephen J. Wood^{a,b,d}, Sue M. Cotton^{a,b}, Edith J. Liemburg^e, Kelly A. Allott^{a,b}

^a Orygen, Melbourne, Australia

^b Centre for Youth Mental Health, University of Melbourne, Melbourne, Australia

^c Melbourne School of Psychological Sciences, University of Melbourne, Melbourne, Australia

^d School of Psychology, University of Birmingham, Birmingham, UK

^e Rob Giel Research Center, University of Groningen, University Medical Center Groningen, Groningen, the Netherlands

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ABSTRACT

Objective: There is a need to better understand the interrelationships between positive and negative symptoms of recent-onset schizophrenia spectrum disorders (SSD) and co-occurring depressive symptoms. Aims were to determine: (1) whether depressive symptoms are best conceptualised as distinct from, or intrinsic to, positive and negative symptoms; and (2) bridging symptoms.

Methods: Network analysis was applied to data from 198 individuals with depressive and psychotic symptoms in SSD from the Psychosis Recent Onset Groningen Survey (PROGR-S). Measures were: Montgomery-Åsberg Depression Rating Scale and Positive and Negative Syndrome Scale.

Results: Positive symptoms were just as likely to be associated with depressive and negative symptoms, and had more strong associations with depressive than negative symptoms. Negative symptoms were more likely to be associated with depressive than positive symptoms, and had more strong associations with depressive than positive symptoms. Suspiciousness and stereotyped thinking bridged between positive and depressive symptoms, and apparent sadness and lassitude between negative and depressive symptoms.

Conclusions: Depressive symptoms might be best conceptualised as intrinsic to positive and negative symptoms pertaining to deficits in motivation and interest in the psychotic phase of SSD. Treatments targeting bridges between depressive and positive symptoms, and depressive and such negative symptoms, might prevent or improve co-occurring depressive symptoms, or vice-versa, in the psychotic phase of SSD.

1. Introduction

Co-occurring depressive symptoms significantly contribute to the already large burden of schizophrenia spectrum disorders (SSDs) (Charleson et al., 2016; Rossler et al., 2005), particularly in the early illness stages, yet are often overlooked (Cotton et al., 2012). They have been associated with serious adverse outcomes in SSD: increased risk of non-remission of psychotic symptoms and psychotic recurrence, and violence towards others, self-harm, and suicide (Birchwood, 2003; Birchwood et al., 2000a, 2000b; Uptegrove et al., 2014). Indeed, depressive symptoms are the most significant predictor of suicide in SSD, more so than acting on command hallucinations (Crumlish et al.,

2005; Dutta et al., 2011).

Schizophrenia spectrum disorders are diagnostically conceptualised as non-affective psychotic disorders comprising positive and negative symptoms (American Psychiatric Association, 2013). They are conceptualised differently to affective psychotic disorders, including schizoaffective disorder. In addition to positive and negative symptoms, schizoaffective disorder includes clinically-significant depression or mania for the majority of the total duration of psychotic symptoms (across psychotic and post-psychotic [or residual] phases). While depressive symptoms might not occur for the majority of psychotic symptoms in SSD, they still occur at clinically significant levels in up to 80% of individuals, and might be more common and severe in the

* Corresponding author. Orygen, 35 Poplar Road, Parkville, VIC, 3052, Australia.

E-mail address: sarah.herniman@unimelb.edu.au (S.E. Herniman).

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psychotic phase or when positive psychotic symptoms are present (as opposed to the post-psychotic phase; [Herniman et al., 2019](#)). Rather than being conceptualised as a distinct, superimposed disorder, depressive symptoms might therefore be better conceptualised as intrinsic to SSD, particularly in the psychotic phase ([Birchwood, 2003](#); [Uptegrove et al., 2020](#)). The importance and prevalence of depressive symptoms in SSD underscores the need to interrogate diagnostic conceptualisations that depressive symptoms are distinct from SSD, and to better understand the mechanisms of its co-occurrence in SSD. Such interrogations might further inform the relevance and validity of dimensional models of SSD (e.g., Research Domain Criteria [RDoC]) ([Keshavan et al., 2011](#); [Reininghaus et al., 2019](#)).

Contemporary conceptualisations or symptom network theory posit that mental disorders comprise causal and reinforcing associations among symptoms, and that co-occurrence is due to causal and reinforcing associations between symptoms of one (or more) disorders ([Borsboom, 2017](#); [Cramer et al., 2010](#)). Network analysis is a computational technique best suited to modelling and visually illustrating associations in highly multivariate data, and can determine empirically-driven clusters or communities of symptoms whose associations are especially dense (e.g., a community comprising positive symptoms; [Borsboom, 2017](#); [Cramer et al., 2010](#)). The degree of distinctiveness or interrelatedness of symptom-level, cross-community associations determines whether communities are best conceptualised as distinct from (and therefore comorbid), or intrinsic to (same disorder), one another. If *positive–depressive* associations (relative to *positive–negative* symptoms) are relatively sparse and weak compared to *positive–positive* associations, then depressive symptoms might be best conceptualised as distinct from positive symptoms of SSD, and vice-versa. Furthermore, symptoms with the most and strongest cross-community associations are considered to have the greatest influence in connecting or bridging communities and therefore, might represent important targets to treat or disintegrate co-occurrence ([Borsboom, 2017](#); [Cramer et al., 2010](#)). Thus, research modelling the networks of positive, negative, and depressive symptoms and narrowing in on cross-community associations and bridges might reveal important insights into the conceptualisation and mechanisms of co-occurring depressive symptoms in SSD.

