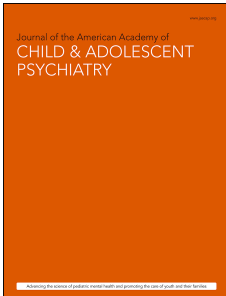


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The Centrality of Doubting and Checking in the Network Structure of Obsessive-Compulsive Symptom Dimensions in Youth

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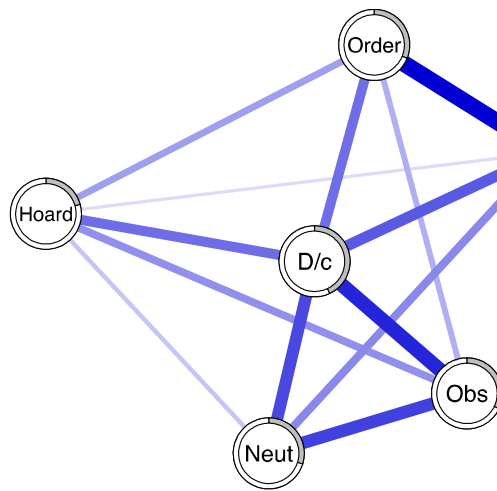
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Schoolchildren



Children with OCD

D/c: Doubting/checking
Obs: Obsessing
Wash: Washing
Hoard: Hoarding
Order: Ordering
Neut: Neutralizing

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RH = Network Structure of OCD in Children

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Editorial

Supplemental Material

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Abstract

Objective. Obsessive-compulsive disorder (OCD) is a heterogeneous condition with well-established symptom dimensions across the lifespan. The objective of the present study was to use network analysis to investigate the internal structure and central features of these dimensions in unselected schoolchildren and in youth with OCD.

Method. We estimated the network structure of OCD symptom dimensions in 6,991 schoolchildren and 704 youth diagnosed with OCD from 18 sites across six countries. All participants completed the Obsessive-Compulsive Inventory - Child Version.

Results. In both the school-based and clinic-based samples, the OCD dimensions formed an interconnected network with doubting/checking emerging as a highly central node, i.e. exerting strong influence over other symptom dimensions in the network. The centrality of the doubting/checking dimension was consistent across countries, genders, age groups, clinical status, and tic disorder comorbidity. Network differences were observed for age and gender in the school-based but not the clinic-based samples.

Conclusion. The centrality of doubting/checking in the network structure of childhood OCD adds to classic and recent conceptualizations of the disorder in which the important role of doubt in disorder severity and maintenance is highlighted. The present results suggest that doubting/checking is a potentially important target for further research into the etiology and treatment of childhood OCD.

Key words: obsessive-compulsive disorder, network analysis, dimensions, children, Obsessive Compulsive Inventory

Introduction

Recurrent and persistent distress-provoking thoughts, urges, or images (obsessions) and distress-reducing repetitive behavioral or mental acts (compulsions) are the cardinal diagnostic features of obsessive-compulsive disorder (OCD).¹ These symptoms can take on a multitude of forms, which pose challenges to both researchers and clinicians aiming to identify etiological and maintaining mechanisms in the disorder and more effective treatment approaches.² One approach to understanding and qualifying the heterogeneity of OCD is a multidimensional framework based on symptom dimensions related to: 1) Symmetry: symmetry obsessions and repeating, ordering, and counting compulsions; 2) Forbidden Thoughts: aggression, sexual, religious, and somatic obsessions and checking compulsions, 3) Cleaning: contamination obsessions and cleaning compulsions, and 4) Hoarding: hoarding obsessions and compulsions.^{2,3} These dimensions have been found to be fairly consistent across youth and adult patient samples, with some individual studies showing partially age-dependent structures.^{3,4} Research to establish the validity of these dimensions has primarily involved factor and principal component analytic studies³ and to a lesser extent studies examining the relationship between individual symptom dimensions and heritability^{5,6}, neural substrates^{7,8}, cognitive functioning⁹, comorbidity^{4,10}, and treatment outcome^{11,12}. Although hoarding disorder is now recognized as separate from OCD in DSM-5 and ICD-11, the differential diagnosis with OCD is still important as hoarding symptoms can be conceptualized as obsessions and compulsions in a minority of children and adults with OCD.^{13,14} Beyond the fact that youth with OCD tend to have symptoms within several dimensions¹⁵ and that the severity of scores on these dimensions tend to correlate with each other in the moderate to strong range¹⁶, little is known about the interrelatedness of symptom dimensions in OCD.

