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Co-occurring internalizing and externalizing psychopathology in childhood and adolescence: a network approach

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Abstract

The network approach suggests that psychopathology arises from complex associations between symptoms and may offer insight into the mechanisms that underpin psychiatric comorbidities. The transition from childhood to adolescence is a key period in the development of psychopathology, yet has rarely been considered from a network perspective. As such, the present study examined the network structure of internalizing and externalizing psychopathology from middle childhood through adolescence using data from the Avon Longitudinal Study of Parents and Children (ALSPAC; $n = 4405$). Eight DSM-IV disorders were assessed using maternal reports when children were aged 7.5, 10.5 and 14 years. Weighted, undirected networks were estimated and the relative importance of each node was assessed using three common measures of node centrality; strength, betweenness, and closeness. A consistent network structure emerged at all three time points; nodes clustered together in two regions of space broadly reflecting the internalizing and externalizing spectra. Permutation tests supported structural invariance across this developmental period. These spectra were bridged by numerous disorder-level interactions, the most consistent of which was between depression and oppositional defiant disorder (ODD). Furthermore, inspection of the centrality indices indicated that generalised anxiety disorder and ODD were the most central disorders in the networks. These findings demonstrate that symptom/disorder-level interplay and reciprocal influence are plausible mechanisms for the association between internalizing and externalizing psychopathology in childhood/adolescence.

Keywords Psychopathology · Comorbidity · ALSPAC · Network analysis · Internalizing · Externalizing

Introduction

Psychiatric comorbidities occur with greater-than-chance frequency [1] and are associated with increased symptom severity and a poorer overall prognosis [2–5]. The mechanisms by which psychiatric symptoms and disorders are related, however, remain poorly understood. Hierarchical dimensional models, which have long been favoured in child and adolescent psychiatric research, account for comorbidity

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by framing psychopathology as a small number of broad transdiagnostic dimensions (e.g. internalizing, externalizing). However, due to strong associations between the dimensions themselves, a general psychopathological factor, p, has been proposed to explain the co-occurrence of virtually all psychiatric symptoms and disorders [6, 7]. Although this general factor has been supported in both adult [6, 7] and child samples [8, 9], a consistent interpretation of the p-factor has so far proven elusive [6–11]. The most popular interpretation posits that p reflects a shared aetiological factor, or set of factors (e.g. genetic vulnerability, personality, environmental factors) that predispose individuals to any and all forms of psychopathology [11].

In recent years, an alternative school of thought, the network approach, has gained considerable momentum. This perspective posits that psychiatric disorders reflect complex networks of locally associated symptoms [12]. In such models, variables are presented graphically as nodes (points in space) and the associations between nodes are presented as edges (lines, with thickness denoting strength). This

approach assumes that the effects of causal factors spread throughout networks via direct, symptom-level interactions and reinforcement (as opposed to causal factors influencing all symptoms simultaneously) [12]. Borsboom and Cramer [12] provide the following chain as an example; chronic stress → depressed mood → self-reproach → insomnia → fatigue → concentration. As such, the network approach accounts for comorbidity through 'bridging edges'; i.e. direct associations that serve to link reasonably distinct clusters of symptoms/disorders [12, 13]. Under such an interpretation, p represents the statistical reduction of a plethora of lower-level interactions between different components of psychopathology. The main advantage of the network approach is that, by focussing on local interactions, we can determine not only how important a symptom/disorder variable is in terms of its overall connectivity (aka centrality), but also where a symptom/disorder is important within the network (i.e. the strongest edges).

Although an abundance of network studies has been published recently, the majority have focussed their enquiry on the structure of single disorders [14, 15], or a narrow range of comorbid disorders [16]. To our knowledge, only two studies have used network methods to model broader psychiatric comorbidity; Boschloo and colleagues [17] examined the network structure of 120 symptoms from 12 supposedly distinct DSM-IV disorders in the second wave of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC, $N = 34,653$). They found that, although symptoms clustered in a manner broadly consistent with the DSM structure, all 120 symptoms were connected, either directly or indirectly, and each cluster was connected to at least three others. Boschloo et al. [18] then examined the network structure of emotional and behavioural problems in a large sample of pre-adolescents (mean age 11.1 years; $N = 2175$). Ninety-five symptoms were assessed using the Youth Self-Report [19], and in the resultant network symptoms clustered together in patterns broadly reflective of the YSR domains. Connections were generally stronger and more common within, rather than between, these domains; however, numerous symptom pairs served to link domains, suggesting that the domain boundaries were not as defined as had previously been assumed in factor analytic studies.