To date, no studies have used network analysis to examine the degree of distinctiveness or interrelatedness of cross-community associations and bridges between positive and depressive symptoms, and negative and depressive symptoms in SSD. Nonetheless, associations can be extrapolated from previous research to provide preliminary insights. *Hallucinations* and *delusions* have been associated with depressive symptoms (albeit based on sum score; [Birchwood, 2003](#); [Birchwood et al., 2000a](#); [Birchwood et al., 2000b](#); [Uptegrove et al., 2014](#)), and *suspiciousness* with *suicidal ideation* ([van Rooijen et al., 2017](#)), particularly when voices were perceived to be threatening towards, have power over (omnipotence), or greater social rank than the individual themselves ([Birchwood, 2003](#); [Birchwood et al., 2000a, 2000b](#); [Uptegrove et al., 2014](#); [van Rooijen et al., 2017](#)). Thus, *hallucinations*, *delusions*, and *suspiciousness* might contribute to depressive symptoms, and represent bridges of co-occurrence. Regarding negative symptoms, those reflective of motivation and interest deficits (i.e., *emotional* and *social withdrawal*) have been specifically associated with the depressive symptom *inability to feel* (items from Montgomery–Åsberg Depression Rating Scale [MADRS]; [Herniman et al., 2020](#)), and *hopelessness*, *morning depression*, and *early wakening* (items from Calgary Depression Rating Scale; [van Rooijen et al., 2017](#)). Unlike positive symptoms, however, these associations have largely been attributed to phenomenological overlap. However, a recent meta-regression challenged this attribution, finding that negative and depressive symptoms were associated even without overlapping symptoms ([Herniman et al., 2019](#)). Negative symptoms might contribute to depressive symptoms, or vice-versa. Though informative, these existing studies primarily using bivariate associations lack the statistical sophistication required to capture complexities of the

phenomena and sufficiently answer questions about conceptualisation and mechanisms of co-occurring depressive symptoms in SSD.

Using network analysis, the aims of the current study were twofold, to determine: (1) whether the symptom community constituting depressive symptoms is best conceptualised as distinct from, or intrinsic to, symptom communities constituting positive and negative symptoms in the psychotic phase of SSD; and (2) the specific symptoms bridging between communities. We hypothesised that depressive symptoms would be highly interrelated with, and therefore better conceptualised as intrinsic to symptoms of the positive and negative communities in the psychotic phase of SSD. It was also hypothesised that *hallucinations*, *delusions*, and/or *suspiciousness* would be among the symptoms bridging between depressive and positive communities, and symptoms pertaining to motivation and interest deficits between depressive and negative communities.

2. Method

2.1. Participants

This study involved secondary analysis of data from the Psychosis Recent Onset Groningen Survey (PROGR-S; [Herniman et al., 2020](#); [Herniman et al., under review](#); [Liemburg et al., 2014](#)). The eligibility criteria for PROGR-S has been described elsewhere ([Liemburg et al., 2014](#)). Briefly, participants resided in the Groningen province of the Netherlands and were referred to a psychiatric institution with a suspected recent-onset psychotic episode (<2 years) that was yet to be treated, or emergency treatment was recently initiated allowing for more detailed clinical assessment. Diagnoses were based on the Diagnostic and Statistical Manual of Mental Disorders–Fourth Edition (DSM-IV; [American Psychiatric Association, 1994](#)) criteria and confirmed using the Schedules for Clinical Assessment in Neuropsychiatry (SCAN; [Wing et al., 1990](#)). There were no exclusion criteria based on age, substance use, or ethnicity.

PROGR-S participants (recruited 1997–2009) with complete Montgomery–Åsberg Depression Rating Scale (MADRS) ([Montgomery and Åsberg, 1979](#)) data were eligible for the current study, and additional exclusion criteria were applied. First, those without a DSM-IV-defined psychotic disorder or who had a psychotic disorder due to a medical condition, as well as those ≥ 40 years of age, were excluded to avoid organic- and dementia-related psychotic disorders. Second, participants with an affective psychotic disorder, including schizoaffective disorder, major depressive disorder (MDD) and bipolar I disorder with psychotic features, were excluded to avoid confounds between illness characteristics and depressive symptoms *per se* ([Cotton et al., 2012](#); [Herniman et al., 2019](#)). Last, participants were also excluded if they did not currently have clinically-defined depression (defined as a MADRS score >10 with at least one of reported sadness, pessimistic thoughts, or suicidal thoughts scoring at least one ([Herniman et al., 2020](#))) and positive psychotic symptom(s) (defined as at least one score of ≥ 3 on any PANSS_p item ([Herniman et al., 2020](#); [Uptegrove et al., 2014](#))).

The final participant group therefore comprised individuals in the psychotic phase of a recent-onset SSD disorder (including schizophrenia, schizophreniform disorder, delusional disorder, brief psychotic disorder, substance-induced psychotic disorder, and psychotic disorder NOS) with co-occurring clinically-defined depression.

2.2. Procedure

Participants provided verbal- and written-informed consent ([Liemburg et al., 2014](#)). Procedures were conducted in accordance with local and international rules confirmed by the local ethical committee of the University Medical Center of Groningen.

2.3. Measures

Depressive symptoms were measured using the Montgomery–Åsberg Depression Rating Scale (MADRS) (Montgomery and Åsberg, 1979), and positive and negative symptoms using the positive and negative subscales of the Positive (PANSS_P) and Negative Syndrome Scale (PANSS_N) (Kay et al., 1987). The MADRS and PANSS have sound psychometric properties in SSD (Herniman et al., 2020; Kay et al., 1987).