Network theory, as applied to psychopathology, asserts that the co-occurrence of symptoms or symptom dimensions from within a disorder (or from different disorders) may arise in part because there are causal relationships between the different symptoms, with individual symptoms having their own unique mechanisms of interaction (biological, psychological, and social) with other symptoms, and with the resultant symptom-to-symptom relationships forming a dynamic, interrelated network structure.¹⁷ Statistical techniques have been developed to explore the structure and internal dynamic of such networks.¹⁸ Within this analytical framework, a psychological network consists of *nodes* and *edges*. Nodes represent variables of interest – for example symptoms, symptom dimensions, cognitive functions, or behavioral patterns – and edges the unique statistical relationships between these nodes when all other relations in the network have been accounted for. Specifically, a regularized partial correlation network is estimated and the specific impact of different nodes is inferred.¹⁸ With these techniques, central nodes within a network, assumed to play a role as strong drivers of the whole network, are identified and can be used to inform assessment strategies, treatments, and the identification of early warning signs across diverse forms of psychopathology.¹⁷

Recent work employing the network perspective has helped identify the network structures of depression and anxiety¹⁹, schizotypal traits²⁰, and posttraumatic stress disorder²¹. Regarding OCD, four network analyses have been carried out. Ruzzano, Borsboom, Geurts²² explored the associations between OCD and autism-related restricted and repetitive behaviors in a group of 213 children with neurodevelopmental disorders. The authors found, by using a series of network analyses, that OCD and autism were distinct syndromes linked together by unusual sensory interests. McNally, Mair, Mugno, Riemann²³ used a network approach to explore the associations between OCD and depression in 408 adults with OCD. The two disorders were connected through depressive sadness and distress arising from obsessions and compulsions. In the only network analysis of youth with OCD (N=87), OCD and depression

were found to form distinct symptom networks connected through obsessive symptoms and depression-related sadness, guilt, and concentration problems.²⁴ In the fourth study, the items of the Revised Children's Anxiety and Depression Scale were analyzed using network techniques in a large sample of treatment-seeking children, and the six OCD items of the scale formed into two clusters: a compulsion-related cluster and a separate obsession-related cluster that was strongly linked to general anxiety.²⁵

Although informative, these studies did not examine the relationship among the broader symptom dimensions of OCD; the present study aimed to help fill this gap in the literature. Our study had three aims. First, we aimed to estimate the network structure of OCD symptom dimensions in two large multi-national samples of unselected schoolchildren and young people diagnosed with OCD. Given the paucity of network research on OCD, the present study was intended to be exploratory in nature, i.e. with no a priori assumptions about which symptom dimension might act as central nodes or about the relationships between the dimensions. This assumption-free approach meshes well with the data-driven statistical techniques used in network analysis.¹⁸ Second, we aimed to explore possible network differences related to gender, age, country of origin, and clinical status. Third, based on evidence that the symptom profile and treatment responsiveness of youth who meet diagnostic criteria for OCD and tic disorders may differ from those with OCD alone^{26,27}, we aimed to compare the OCD symptom dimension networks in OCD sufferers with and without a history of tic disorder.

Method

Participants

Participants were previously recruited to various studies of OCD. The Obsessive-Compulsive Inventory-Childhood Version (OCI-CV) was administered to 6,991 schoolchildren in Chile,

Italy, Spain, and Turkey, and to 704 children and adolescents with a diagnosis of OCD from Italy, Spain, Sweden, and the USA. Table 1 summarizes the sociodemographic and clinical characteristics of the participants by country and place of recruitment (schools versus clinics). All data were collected as part of research projects that were approved by regional ethics committees and in accordance with the World Medical Association's Declaration of Helsinki on medical research involving human participants. Detailed characteristics of each of the samples have been reported in previous publications.²⁸⁻³⁵

Insert Table 1 Around Here

Measures

Obsessive Compulsive Inventory – Child Version (OCI-CV; Foa et al., 2010). The OCI-CV is a 21-item self-report measure of OCD symptoms over the past month; each item is rated on a 3-point frequency scale (0 = *Never* to 2 = *Always*). The measure yields scores on six symptom dimensions that are broadly consistent with the most accepted symptom structure of the disorder: (1) doubting/checking; (2) obsessing; (3) hoarding; (4) washing; (5) ordering; and (6) neutralizing (counting/repeating). The OCI-CV has demonstrated good psychometric properties in both school and clinic-based samples of children and adolescents.^{16,28,29,31-34} The six symptom dimensions obtained in the original validation study¹⁶ have been largely replicated in one other clinical sample²⁸ and in five school-based samples^{29,31-34}. Means and standard deviations and internal consistency coefficients (Cronbach's and ordinal alpha) for the OCI-CV dimension scores are presented in Table S1 and Table S2, available online. The internal consistency coefficients were generally higher in the clinic- than in the school-based sample with coefficients in both samples overall being in the adequate range.