Further studies of broad comorbidity networks may help unpack the overlap between higher order dimensions of psychopathology and provide a more complete view of psychiatric comorbidity. The present study expands on previous work in two ways. This is the first study to examine the network structure of comorbid internalizing and externalizing at the disorder level (i.e. where nodes in the network reflect distress/impairment aggregates from internalizing and externalizing symptom groups). To date, network analysis has mainly been used to model the association between symptoms, assuming that symptoms are the base level of psychopathological expression. However, as Borsboom et al. [12] note, symptoms themselves may be broken down into networks of emotional, behavioural and external factors; e.g. difficulty sleeping may be understood in terms of the interplay between mood, melatonin production, routine, caffeine intake and/or screen time. As such, network analysis is flexible and may be used to study psychopathology at various levels of complexity [20]. Indeed, there has been an increase in studies that have examined psychopathology at the construct level [20–23], and this approach has the advantage of reducing the amount of nodes and edges in a network, in turn simplifying interpretation [24]. As the aim of the present study was to provide a network analogue to p (which has primarily been modelled at the disorder-level), we chose to focus our enquiry at the disorder level (e.g. depression, general anxiety, hyperactivity).

Second, this study expands our knowledge of the network structure of psychopathology in childhood and adolescence, and explores whether this structure changes over this key developmental period. The transition from childhood through adolescence is a period marked by significant biological, cognitive and socio-environmental change. It is during this period that psychopathology commonly emerges [1, 25]. Furthermore, disorders that emerge during this period typically serve as precursors to similar problems later in life [26]. As such childhood/adolescence is an ideal period to focus on when examining direct associations between symptoms and/or disorders and may offer key insights into the development of psychiatric sequelae. To date, only one study has focussed on this age group [18]; however, the network structure was examined at only one time point (age 11). The present study examined the network structure of psychopathology (internalizing and externalizing) within a single cohort across three time points (7.5, 10.5, and 14 years) and tested whether this structure remained stable over this period. Although this study was exploratory in nature, it was predicted that disorders would form two distinct clusters of nodes analogous to the internalizing and externalizing dimensions of psychopathology. No a priori hypotheses were made regarding potential 'bridging edges'.

Method

Sample

Data were from the Avon Longitudinal Study of Parents and Children (ALSPAC). The ALSPAC is a prospective cohort study of children born in the English county of Avon between April 1st 1991 and December 31st 1992 ($N = 14,062$). The sample is broadly representative of the overall population of children in the UK [27, 28]. Data were collected using self-report postal questionnaires (completed

by the study mothers and mother's partners) and via yearly clinics for the study children from the age of 7.5 years [27, 28]. The study website contains details of all the data that are available through a fully searchable data dictionary (http://www.bris.ac.uk/alspac/researchers/data-access/data-dictionary/). Ethical approval for the study was obtained from the ALSPAC Ethics and Law Committee and the Local Research Ethics Committees. Further detailed descriptions of the ALSPAC can be found elsewhere [27].

Measures

Disorders were assessed using maternal report versions of the Development and Wellbeing Assessment (DAWBA) [29]. This structured clinical interview is used to assign psychiatric diagnoses to 5–16 year olds. It is used to assess fourteen distinct symptom profiles corresponding to ICD-10 and DSM-IV diagnostic criteria. The symptom profiles used in the present analysis were those assessed consistently across the three waves; specific phobia (SPP), social phobia (SOP), posttraumatic stress (PTSD), generalized anxiety (GAD), depression (DEP), attention deficit/hyperactivity disorder (ADHD), oppositional/defiant disorder (ODD) and conduct problems (CD). Official diagnoses were only available at the 7.5 year assessment. To make the use of data from subsequent time points, a comprehensive recoding strategy was employed. Mirroring the structure of the DSM, the DAWBA employs skip patterns; mothers are first asked whether children display core symptoms, followed by questions related to distress and burden associated with symptoms. To create quasi-diagnostic variables that closely mirrored DSM-IV diagnoses, disorders were deemed present if study mothers reported the requisite symptom profiles (including core symptoms) and significant burden or distress associated with these symptom profiles. In the case of ODD, teacher complaint was used in place of distress. For CD, a binary variable reflecting 'any frequent/definite troublesome behaviour' was computed, as per ALSPAC codebook guidelines. This recoding process resulted in eight binary quasi-diagnostic variables at each of the three time points. More detailed descriptions of this recoding process are available in the online supplementary materials.