2.4. Statistical analyses

Statistical analyses were conducted in R (V4.0.3). Assumption screening were undertaken and descriptive statistics and frequency counts were obtained for sample characterization (Tabachnick and Fidell, 2013; Troyanskaya et al., 2001).

2.4.1. Network estimation

To estimate the network, regularised, partial correlation networks were conducted in accordance with current recommendations (Epskamp et al., 2018; Epskamp and Fried, 2018). Specifically, Graphical Gaussian Models using the Least Absolute Shrinkage and Selection Operator (LASSO; Tibshirani, 1996) and the Extended Bayesian Information Criterion (EBIC; hyperparameter λ set to 0) were used (Chen and Chen, 2008). This procedure shrinks correlations towards zero and sets trivially small correlations to zero, eliminating spurious associations, resulting in a sparse graphical model comprising the strongest associations. All non-zero associations in a network with LASSO regularisation are considered sufficiently strong and meaningful (Epskamp et al., 2018; Epskamp and Fried, 2018).

2.4.2. Network analysis

2.4.2.1. Communities. Community analysis using the well-established *spinglass algorithm* was conducted in accordance with recommendations (Fried, 2016): the spinglass algorithm was conducted 1,000 times, and the median number of communities was obtained. A seed was then found that produced this median number of communities, and consequently set to this seed to allow for replicability (Fried, 2016).

2.4.2.2. Interrelatedness or distinctness. To determine the interrelatedness between symptoms, we analysed the number and strength of within-community and cross-community associations. Using Chi-square (χ^2), the proportion of non-zero, cross-community associations (possible associations defined as: $n^*(n-1)/2$, where n is the number of symptoms/nodes within the network) between positive and depressive communities (positive—depressive associations) was compared to the proportion of non-zero positive—negative associations (Choi et al., 2017; Knefel et al., 2016). Only associations that were positive in direction were considered in χ^2 analyses.

Also using χ^2 , the proportion of positive—depressive associations exceeding the strength of the weakest, non-zero association amongst positive symptoms (positive—positive associations) was compared to the proportion of positive—negative associations exceeding the strength of the weakest, non-zero positive—positive association. The weakest within-community association amongst positive symptoms was used as a reference point since non-zero associations are sufficiently strong and meaningful (Epskamp et al., 2018; Epskamp and Fried, 2018). Again, only associations positive in direction were considered in χ^2 analyses. This approach was then repeated to determine the relative interrelatedness or distinctiveness of depressive with negative symptoms.

2.4.2.3. Bridge symptoms. The *bridge expected influence* was calculated in accordance with recommendations (Heeren et al., 2018; Jones et al., 2018, 2019). *Bridge expected influence* is the sum of a symptoms' associations with symptoms of the other community—without taking the

absolute value of edges before summing them. This is indicated when networks comprise associations that are positive and negative in direction (Robinaugh et al., 2016). There is no consensus on what constitutes bridge significance. In accordance with recommendations, the top 20% of symptoms with the greatest values were considered most meaningful (Jones et al., 2019).

2.4.3. Network accuracy and stability

Accuracy and stability of edge-weights was examined using nonparametric and case-dropping subset bootstrapping procedures (Epskamp et al., 2018; Epskamp and Fried, 2018). Details and results of these are reported in Supplementary.

3. Results

3.1. Participant flow

Six hundred and fifty-nine of the 718 (92%) PROGR-S participants had complete MADRS data (Liemburg et al., 2014). Of the 659, 62.8% ($n = 414$) did not meet the eligibility criteria (Supplementary). 187 were excluded due to ≥ 40 years of age, organic or affective psychotic disorder. Of the remaining 472 individuals, 48.1% ($n = 227$) did not have clinically-significant depressive symptoms (and were excluded) and 51.9% ($n = 245$) did. Of the remaining 245 with SSD and depressive symptoms, 80.8% or 198 individuals were experiencing positive psychotic symptoms, and comprised the final sample.

3.2. Demographic and clinical characteristics

Table 1 presents the demographic and clinical characteristics of the sample ($N = 198$). The average age was 25.28 years ($SD = 5.85$). Most were male (78.8%, $n = 156$) and had a diagnosis schizophrenia (61.0%, $n = 121$).

Table 1

Demographic and clinical characteristics of individuals with recent onset schizophrenia spectrum disorders with clinically significant depression ($N = 198$).

Variable	M (SD) or % (n)
Demographic characteristics	
Age (years)	25.28 (5.85)
Gender (%female)	21.2% ($n = 42$)
Highest level of education completed ($n=196$)	
Elementary/primary school	19.4 (38)
Secondary/high school	53.6 (105)
Vocation/TAFE	23.9 (47)
University degree	3.1 (6)
Occupation ($n=189$), %(n)	
Paid job	28.0 (53)
Student	18.5 (35)
Voluntary job	6.3 (12)
Running household	1.1 (2)
Unemployed	46.0 (87)
Illness characteristic	
Diagnoses	
Schizophrenia	61.1 (121)
Psychotic disorder NOS	17.2 (34)
Schizophreniform disorder	7.0 (14)
Brief psychotic disorder	4.5 (9)
Substance induced psychotic disorder	7.5 (15)
Delusional disorder	2.5 (5)
Total scale scores	
MADRS total score (range 0–60)	20.13 (1.31)
PANSS _P total score (range 1–49)	15.41 (4.55)
PANSS _N total score (range 1–49)	16.92 (6.25)
Functioning (GAF)	51.42 (11.86)

Notes. M = mean; SD = standard deviation; MADRS = Montgomery–Åsberg Depression Rating Scale; PANSS_P=Positive Subscale of the Positive and Negative Syndrome Scale; PANSS_N=Negative Subscale of the Positive and Negative Syndrome Scale; GAF = Global Assessment of Functioning.