In the clinical samples, the diagnosis of OCD was established using structured diagnostic interviews, either the Kiddie Schedule for Affective Disorders and Schizophrenia or the Mini International Neuropsychiatric Interview for Children and Adolescents.^{36,37} OCD severity was assessed via interview using the 10-item, Children's Yale-Brown Obsessive Compulsive Scale.³⁸ The CY-BOCS assesses time, distress, impairment, resistance, and control related to obsessions and compulsions, resulting in a total severity score of 0 to 40. The means and standard deviations for the CY-BOCS for the clinical samples (by country) are reported in Table 1. Information about tic disorders was available for 543 of the clinic-based participants, of whom 156 (29%) had a lifetime history of tic disorder. Presence/absence of lifetime history of tic disorder was established using the structured diagnostic interviews listed above.

Statistical Analyses

Model fit, network estimation and network inference

Prior to undertaking the network analyses, the model fit of the OCI-CV dimension structure proposed in the original validation study¹⁶ was investigated in the school- and clinic-based samples via confirmatory factor analyses using the R-package *lavaan*. Missing data was handled through full information maximum likelihood estimation.

Network analyses were carried out using the R-package *bootnet* which estimates the regularized partial correlation networks among the study variables. Before analyzing the network structure of the OCD symptom dimensions, we estimated the network structure of the 21 individual symptom items from the OCI-CV separately for the school- and clinic-based samples. When estimating the individual symptom networks, listwise deletion was used and the estimations were based on 6666 school-based (4.6% omitted) and 683 clinic-based (3.0%

omitted) participants. When estimating the dimension networks, we imputed missing data separately for each subsample using an expectation-maximization algorithm before computing the dimension scores. Predictability, which refers to the degree to which a specific node value can be predicted by other nodes in the network³⁹, was calculated using the R-package *mgm* and graphically displayed as a circle surrounding the node. Predictability estimates in the symptom networks were based on categorically coded items (individual symptoms) while continuously coded scores (sum scores) were used when estimating predictability in the symptom dimension networks. The centrality of each node was estimated using three different metrics: node strength, closeness, and betweenness.⁴⁰ Node strength estimates the degree to which a node is directly connected with other nodes in the network. Closeness estimates the degree to which a node is indirectly connected to other nodes in the network. Betweenness estimates how important a node is in connecting other nodes in the network. Z-standardized centrality estimates are presented throughout. Raw estimates for the school- and clinic-based dimension networks can be found in Figure S1, available online.

Network robustness

Edge-weight accuracy was explored by running 1,000 bootstraps to produce 95% confidence intervals for all edges in the symptom dimension networks. We explored the stability of the centrality estimates by estimating the *correlation stability coefficient* (CS-coefficient); a metric that describes the proportion of the total number of cases that can be excluded before a correlation of $\geq .70$ between the original network and the new network (estimated only on non-excluded cases) is violated.⁴⁰ The maximum value for a CS-coefficient is 0.75, with coefficients > 0.50 indicative of network robustness.⁴⁰

Network comparisons

All network comparisons were carried out using permutation techniques with the R-package *NetworkComparisonTest*. First, networks were compared on overall network structure. If differences in structure were present, specific edge-weight differences were examined using a Holm-Bonferroni correction for multiple comparisons. Networks were also compared on overall network connectivity, i.e. the sum of all edge values in the network. A total of 12 comparisons were carried out and to control for the familywise error, we used a Bonferroni correction resulting in an alpha level of .004. We used 5,000 permutations for each estimation.

Results

Model fit and symptom network

Detailed results of the confirmatory factor analysis for the six original OCI-CV symptom dimensions¹⁶ are presented in the Table S3, available online. Briefly, the six-factor model provided a good fit to the OCI-CV data in both the school- and clinic-based samples. The observed network structure of the individual OCD symptoms, estimated for the school- and clinic-based samples separately (Figure 1 a and b), provided further evidence of the validity of the six-dimension structure of the original OCI-CV (detailed information about these networks can be found in Figure S2 and Table S4, available online).

Dimension networks

The OCD symptom dimension networks for the school- and clinic-based samples are depicted in Figure 1 (c and d). For the schoolchildren, the mean predictability of all nodes in the network was 0.313, indicating that 31.3% of the variance in nodes (dimensions) could be accounted for by variance in the other network nodes. The doubting/checking dimension had

the highest predictability score (0.431), followed by obsessing (0.321), ordering (0.311), washing (0.310), neutralizing (0.299), and hoarding (0.208). In the clinic-based samples, the dimension network had a mean predictability of 0.210. Again, the doubting/checking node had the highest predictability score (0.369), followed by ordering (0.242), neutralizing (0.236), obsessing (0.195), hoarding (0.138), and washing (0.082).