Missing data

There is a lack of consensus as to how missing data should best be handled in network analysis [30]. The present study used the most common current practice, listwise deletion [14, 30, 31]. Complete data were available for 4405 maternal reports (DAWBA) at ages 7.5, 10.5 and 14, and this subsample was used for analysis.

Statistical analysis

Networks were constructed using the R package 'Isingfit' [32] which was developed to construct weighted undirected networks using binary data. This package uses the elasso method; based on the Ising [33] model, each variable is regressed on all other variables iteratively with a lasso penalty (l1) imposed on the regression coefficients that helps identify the simplest network by balancing sparsity and goodness of fit [18]. The l1 process identifies the best fitting network structure by specifying competing models with different levels of sparsity, and comparing the models using the extended Bayesian information criteria (EBIC) [34]. The edges in these networks are the mean values of the two logistic regression coefficients (i.e. node A predicting node B, and node B predicting node A), which can be interpreted similar to partial correlations. 'Isingfit' was used to construct networks using the 8 binary psychological disorder variables at ages 7.5, 10.5 and 14 years. The resultant networks were then graphically illustrated using the 'qgraph' package [35]. This package uses the Fruchterman–Reingold algorithm to place nodes with stronger and/or more connections closer together [36].

The relative importance of each node to the overall network structure was quantified using three common measures of node centrality. Strength is calculated for each node by summing its weighted connections with other nodes [37]. A node that is high in strength strongly and directly transmits its effects throughout the network [37]. Closeness reflects the average distance from a node of interest to all other nodes in a given network [37]. High closeness means a node is strongly influenced by changes in other nodes in the network [37]. Betweenness is calculated by counting the number of times a node of interest lies on the shortest path between two other nodes [37]. Nodes that are high in betweenness are important for transmitting effects between other nodes in the network. For all measures of centrality, higher values (presented as z-scores) are indicative of greater importance to the network as a whole [38].

Recently, the accuracy and stability of networks have received attention in the literature [39]. Accuracy and stability refer to the degree of certainty with which we can interpret the rank ordering the various edge weights and centrality indices. Network accuracy and stability were assessed using the guidelines of Epskamp, Borsboom, and Fried [39]. First, bootstrapped 95% confidence intervals (CIs) were used to examine the accuracy of network edges. Second, the stability of the order of the centrality indices (strongest to weakest) was examined using a subsetting bootstrap method, i.e. by re-estimating the network based on increasingly smaller subsets of the original sample. The underlying logic of this method is that if the order of centrality estimates from a network based on a small subset is highly correlated

to the order of the centrality from the original network, the centrality estimates can be considered stable [39]. Stability analyses were conducted using the R package 'bootnet' [39].

To test for changes in the relationships between internalizing and externalizing disorders over time, structural invariance was examined using the 'Network Comparison Test' (NCT) package in R [40]. NCT tests the null hypothesis $A_1 = A_2$, where A_1 and A_2 are matrices containing the strengths of connections in two separate networks [40]. The NCT procedure involves non-parametric permutation testing and is conducted in three phases [40]. First the two networks in question are estimated and the maximum difference in edge strength between two given networks (*M*) is calculated and serves as the test statistic [40]. For the second step, cases are repeatedly randomly swapped between groups and the networks and test statistics re-estimated. Third, a reference distribution is created from these test statistics and statistical significance is determined, with the *p* value equal to the proportion of test statistics that have an equal or higher value than the observed test statistic [40].

Results

Descriptive statistics

Table 1 shows the frequencies and relative percentages of the disorders at the different time points. Across time, GAD was the most common disorder, followed by SPP. PTSD was the least endorsed disorder. Bivariate correlations between disorders are presented in the online supplementary materials (Table S1).

Association networks

The association networks, constructed separately at each time point, are presented in Fig. 1. Similar patterns of association were observed; two distinct clusters of nodes emerged, reflecting internalizing and externalizing disorders. Within the internalizing cluster, GAD was placed centrally and demonstrated moderate to strong associations with all other disorders. Within the externalizing cluster, thick edges indicated strong associations between ODD and ADHD at all three time points. Relationships between ADHD and CD, however, were comparatively weak. Indeed, ODD appeared to bridge the associations between CD and ADHD at the different time points.