3.3. Network

Fig. 1 presents the regularised, partial correlation network. The left panel (1A) was coloured according to scale, and the right (1B) according to communities. All symptoms were connected either directly or indirectly via other symptoms in the network. 37.7% ($n = 104$) of the possible 276 edges were $>zero$.

3.3.1. Communities

Six spinglass communities were identified and presented in Fig. 1B. The depressive mood and thinking community comprised *apparent sadness, reported sadness, inner tension, pessimistic thoughts, and suicidal thoughts*. The positive symptom community comprised *delusions, conceptual disorganisation, hallucinatory items, grandiosity, suspiciousness, and stereotyped thinking*. Two negative symptom communities emerged; the first pertained to deficits in expressive functions (*blunted affect, poor rapport, difficulty in abstract thinking, lack of spontaneity and flow of conversation*), and the second to motivation and interest (*concentration difficulties, lassitude, inability to feel, emotional withdrawal, passive social withdrawal*).

3.3.2. Interrelatedness or distinctness

Amongst depressive symptoms (*apparent sadness, reported sadness, inner tension, pessimistic thoughts, suicidal thoughts*), 80% ($n = 8$) of the possible 10 edges were $>zero$. The strongest edge emerged between *apparent sadness* and *reported sadness* (regularised, partial r [termed r hereafter]; $r = 0.31$), and weakest between *reported sadness*–*pessimistic thoughts* ($r = 0.04$).

3.3.2.1. Positive—depressive associations. Amongst positive symptoms (*delusions, conceptual disorganisation, hallucinatory items, grandiosity, suspiciousness, stereotyped thinking*), 60.0% ($n = 9$) of the possible 15 edges were $>zero$. The strongest non-zero association emerged between *delusions*–*suspiciousness* ($r = 0.31$), and weakest between *hallucinatory behaviour*–*suspiciousness* ($r = 0.01$).

Across positive and depressive symptoms, 33.3% ($n = 10$) of the possible 30 associations were $>zero$; 20.0% ($n = 6/30$) were positive in direction. The proportion of non-zero, positive associations between positive and depressive symptoms (20.0%) was equivalent to the proportion of associations between positive and negative symptoms regarding expressive deficits (25.0%), $\chi^2(1) = 1.42$, 95%CI = -3.24 ,

13.16, $p = 0.234$, and positive and negative symptoms regarding motivation and interest (23.3%), $\chi^2(1) = 0.63$, 95%CI = -4.83 , 11.38, $p = 0.426$.

Of associations between positive and depressive symptoms, 83.3% ($n = 5/6$) exceeded the strength of the weakest, non-zero association amongst positive symptoms ($r = 0.01$). This proportion was equivalent to the proportion of associations between positive and negative symptoms regarding expressive deficits (83.3%, $n = 5/6$) exceeding the strength of the weakest, non-zero association amongst positive symptoms ($r = 0.01$), $\chi^2(1) = 0.00$, 95%CI = -7.38 , 7.39, $p = 1.000$. This proportion was significantly greater than the proportion of positive and negative symptoms regarding motivation and interest deficits (57.1%, $n = 4/7$) exceeding the strength of the weakest association amongst positive symptoms ($r = 0.01$), $\chi^2(1) = 32.40$, 95%CI = 17.33, 34.52, $p < 0.001$.

3.3.2.2. Negative(expressive deficits)—depressive associations. Amongst negative symptoms regarding expressive deficits (*blunted affect, poor rapport, difficulty in abstract thinking*), 83.3% ($n = 5$) of the possible 6 edges were $>zero$. The strongest non-zero association emerged between *poor rapport*–*lack of spontaneity and flow of conversation* ($r = 0.47$), and weakest between *poor rapport*–*difficulty in abstract thinking* ($r = 0.03$).

Across negative symptoms regarding expressive deficits and depressive symptoms, 35% ($n = 7$) of the possible 20 cross-community edges were $>zero$; 10% ($n = 2/20$) were positive in direction. The proportion of non-zero, positive associations between negative symptoms regarding expressive deficits and depressive associations (10%) was significantly lower than the proportion of such negative symptoms with positive symptoms (25%), $\chi^2(1) = 15.39$, 95%CI = 7.58, 22.33, $p < 0.001$.

Of the associations between negative symptoms (expressive deficits) and depressive symptoms, 50.0% ($n = 1/2$) exceeded the strength of the weakest, non-zero association amongst such negative symptoms ($r = 0.03$). This was significantly lower than the proportion of associations between such negative symptoms and positive symptoms (66.7%, $n = 4/6$) exceeding the strength of the weakest association amongst such negative symptoms ($r = 0.03$), $\chi^2(1) = 11.33$, 95%CI = 6.99, 25.97, $p < 0.001$.