Insert Figure 1 Around Here

Centrality measures for the OCD symptom dimension networks are presented separately for the school- and clinic-based samples in Figure 2. For both the school- and clinic-based samples, doubting/checking was by far the most central symptom dimension according to all three centrality measures. The centrality of doubting/checking held true for all estimated networks in the study as represented by the predictability estimates across the school-based subsamples (Table 2). Obsessing and neutralizing, as well as hoarding and ordering, were interconnected in the dimension networks in both the school- and clinic-based samples.

Given the apparently central role played by doubting/checking in the networks, we carried out correlational analyses between the predictability estimates and the standardized standard deviations for the individual symptom dimensions separately for the school- and clinic-based samples to investigate whether the centrality estimates were dependent on differential variability of the symptom dimensions. The observed correlations ($r = -.33$ in the school-based samples; $r = -.56$ in the clinic-based samples) suggest that the centrality of doubting/checking was not dependent on larger variation within that particular symptom dimension.

Insert Figure 2 Around Here

Insert Table 2 Around Here

Network robustness

The robustness metrics for the symptom dimension networks in the school-based and clinic-based samples were excellent. Edge-weight accuracy was high, as indicated by the narrow 95% confidence intervals around the estimates. The maximum possible CS-coefficient of 0.75 was obtained for node strength, closeness, and betweenness in the school-based dimension network. In the clinic-based samples, the CS-coefficient for node strength was equally high (0.75), while the CS-coefficients for betweenness and closeness were both 0.67. Thus, the observed network estimates for the OCD symptom dimension networks in both the school- and clinic-based samples were very robust. See Figures S3 and S4, available online, for graphical descriptions of the robustness metrics.

Network comparisons

School-based versus clinic-based samples. The network structure of the OCD symptom dimensions differed between the school- versus clinic-based samples for overall network structure ($M = .26$; $\hat{p} < .001$; \hat{p} is hereafter used for all p-values estimated through permutation). Post hoc tests revealed that there were four statistically significant edge-weight differences between the two networks: washing was more strongly connected to ordering ($\hat{p} < .001$) and neutralizing ($\hat{p} < .001$) and obsessing to hoarding ($\hat{p} < .01$) in the school-based samples; and ordering more strongly connected to neutralizing ($\hat{p} < .01$) in the clinic-based samples. Compared to the clinic-based samples, the network structure in the school-based samples had a higher degree of overall connectivity ($S = .58$; $\hat{p} < .001$). Because unequal sample sizes can affect network comparisons⁴¹, we carried out a sensitivity analysis where

we randomly selected an equally sized sample of school-based participants. The results were very similar (network structure: $M = .25$; $\hat{p} < .001$; overall connectivity: $S = .48$; $\hat{p} < .001$) and are reported in detail in Supplement 1, available online.

Younger children versus adolescents; Girls versus boys. Using data from the school-based samples, children (< 13 years) differed from adolescents (> 12 years) in their overall network structure ($M = .12$; $\hat{p} < .001$), with three statistically significant edge weight differences: neutralizing was more strongly connected to obsessing ($\hat{p} < .001$) and washing ($\hat{p} < .01$) and less strongly connected to ordering ($\hat{p} < .01$) for adolescents than for children. The network for adolescents was also more strongly interconnected than the network for children ($S = .40$; $\hat{p} < .001$). No age-related differences were found for network connectivity ($\hat{p} = .47$) or network structure ($\hat{p} = .55$) in the clinic-based samples.

In the school-based samples, the dimension networks of girls and boys did not differ for overall network connectivity ($S = .05$; $\hat{p} = .10$), nor for overall network structure using our Bonferroni corrected alpha level ($M = .08$; $\hat{p} = .01$). In the clinic-based samples, no differences were observed between boys and girls for overall network connectivity ($\hat{p} = .90$) or network structure ($\hat{p} = .98$). Means and standard deviations for girls and boys and younger and older children, respectively, can be found in Table S1, available online. Further, detailed information about these networks can be found in Figure S5, also available online.

Country by country differences. In Tables S5 and S6, available online, country-to-country differences for network structure and connectivity are presented, and in Figure S6, also available online, centrality estimates for all countries are presented. Overall, few differences emerged with the exception that the Turkish sample had a more strongly interconnected network with stronger edge weights. As the mean age of the participants in the Turkish sample was higher than in the other country samples, we carried out the network comparisons again but included age when estimating the networks, and the differences in

overall network connectivity between countries disappeared. However, differences in network structure remained largely unchanged. Additional post-hoc analyses of overall network estimates with and without Turkish participants only revealed small differences. Results of the post hoc country comparisons that included age and for estimates with and without Turkish participants can be found in Table S7, Table S8, and Supplement 2, available online.

OCD participants with and without a lifetime history of tic disorder. No significant differences were observed in the symptom dimension network structures of OCD sufferers (clinic-based samples only) with versus without a lifetime history of tic disorder ($M = .12$, $\hat{p} = .82$; $S = .04$, $\hat{p} = .91$).