GAD appeared to lie at the heart of the network as a whole, due to its central placing at all three time points. An inspection of the centrality indices (Fig. 2) corroborated this observation; across time GAD consistently scored highest on the measures of strength, closeness and betweenness. Within the externalizing cluster, ODD was the most central node

Table 1 Frequencies and relative percentages of measured indicators by assessment period

	7.5 years	10.5 years	14 years
SPP			
Present	209 (4.7%)	635 (14%)	446 (10.1%)
Absent	4196	3770	3959
SOP			
Present	162 (3.6%)	197 (4.5%)	236 (5.4%)
Absent	4243	4208	4169
PTSD			
Present	63 (1.4%)	100 (2.3%)	134 (3%)
Absent	4342	4305	4271
GAD			
Present	222 (5%)	514 (11.7%)	541 (12.3%)
Absent	4183	3891	3864
DEP			
Present	201 (4.5%)	412 (9.4%)	464 (10.5%)
Absent	4202	3993	3941
ADHD			
Present	230 (5.5%)	340 (7.7%)	441 (10%)
Absent	4175	4065	3964
ODD			
Present	163 (3.7%)	190 (4.3%)	245 (5.6%)
Absent	4242	4215	4160
CD			
Present	256 (5.8%)	184 (4.2)	230 (5.2%)
Absent	4242	4221	4175

SPP specific phobia, *SOP* social phobia, *PTSD* post-traumatic stress disorder, *GAD* generalized anxiety disorder, *DEP* major depression, *ADHD* attention deficit hyperactivity disorder, *ODD* oppositional/defiant disorder, *CD* conduct disorder

at ages 10.5 and 14 years, whereas ADHD demonstrated greater betweenness and closeness at age 7.5 years. Cross-cluster associations were common, although generally of smaller magnitude compared to the within-cluster associations. The most consistent bridging edge was DEP-ODD, which consistently appeared within the 10 strongest edges (Fig S1). The edge GAD-ADHD was also significant at each time point. Other edges were less consistent. For example, the edge SOP-ADHD was moderately strong at ages 10.5 and 14 years, but non-significant at age 7.5.

The bootstrapped 95% confidence intervals for the edges are presented in the online supplementary materials (Fig S1). Although there was considerable overlap among the CIs, the strongest edges demonstrated little overlap, suggesting statistically significant differences in the strengths of these associations. As such, the networks were moderately accurately estimated, and the order of the edge weights in each of the three networks can be interpreted with some degree of confidence [48]. The results from the subsetting bootstrap method are presented in the online supplementary
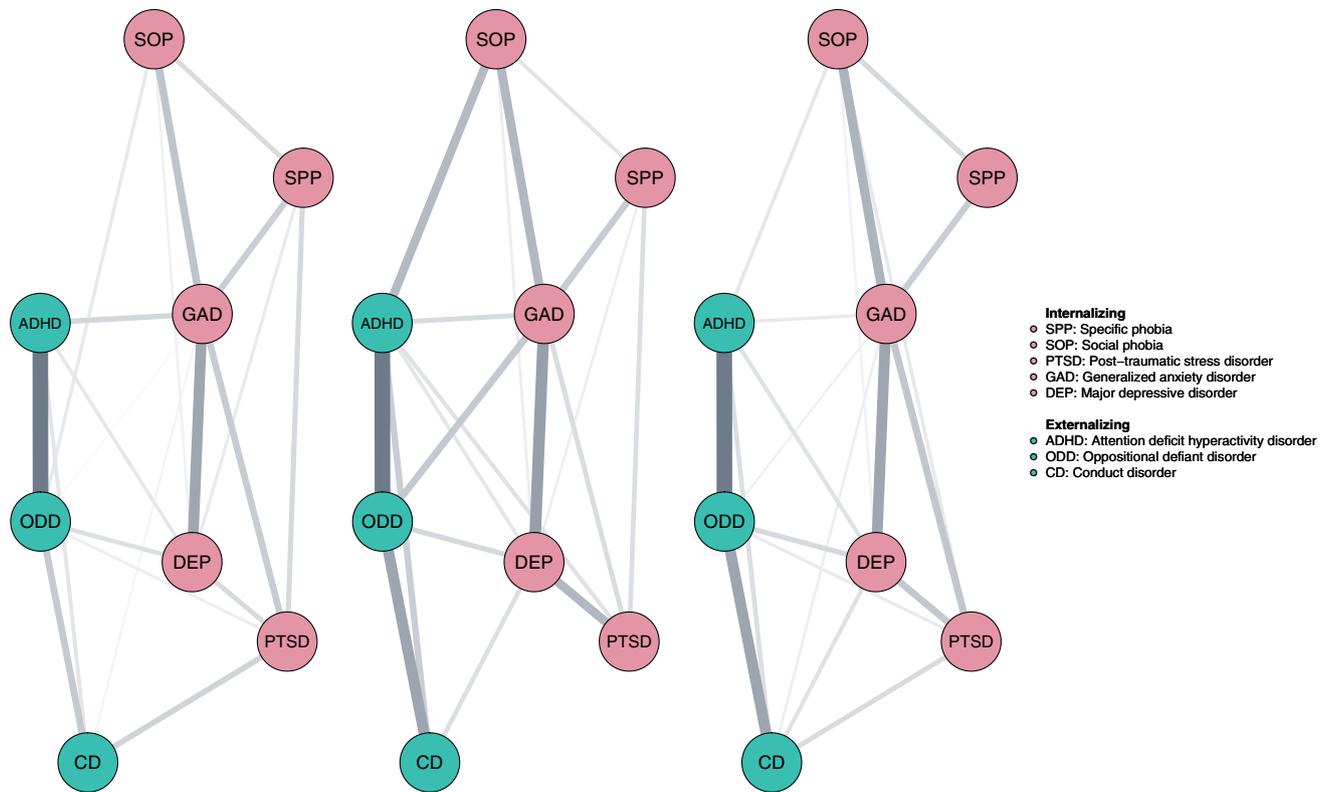
Fig. 1 Association networks at ages 7.5, 10.5, and 14 years. Line thickness denotes strength of association. All edges are positive