3.3.2.3. Negative (motivation and interest deficits)—depressive associations. Amongst negative symptoms regarding motivation and

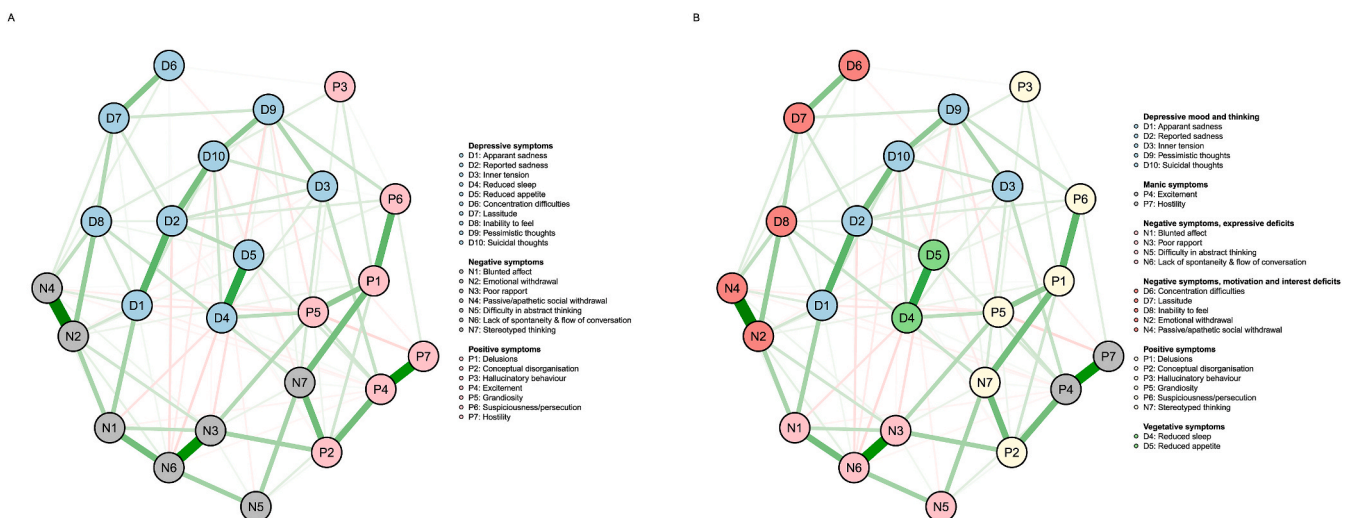


Fig. 1. The networks comprising regularised, partial correlations between depressive, positive, and negative symptoms in the psychotic phase of recent-onset schizophrenia spectrum disorders (SSD) with co-occurring clinically-defined depression.

Figure notes. Green edges represent positive, regularised, partial correlations (conditional dependence associations), and red edges represent negative, regularised, partial correlations. Thicker edges represent stronger correlations.

interest deficits (concentration difficulties, lassitude, inability to feel, emotional withdrawal, passive social withdrawal), 70.0% (n = 7) of the possible 10 edges were >zero. The strongest edge emerged between emotional withdrawal—passive social withdrawal (r = 0.54), and weakest between concentration difficulties—passive social withdrawal (r = 0.05).

Across negative symptoms regarding motivation and interest deficits and depressive symptoms, 40.0% (n = 10) of the possible 25 cross-community associations were >zero; 36% (n = 9/25) were positive in direction. The proportion of non-zero, positive associations between negative symptoms regarding deficits in motivation and interest and depressive symptoms (36%) was significantly greater than the proportion of associations between such negative and positive symptoms (23.3%), $\chi^2(1) = 7.64$, 95%CI = 3.70, 21.42, p = 0.006.

Of the associations between negative symptoms (motivation and interest) and depressive symptoms, 55.6% (n = 5/9) exceeded the strength of the weakest, non-zero association amongst such negative symptoms (r = 0.05). This was significantly greater than the proportion of associations between such negative and positive symptoms (28.6%, n = 2/7) exceeding the strength of the weakest association amongst such negative symptoms (r = 0.05), $\chi^2(1) = 29.53$, 95%CI = 17.40, 35.93, p = 0.001.

3.3.3. Bridge symptoms

3.3.3.1. Positive—depressive bridges. The positive symptoms of suspiciousness and stereotyped thinking had the greatest bridge expected influence in connecting depressive and positive symptoms (respectively 0.17, 0.12). Fig. 2 presents the regularised, partial correlation network respectively highlighting such bridge symptoms and their cross-disorder associations—each are presented in two separate panels (Fig. 2A and B). Suspiciousness had the greatest cross-community association with pessimistic thoughts (r = 0.10; Fig. 2A), and stereotyped thinking with inner tension (r = 0.08; Fig. 2B).

3.3.3.2. Negative (expressive deficits)—depressive bridges. The depressive symptom apparent sadness and negative symptom blunted affect had the greatest bridge expected influence in connecting depressive and negative symptoms pertaining to expressive deficits (respectively 0.20, 0.17). As seen in Fig. 3, apparent sadness and blunted affect had the greatest cross-community association with one another (r = 0.17).

3.3.3.3. Negative (motivation and interest deficits)—depressive bridges. The depressive symptom apparent sadness and negative symptom lassitude had the greatest bridge expected influence in connecting depressive and negative symptoms regarding motivation and interest deficits (respectively 0.26, 0.21). As seen in Fig. 4, apparent sadness has the greatest cross-community association with inability to feel (r = 0.08), and lassitude with reported sadness (r = 0.09).

4. Discussion

To our knowledge, this is the first study to use contemporary statistical modelling to determine whether depressive symptoms are best conceptualised as intrinsic to SSD, or a distinct, superimposed comorbid disorder, and what symptoms connect the two.

4.1. Interrelatedness or distinctness of depressive symptoms

More than half (51.9%) with SSD had clinically-significant depressive symptoms (just under did not, 49.1%), most of whom (80.8%) were in the psychotic phase or experiencing positive psychotic symptoms, comprising the analytical sample (N = 198).