Discussion

The symptoms of OCD are highly heterogeneous but can be categorized within well-established symptom dimensions. By applying a network analytical approach to these dimensions in two large multinational samples of children and adolescents recruited from schools and OCD clinics, a robust network structure was observed wherein doubting and checking played a strong central role in relation to all other symptom dimensions. This result was replicated across nationalities, genders, ages, and school- and clinic-based samples. From a network perspective⁴², this finding suggests that doubting and checking (or the processes that underpin these symptoms) may play a particularly important role in the development and/or maintenance of other OCD symptom dimensions in children and adolescents.

Doubt has played an important, if not central, role in classic descriptions of OCD dating back more than 100 years. Building on 19th century conceptualizations of OCD as the insanity of doubt (e.g., Legrand du Saullé's *folie du dout avec delire du toucher*), Pierre Janet described the symptoms of OCD as being motivated by an inner sense of imperfection or more precisely *incompleteness* (*les sentiments d'incomplétude*), which flowed from a

perception that one's actions had not been completed in a satisfactory way⁴³. This aspect of Janet's description of OCD is supported by contemporary investigations that find incompleteness to be an important motivational factor in OCD.⁴⁴ Szechtman, Woody⁴⁵ defined OCD as a disorder of security motivation, wherein a recurrent inability to reach a completion signal (e.g., a feeling of just knowing) prevents termination of an underlying security motivation system, which in turn activates obsessions and compulsions. More recently, Lazarov, Liberman, Hermesh, Dar⁴⁶ have argued that the pathological doubt in OCD arises from a diminished capacity to assess one's own internal states which leads to an overreliance on external proxies, including highly idiosyncratic rules and rituals, thereby producing the heterogeneous symptom picture common in OCD. In a similar vein, Nestadt, Kamath, Maher, Krasnow, Nestadt, Wang, Bakker, Samuels⁴⁷ proposed that the doubt, uncertainty and lack of confidence that is at the core of OCD, reflects underlying neurocognitive deficits that make it difficult for the individual to integrate information to reach a decision, which in turn leads to compulsive behaviors. By contrast, Gangemi, Mancini, Dar⁴⁸ argue that pathological doubt in OCD is not dependent on information gathering processes but instead reflects a fundamental distrust in information obtained through the senses in favor of hypothesized possibilities that negate the value of sensory information. The above is not meant to be an exhaustive review of theoretical models of OCD, rather an illustration of the importance that pathological doubt (and the checking behavior that typically results from it) has had in diverse conceptualizations of OCD across the years.

Aside from the shared centrality of doubting/checking in the symptom dimension network of OCD, some differences between the clinic- and school-based networks emerged. In the clinic-based network, washing was the least interconnected node with edges appearing only in relation to doubting/checking and ordering, while in the school-based network

washing was connected to multiple nodes. Further, in the clinic-based network, ordering and neutralizing were strongly interconnected while only a weak connection between these nodes was found in the school-based network. The reasons for these differences and their significance are currently unclear but may provide interesting clues on how OCD symptoms, which are dimensional in nature (cf. categorical), and therefore present in various degrees in the general population, can become pathological in some individuals. The individual symptom items of the OCI-CV subscale of doubting/checking were much more strongly interconnected in the clinic- versus school-based samples. While the reasons for this are unclear, it may be that pathology emerges when doubting becomes paired with a physical act (e.g., checking), which in turn can give rise to the pathological levels of doubt often seen in OCD. Future studies may want to separate the constructs of doubting and checking to better understand their respective influence on OCD. In general, the symptom dimensions were more strongly interconnected in the school- than in the clinic-based samples, a finding that is in line with numerous other network studies showing higher connectivity in non-clinical versus clinical samples.⁴⁹

The present study included children from a very wide age range and it is important to address results which might suggest any apparent age-related or developmental processes. Overall, the network structure, including the centrality of doubting/checking, was stable and robust in pre-pubertal and adolescent participants and regardless of sample source (school versus clinics). However, some significant differences emerged when comparing older and younger children in the school-based samples with the network of older children being more interconnected. Perhaps, with advancing age, some symptom dimensions, predominantly doubting/checking, begin to exert a wider influence on other aspects of behavior leading to the development of more varied symptoms within the network. Developmental differences related to clinical OCD have emerged in previous research⁵⁰, however, such differences have

been found mostly in child versus adult comparisons. In the present study, only youth were included which might explain the network consistencies across age in the clinic-based sample.