materials (Fig S2). Overall, the network centrality indices appeared highly stable; the correlations between the measures of centrality using the full sample and a subset of 30% ranged from approximately 0.5–0.85. This indicates that, even when 70% of the sample were randomly removed, the order of the centrality indices remained stable, suggesting a robust estimation of centrality. Overall, strength was the most stable of the three indices, and betweenness the weakest.

With regard to structural invariance, after applying a Bonferroni adjustment to account for multiple testing, the non-parametric permutation tests found no significant difference in overall network structure (Fig S3). As such, the network structure was considered broadly stable over time.

Discussion

The present study sought to examine the network structure of internalizing and externalizing disorders assessed between middle childhood and early adolescence. To our knowledge, this is the first study to take a network approach to the modelling of internalizing and externalizing at the disorder level. Furthermore, this is the first study to apply

network techniques to a cohort of children assessed from middle childhood through adolescence. A coherent network structure was identified at three time points (age 7.5, 10.5 and 14 years), and tests of structural invariance indicated that the networks remained generally stable, despite the many biological, cognitive and social changes that typically occur over this developmental period. As predicted, two regions of clustered nodes emerged, reflecting strong associations between internalizing disorders, and externalizing disorders. These clusters were most strongly bridged via the edges GAD-ADHD, and DEP-ODD. The centrality indices indicated that GAD and ODD were most important to the networks as a whole. An examination of the robustness of the centrality indices suggested that they could be interpreted with a degree of confidence.

Internalizing and externalizing as networks

Borsboom and colleagues [41] suggested that, if modelled using network techniques, traditional hierarchical measurement models of psychopathology would be reflected in clusters of highly associated nodes, analogous to the higher order dimensions of internalizing and externalizing. The findings of the present study support this claim. While

Fig. 2 Centrality statistics for association networks at the three time points. *SPP* specific phobia, *SOP* social phobia, *PTSD* post-traumatic stress disorder, *GAD* generalized anxiety disorder, *DEP* major depression, *ADHD* attention deficit hyperactivity disorder, *ODD* oppositional defiant disorder, *CD* conduct disorder. Centrality values (*y* axis) presented as *z*-scores

this finding may not be surprising (both network and latent variable models are derived from covariance), it offers a different interpretation of psychiatric comorbidity. This perspective suggests that, rather than a single causal factor (or amalgam of causal factors) driving the association between symptoms/disorders, causal factors spread their effects throughout psychopathological networks via local interactions and reinforcement. In other words, higher order dimensions (e.g. p) may be capturing a plethora of local-level interactions. Under this interpretation, the dimensions of internalizing and externalizing are correlated due to certain disorders (which themselves are comprised of networks of associated symptoms) acting as 'bridges' between these two broad spectra.