We found that positive symptoms were just as likely to be associated with depressive symptoms compared to negative symptoms pertaining to deficits in expressive functions as well as motivation and interest. Positive symptoms had significantly more strong associations with depressive symptoms compared to negative symptoms pertaining to motivation and interest, and an equivalent number with depressive and negative symptoms pertaining to expressive deficits. Negative symptoms regarding deficits in motivation and interest were significantly more likely to be associated with depressive symptoms compared to positive symptoms, and such negative symptoms had significantly more strong associations with depressive symptoms compared to positive symptoms. In contrast, negative symptoms regarding expressive functions were significantly more likely to be associated with positive symptoms than depressive symptoms, and such negative symptoms had significantly more strong associations with positive than depressive symptoms.

These findings indicate that depressive symptoms are highly interrelated with positive symptoms and negative symptoms pertaining to deficits in motivation and interest, and might therefore be best conceptualised as intrinsic to such symptoms in the psychotic phase of SSD (Birchwood et al., 2000a; Koren et al., 1993). Symptoms that bridge

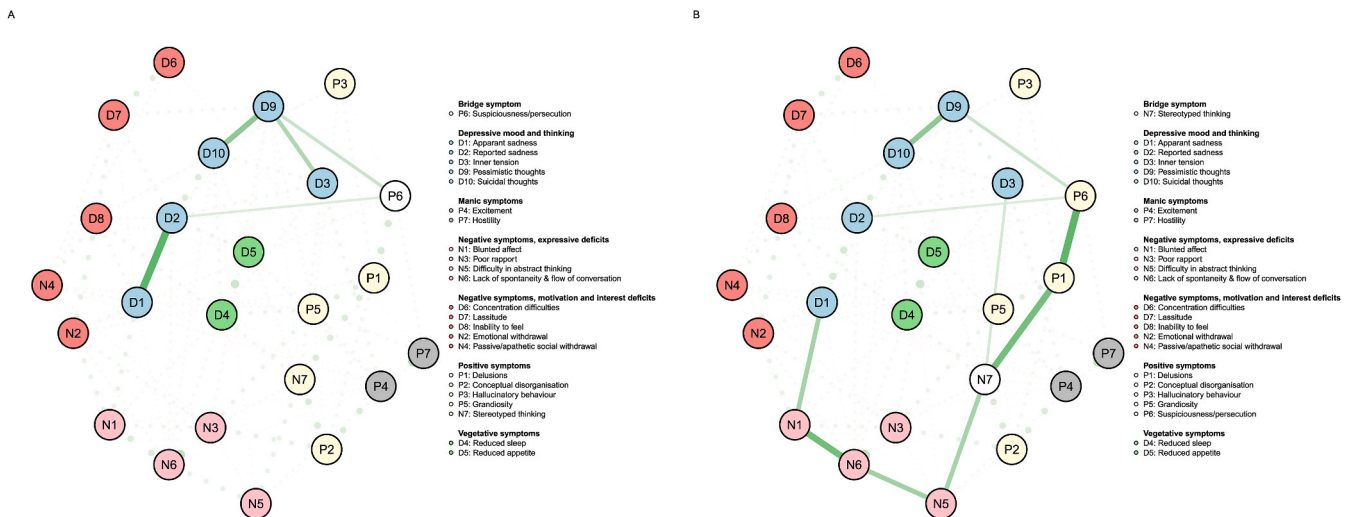


Fig. 2. The network highlighting bridges and symptom-level associations between depressive and positive symptom communities in the psychotic phase of schizophrenia spectrum disorders with co-occurring clinically-defined depression.

Figure notes. Green edges represent positive, regularised, partial correlations (conditional dependence associations), and red edges represent negative, regularised, partial correlations. Thicker edges represent stronger correlations.

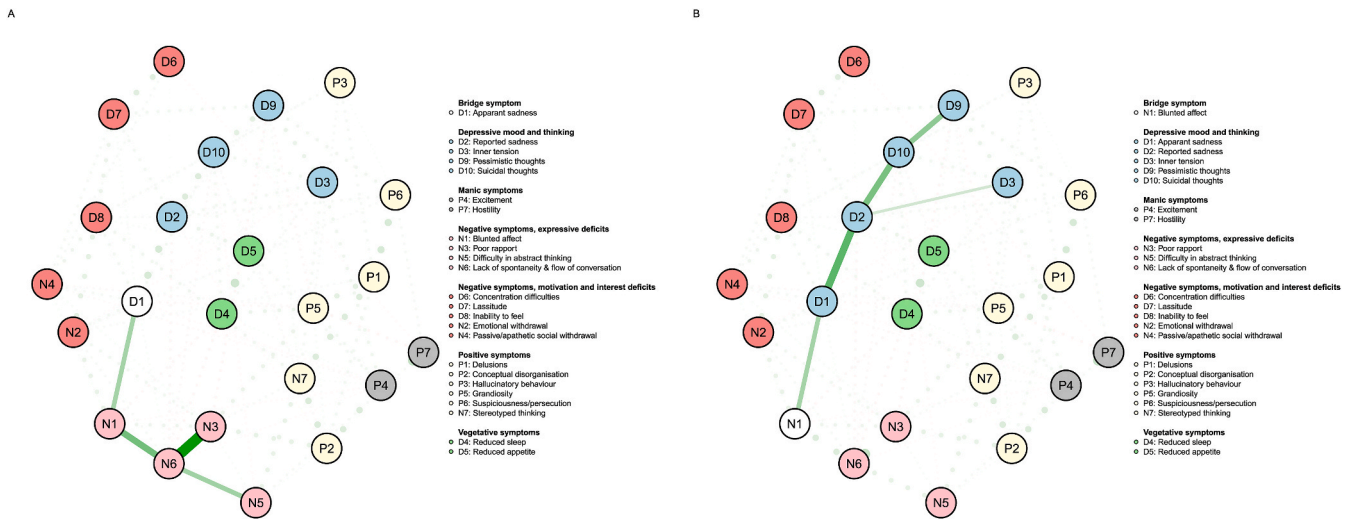


Fig. 3. The network highlighting bridges and symptom-level associations between depressive and negative symptom community pertaining to expressive deficits in the psychotic phase of schizophrenia spectrum disorders with co-occurring clinically-defined depression.