Despite the evidence of a tic-related subgroup within childhood OCD²⁶, we found no network differences between children with and without a lifetime history of tic disorder in the clinic-based samples. If replicated, these findings suggest that the centrality of doubting and checking in OCD is independent of tic-related status. This would suggest that successful treatment of symptoms within this central, doubting/checking dimension should result in similar levels of improvement in patients with OCD with and without comorbid tics; a suggestion consistent with the similar effects of exposure plus response prevention in these groups.²⁶ Similarly, it is reasonable to ask whether changes in doubting and checking might be necessary to improvement in all OCD symptoms in children and adolescents with the disorder, and the lack of such changes may help explain partial and non-responses to evidence-based OCD treatments. This remains an open question because studies evaluating the influence of OCD symptom dimensions on treatment outcome have relied upon the adult and childhood versions of the Y-BOCS checklist, which mainly covers topographical aspects of symptoms; because doubt can be associated with a number of obsessions and compulsions across symptom dimensions, the use of Y-BOCS may not be ideally suited for the examination of the relation between doubt and treatment outcome. Given the central role played by doubt in the present study, there is a need for future studies investigating its role in the treatment of OCD and also the development of doubt-specific measures.

Finally, hoarding was the least influential node in the school-based network, providing further empirical support for Hoarding Disorder as a diagnosis separate from OCD in DSM-5. Nevertheless, the same pattern was not as pronounced in the clinic-based network, in which washing (not hoarding) was the least interconnected node, with its only substantial edge emerging in relation to doubting/checking. There is some evidence that adult patients with

contamination symptoms differ from other patient groups with OCD in their basic cognitive functioning⁵¹ and neural substrates⁸. The present study suggests that more research is needed to delineate possible differences in etiology and clinical correlates of patients with washing/contamination symptoms.

There are several limitations that need to be taken into account. First, all analyses were based on a single self-report measure that overlaps but does not perfectly correspond to the symptom dimensions established with the Y-BOCS/CY-BOCS symptom checklist; for example, the OCI-CV yields dimensional scores in contrast to the binary scoring of the CY-BOCS and some of its symptom dimensions (e.g., doubting/checking and neutralizing) tap into potentially functional aspects of OCD that cut across several of the traditional symptom dimensions based on the CY-BOCS. Future studies are needed to examine to what extent the current results are measure-dependent. Specifically, given that most work on OCD symptom structure has been based on the CY-BOCS, network analyses using CY-BOCS data are warranted. Second, all network estimations were performed on cross-sectional data and longitudinal/experimental research is needed to directly address questions about causality. Third, a number of statistically significant differences emerged between subgroups of children in the school-based sample regarding network connectivity and structure (i.e., younger versus older children, boys versus girls). However, it is unclear from our results whether these differences are meaningful in regard to the clinical aspects of OCD. Finally, the school-based samples were primarily recruited from southern/southeastern Europe and South America while the clinical samples were primarily recruited from northern Europe and USA. Thus, the differences found between the clinic- and school-based samples may also partly reflect cultural differences.

In sum, doubting/checking clearly emerged as a central dimension across all clinical and non-clinical networks. The present study adds to the OCD literature by suggesting that

doubting/checking is a potentially important target for further research into the etiology and treatment of childhood OCD. Longitudinal studies involving both clinical samples and at-risk youth are needed to determine if this symptom dimension constitutes a vulnerability factor for symptom development and relapse. In a similar vein, it will be important to examine the network structure of OCD symptoms and symptom dimensions in adults. If doubting/checking is a central node in the network of adults, this would lend further support to the notion that this aspect of OCD is central to the development and persistence of the disorder. If other symptom dimensions emerge as central nodes in adults, this may suggest variation in maintaining mechanisms across the lifespan with further implications for treatment.

References

1. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 5th ed. Washington, DC2013.
2. Mataix-Cols D, Rosario-Campos MC, Leckman JF. A multidimensional model of obsessive-compulsive disorder. *The American journal of psychiatry*. 2005;162(2):228-238.
3. Bloch MH, Landeros-Weisenberger A, Rosario MC, Pittenger C, Leckman JF. Meta-analysis of the symptom structure of obsessive-compulsive disorder. *American Journal of Psychiatry*. 2008;165(12):1532-1542.
4. Hojgaard DR, Mortensen EL, Ivarsson T, et al. Structure and clinical correlates of obsessive-compulsive symptoms in a large sample of children and adolescents: a factor analytic study across five nations. *European child & adolescent psychiatry*. 2016.