The nature of these interactions (i.e. edges), however, is far from clear and serves to further emphasise the complexity of psychiatric comorbidity. Given that the analysed data were cross-sectional (within-time points), a significant edge could represent a multitude of possible relationships. First, it is possible that disorders directly influence each other. For example, there is a long history of research looking at the comorbid anxiety and depression, with evidence suggesting that anxiety tends to precede and lead to subsequent depression [42]. One proposed mechanism for such a relationship is that cognitive/neurophysiological processes (e.g. sustained heightened physiological arousal) may lead to an exhaustion of the body which manifests as depression [43]. Other edges may reflect more indirect associations, e.g. the edges ODD-DEP and ADHD-GAD in the current networks. Developmental cascade models have long suggested that externalizing behaviour may indirectly lead to internalizing problems through mediating variables [44–46]. To illustrate, frequent disruptive behaviour in childhood/adolescence may lead to negative reactions from parents, teachers and/or peers, e.g. shouting, punishment, ostracisation from peer group, and/or academic failure. Such negative outcomes may in turn foster feelings of irritability, distress and worthlessness within the child, and if left unchecked, these experiences may eventually progress to levels of clinical significance [45, 46]. Edges in any given network may also represent spurious associations due to an unmeasured common cause. For example, shared biological (e.g. genes) or environmental (e.g. trauma) risk factors may influence the development of multiple symptom domains simultaneously [42]. If these risk factors are not represented in a given network, this may give rise to non-causal associations between disorders. Edges are further complicated by the possibility of bidirectional feedback loops, equifinality (multiple risk factors, pathways and processes leading to similar outcomes), and multifinality (specific risk factors leading to multiple outcomes) [47].

Given that the networks in the present study were undirected and cross-sectional, any causal interpretations, such as those described above, are purely speculative. The aim of the present study, however, was not to infer strict causal relationships but to demonstrate how network analysis can be used to quantify the importance of disorders and identify key associations between disorder pairs and as such generate hypotheses regarding the complex mechanisms that drive psychiatric comorbidity. For example, in the present study, GAD and ODD were identified as the two most influential nodes within wider comorbidity networks, suggesting that symptoms within these disorders may be influential in the initiation and/or maintenance of comorbid psychopathology. Furthermore, a number of significant edges bridged the spectra of internalizing and externalizing, the strongest of which was the edge ODD-DEP. This suggests that local-level interactions between these two disorders may go some way to explaining the correlations between internalizing and externalizing when modelled as continuous dimensions [24].

Strengths and limitations of the present study

The main strength of the present study was the large sample size relative to the number of parameters estimated [49]. With regard to limitations, diagnostic data were not available for the participants at all three of the time points; therefore, a comprehensive recoding strategy was adopted. It must be noted, however, that the diagnostic algorithms used to create the quasi-diagnostic variables were based on skip patterns (i.e. those who did not endorse 'core' symptoms were scored as having no disorder, and subsequent distress and burden were not assessed). This likely introduces an element of bias to the data in favour of DSM scoring conventions. Similar bias likely affects all analyses that employ DSM skip structures.

Skip patterns are particularly problematic when using symptom-level data, as they introduce deterministic dependencies (i.e. secondary symptoms can only be endorsed if primary symptoms are first endorsed, thus artificially inflating correlations between these symptom pairs). However, this was not the case in the present study, as a diagnosis of one disorder was not dependent on the diagnosis of another disorder. Finally, any study that employs network analysis comes with the caveat that this approach is highly divisive. Indeed, this has been evidenced by a series of back-and-forth papers focussed on the replicability of networks [50–52]. A methodological critique of network analysis and/or traditional latent variable models is beyond the scope of this article (for recent reviews, see [13, 48, 50–52]); however, our findings do appear to support the replicability of psychopathological networks within a cohort of children and adolescents assessed repeatedly over a period of significant development.

Conclusion

In conclusion, the present study sought to model internalizing and externalizing disorders in childhood and adolescence as a series of networks. A consistent and relatively stable network structure emerged across time, in which nodes formed two clusters broadly reflecting internalizing and externalizing. The two domains appeared to be linked through numerous bridging edges, and generalized anxiety disorder (GAD) and oppositional defiant disorder (ODD) were the most influential nodes in the networks. These findings offer a plausible interpretation of the *p*-factor model of comorbidity; i.e. the correlations between internalizing and externalizing dimensions may be due to direct associations between symptoms and/or disorders.

Compliance with ethical standards

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