Figure notes. Green edges represent positive, regularised, partial correlations (conditional dependence associations), and red edges represent negative, regularised, partial correlations. Thicker edges represent stronger correlations.

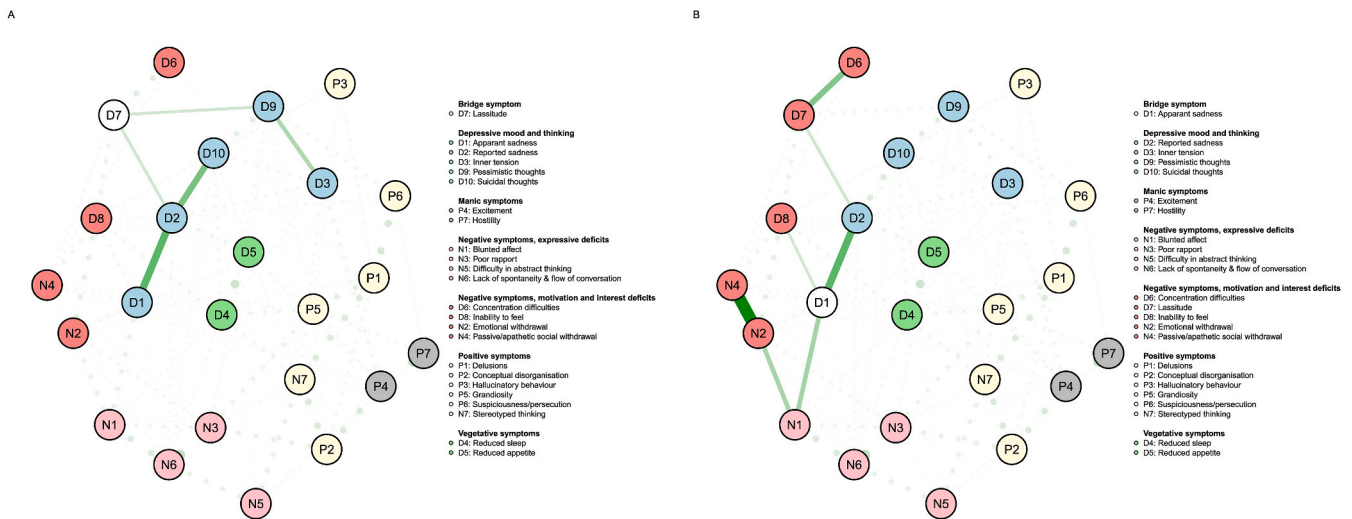


Fig. 4. The network highlighting bridges and symptom-level associations between depressive and negative symptom community pertaining to motivation and interest deficits in the psychotic phase of schizophrenia spectrum disorders with co-occurring clinically-defined depression.

Figure notes. Green edges represent positive, regularised, partial correlations (conditional dependence associations), and red edges represent negative, regularised, partial correlations. Thicker edges represent stronger correlations.

between positive and depressive symptoms, and between negative symptoms regarding deficits in motivation and interest and depressive symptoms, and their strongest cross-community associations, might provide important insights into the mechanisms underlying co-occurring depressive symptoms in the psychotic phase of SSD. As such, these bridges and cross-community associations (and not depressive symptoms—negative symptoms of expressive deficits) are specifically discussed next.

4.2. Bridge symptoms and strongest cross-community associations

We found that positive symptoms *suspiciousness* and *stereotyped thinking* bridged between positive and depressive communities, and that the negative symptom (motivation and interest) of *lassitude* and depressive symptom of *apparent sadness* bridged between negative (motivation and interest) and depressive communities.

Suspiciousness/persecution and *stereotyped thinking* bridged between

positive and depressive symptoms via *pessimistic thinking* and *inner tension*, respectively. This theoretically indicates that *suspiciousness/persecution* and *stereotyped thinking* are associated with *pessimistic thinking* and *inner tension*, which, in turn, might activate other depressive symptoms, leading to depressive disorder. These associations are broadly consistent with previous research, which found that *hallucinations*, *delusions*, and *suspiciousness* were specifically associated with depressive symptoms, particularly when voices were perceived to be threatening toward, have power over (omnipotent), or greater social rank than the individual themselves (Birchwood, 2003; Birchwood et al., 2000a, 2000b; Uptegrove et al., 2014). In this context, *pessimistic thinking* and *inner tension* are an understandable responses, with *pessimistic thinking* potentially functioning as a maladaptive coping mechanism (and not just symptomatic of depression) to reach some kind of resolution (e.g., by asking one-self, “why is this happening to me?”) (Nolan-Hoeksema, 1991; Thomas et al., 2012). However, this might unintentionally reinforce the omnipotence of psychotic experiences, interfere with effective problem

solving (and therefore reaching a resolution), and increase attention towards depressive and psychotic experiences (Nolan-Hoeksema, 1991; Thomas et al., 2012; Watkins and Brown, 2002).