5. Iervolino AC, Rijdsdijk FV, Cherkas L, Fullana MA, Mataix-Cols D. A multivariate twin study of obsessive-compulsive symptom dimensions. *Archives of general psychiatry*. 2011;68(6):637-644.
6. Lopez-Sola C, Fontenelle LF, Verhulst B, et al. Distinct Etiological Influences on Obsessive-Compulsive Symptom Dimensions: A Multivariate Twin Study. *Depression and anxiety*. 2016;33(3):179-191.
7. Mataix-Cols D, Wooderson S, Lawrence N, Brammer MJ, Speckens A, Phillips ML. Distinct neural correlates of washing, checking, and hoarding symptom dimensions in obsessive-compulsive disorder. *Archives of general psychiatry*. 2004;61(6):564-576.
8. van den Heuvel OA, Remijnse PL, Mataix-Cols D, et al. The major symptom dimensions of obsessive-compulsive disorder are mediated by partially distinct neural systems. *Brain*. 2009;132(Pt 4):853-868.
9. Bragdon LB, Gibb BE, Coles ME. Does neuropsychological performance in OCD relate to different symptoms? A meta-analysis comparing the symmetry and obsessing dimensions. *Depression and anxiety*. 2018.
10. Hasler G, LaSalle-Ricci VH, Ronquillo JG, et al. Obsessive-compulsive disorder symptom dimensions show specific relationships to psychiatric comorbidity. *Psychiatry research*. 2005;135(2):121-132.
11. Mataix-Cols D, Marks IM, Greist JH, Kobak KA, Baer L. Obsessive-compulsive symptom dimensions as predictors of compliance with and response to behaviour therapy: results from a controlled trial. *Psychother Psychosom*. 2002;71(5):255-262.
12. Mataix-Cols D, Rauch SL, Manzo PA, Jenike MA, Baer L. Use of factor-analyzed symptom dimensions to predict outcome with serotonin reuptake inhibitors and placebo in the treatment of obsessive-compulsive disorder. *American Journal of Psychiatry*. 1999;156(9):1409-1416.

13. Pertusa A, Frost RO, Mataix-Cols D. When hoarding is a symptom of OCD: A case series and implications for DSM-V. *Behaviour research and therapy*. 2010;48(10):1012-1020.
14. Storch EA, Muroff J, Lewin AB, et al. Development and preliminary psychometric evaluation of the Children's Saving Inventory. *Child Psychiatry & Human Development*. 2011;42(2):166-182.
15. Cervin M, Perrin S, Olsson E, Claesdotter-Knutsson E, Lindvall M. Validation of an interview-only version of the Dimensional Yale-Brown Obsessive-Compulsive Scale (DY-BOCS) in treatment-seeking youth with obsessive-compulsive disorder. *Psychiatry research*. 2019;271:171-177.
16. Foa EB, Coles M, Huppert JD, Pasupuleti RV, Franklin ME, March J. Development and validation of a child version of the obsessive compulsive inventory. *Behavior therapy*. 2010;41(1):121-132.
17. Borsboom D. A network theory of mental disorders. *World Psychiatry*. 2017;16(1):5-13.
18. Epskamp S, Fried EI. A tutorial on regularized partial correlation networks. *Psychological methods*. 2018.
19. Beard C, Millner AJ, Forgeard MJ, et al. Network analysis of depression and anxiety symptom relationships in a psychiatric sample. *Psychological medicine*. 2016;46(16):3359-3369.
20. Fonseca-Pedrero E, Ortuno J, Debbane M, et al. The Network Structure of Schizotypal Personality Traits. *Schizophr Bull*. 2018.
21. Fried EI, Eidhof MB, Palic S, et al. Replicability and Generalizability of Posttraumatic Stress Disorder (PTSD) Networks: A Cross-Cultural Multisite Study of PTSD

- Symptoms in Four Trauma Patient Samples. *Clinical psychological science : a journal of the Association for Psychological Science*. 2018;6(3):335-351.
22. Ruzzano L, Borsboom D, Geurts HM. Repetitive behaviors in autism and obsessive-compulsive disorder: new perspectives from a network analysis. *J Autism Dev Disord*. 2015;45(1):192-202.
23. McNally RJ, Mair P, Mugno B, Riemann B. Co-morbid obsessive-compulsive disorder and depression: a Bayesian network approach. *Psychological medicine*. 2017;47(7):1204-1214.
24. Jones PJ, Mair P, Riemann BC, Mugno BL, McNally RJ. A network perspective on comorbid depression in adolescents with obsessive-compulsive disorder. *Journal of anxiety disorders*. 2018;53:1-8.
25. McElroy E, Patalay P. In search of disorders: internalizing symptom networks in a large clinical sample. *Journal of Child Psychology and Psychiatry*. 2019.
26. Conelea CA, Walther MR, Freeman JB, et al. Tic-related obsessive-compulsive disorder (OCD): phenomenology and treatment outcome in the Pediatric OCD Treatment Study II. *Journal of the American Academy of Child and Adolescent Psychiatry*. 2014;53(12):1308-1316.
27. March JS, Franklin ME, Leonard H, et al. Tics moderate treatment outcome with sertraline but not cognitive-behavior therapy in pediatric obsessive-compulsive disorder. *Biological psychiatry*. 2007;61(3):344-347.
28. Jones AM, De Nadai AS, Arnold EB, et al. Psychometric properties of the obsessive compulsive inventory: child version in children and adolescents with obsessive-compulsive disorder. *Child psychiatry and human development*. 2013;44(1):137-151.