The negative symptom *lassitude* bridged between negative symptoms of motivation and interest and depressive symptoms via *reported sadness*. The depressive symptom *apparent sadness* also bridged between such negative and depressive symptoms via *inability to feel*. The *lassitude–reported sadness* and *apparent sadness–inability to feel* associations are broadly consistent with previous research, finding that *lassitude* and *inability to feel* are among the symptoms previously considered to account for co-occurrence between depressive and negative symptoms (Herniman et al., 2020). *Lassitude* might specifically be associated with *reported sadness*, and *apparent sadness* with *inability to feel*, given no positive feedback loops. That is, an individual experiencing *lassitude* might have difficulty engaging in activities that provide pleasure or a sense of mastery, reinforcing *sadness*. Similarly, *apparent sadness* might contribute to *inability to feel*, given the absence of pleasurable experiences. These bridges and cross-disorder associations might provide preliminary insights into the development, recurrence, or perpetuation of co-occurring depressive symptoms in the psychotic phase of SSD.

4.3. Clinical implications and future research

The current results imply that depressive symptoms might be better conceptualised as intrinsic to positive symptoms and negative symptoms of motivation and interest in the psychotic phase of SSD. The incorporation of depressive symptoms into the diagnostic criteria for SSD would highlight the importance of assessment and treatment of these symptoms in the psychotic phase of SSD, and ultimately improve outcomes. Indeed, the importance of depressive symptoms in psychotic disorders has previously led to the development of the diagnostic entity schizoaffective disorder. However, such an entity has potentially led to clinicians and researchers overlooking the experience of depressive symptoms in individuals without a diagnosis of schizoaffective disorder. These diagnostic issues might point to the relevance and validity of dimensional models of SSD, such as RDoC (Keshavan et al., 2011; Reininghaus et al., 2019).

Assessment and treatment of depression in SSD should occur from first presentation to treatment services (Herniman et al., 2019), particularly given the serious adverse consequences associated with depression including suicide (Conley et al., 2007), and its potential to prevent or interfere with the resolution of psychotic symptoms in SSD (Kuipers et al., 2006; Smith et al., 2006). Until there is robust evidence of the phenotype of depression in the psychotic phase of SSD, assessment should be comprehensive (including at least two different assessment modalities such as diagnostic interview and completion of a depression severity scale; Herniman et al., 2019), emphasise core depressive symptoms including *sadness*, *pessimism*, or *suicidal ideation* (Herniman et al., 2020; Krynicki et al., 2018), and capture atypical symptoms including *increased sleep* and *increased appetite* (Lange et al., 2021).

Given the high interrelatedness between symptoms, treatments targeting specific symptoms such as positive symptoms (or mechanisms that map onto such symptoms) should theoretically improve closely interrelated symptoms such as depressive symptoms, or vice-versa. Indeed, antipsychotic medications appear to not only improve positive symptoms, but also co-occurring depressive symptoms in SSD (Gregory et al., 2017; Siris, 2000). As discussed above, if cognitive appraisals of voices as threatening and omnipotent (Birchwood, 2003; Birchwood et al., 2000a, 2000b; Uptegrove et al., 2014) map onto or bridge psychotic with depressive symptoms in SSD, then treatments targeting such cognitions (include cognitive diffusion and acceptance techniques, Thomas et al. (2013)) should theoretically prevent or improve co-occurring depressive symptoms in SSD. Controlled trials should be conducted to test such hypotheses.

It is unknown whether treatment of negative symptoms pertaining to motivation and interest might improve depressive symptoms, or vice-

versa, in SSD. If negative symptoms such as *lassitude* or *inability to feel* are implicated in the development or maintenance of co-occurring depressive symptoms in SSD, then treatments targeting such symptoms, including behavioural activation, should theoretically prevent or improve co-occurring depressive symptoms in SSD. Indeed, while no research has examined the efficacy of behavioural activation in improving depressive symptoms in SSD, it has been shown to improve negative symptoms in SSD (Choi et al., 2016). Again, controlled trials should test such hypotheses.

4.4. Limitations

The current study had some important limitations. The current study comprised a secondary analysis of data, meaning that such data was not collected for the current purposes of determining network interrelationships between positive, negative, and depressive symptoms in SSD. The current study was cross-sectional, and the network depicting positive, negative, and depressive symptoms of SSD was undirected as a result. Thus, while the current study captures associations, it does not capture information on directionality or whether certain symptoms activate or trigger other symptoms. While symptom-level associations might be bi-directional and involve feedback loops, it is also possible that some symptom-level associations are purely unidirectional. Directionality and temporal causality cannot therefore be inferred from the current analyses. Nonetheless, the current study is the first necessary step towards advancing knowledge on this important topic. Replication as well as prospective, longitudinal studies are needed before firm conclusions can be made regarding causal, symptom-level associations between depressive, positive, and negative symptoms of SSD.

5. Conclusions

Through the use of network analysis, we have shown that depressive symptoms are highly interrelated with both positive symptoms and negative symptoms of motivation and interest, and might therefore be best conceptualised as intrinsic to such symptoms in the psychotic phase of SSD. Symptoms that bridge between depressive and positive symptoms, and between depressive and negative symptoms of motivation and interest might account for such an intrinsic co-occurrence. Treatments targeting specific symptoms within and bridging between depressive and positive symptoms, and depressive and negative symptoms of motivation and interest, might prevent or improve co-occurring depressive symptoms in the psychotic phase of SSD, or vice-versa. However, given the infancy of such research, this area requires further investigation.

Author statement

All authors confirm that they are responsible for all aspects of this research. All authors contributed to the concept and design of this research, analysis and interpretation of the data, and the drafting and revising of the manuscript. All authors have approved the final version of this manuscript, as submitted.

Declaration of competing interest

None relevant to this paper.

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Appendix A. Supplementary data

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