29. Martínez-González AE, Rodríguez-Jiménez T, Piqueras JA, Vera-Villarreal P, Godoy A. Psychometric Properties of the Obsessive-Compulsive Inventory-Child Version (OCI-CV) in Chilean Children and Adolescents. *PloS one*. 2015;10(8):e0136842.
30. Ortiz A, Morer A, Moreno E, Plana M, Cordovilla C, Lázaro L. Clinical significance of psychiatric comorbidity in children and adolescents with obsessive-compulsive disorder: subtyping a complex disorder. *European archives of psychiatry and clinical neuroscience*. 2016;266(3):199-208.
31. Pozza A, Barcaccia B, Dettore D. The Obsessive Compulsive Inventory-Child Version (OCI-CV): Further Evidence on Confirmatory Factor Analytic Structure, Incremental and Criterion Validity in Italian Community Children and Adolescents. *Archives of psychiatric nursing*. 2017;31(3):291-295.
32. Rodríguez-Jiménez T, Godoy A, Piqueras JA, Gavino A, Martínez-González AE, Foa EB. Factor structure and measurement invariance of the Obsessive-Compulsive Inventory-Child version (OCI-CV) in general population. *European Journal of Psychological Assessment*. 2017;33(2):97-103.
33. Rosa-Alcazar AI, Ruiz-Garcia B, Iniesta-Sepulveda M, Lopez-Pina JA, Rosa-Alcazar A, Parada-Navas JL. Obsessive Compulsive Inventory-Child Version (OCI-CV) in a Spanish community sample of children and adolescents. *Psicothema*. 2014;26(2):174-179.
34. Seçer İ. Obsesif kompulsif bozukluk ölçeği çocuk formunun Türkçeye uyarlanması: Güvenirlilik ve geçerlilik çalışması. *Eğitim ve Bilim*. 2014;39(176).
35. Storch EA, Merlo LJ, Bengtson M, et al. D-cycloserine does not enhance exposure-response prevention therapy in obsessive-compulsive disorder. *International clinical psychopharmacology*. 2007;22(4):230-237.

36. Kaufman J, Birmaher B, Brent D, et al. Schedule for affective disorders and schizophrenia for school-age children-present and lifetime version (K-SADS-PL): initial reliability and validity data. *Journal of the American Academy of Child & Adolescent Psychiatry*. 1997;36(7):980-988.
37. Sheehan DV, Sheehan KH, Shytle RD, et al. Reliability and validity of the Mini International Neuropsychiatric Interview for Children and Adolescents (MINI-KID). *The Journal of clinical psychiatry*. 2010;71(3):313-326.
38. Scahill L, Riddle MA, McSwiggin-Hardin M, et al. Children's Yale-Brown Obsessive Compulsive Scale: reliability and validity. *Journal of the American Academy of Child and Adolescent Psychiatry*. 1997;36(6):844-852.
39. Haslbeck JM, Waldorp LJ. How well do network models predict observations? On the importance of predictability in network models. *Behavior research methods*. 2018;50(2):853-861.
40. Epskamp S, Borsboom D, Fried EI. Estimating psychological networks and their accuracy: A tutorial paper. *Behavior Research Methods*. 2018;50(1):195-212.
41. Van Borkulo CD, Boschloo L, Kossakowski J, et al. Comparing network structures on three aspects: A permutation test. *Manuscript in preparation*. 2017.
42. Fried EI, van Borkulo CD, Cramer AO, Boschloo L, Schoevers RA, Borsboom D. Mental disorders as networks of problems: a review of recent insights. *Social Psychiatry and Psychiatric Epidemiology*. 2017;52(1):1-10.
43. Pitman RK. Janet's Obsessions and Psychasthenia: a synopsis. *Psychiatr Q*. 1984;56(4):291-314.
44. Pallanti S, Barnes J, Pittenger C, Eisen J. Incompleteness and harm avoidance in OCD. *Obsessive-compulsive Disorder: Phenomenology, Pathophysiology, and Treatment, NY: Oxford University Press, New York*. 2017.

45. Szechtman H, Woody E. Obsessive-compulsive disorder as a disturbance of security motivation. *Psychol Rev.* 2004;111(1):111-127.
46. Lazarov A, Liberman N, Hermesh H, Dar R. Seeking proxies for internal states in obsessive-compulsive disorder. *Journal of abnormal psychology.* 2014;123(4):695-704.
47. Nestadt G, Kamath V, Maher BS, et al. Doubt and the decision-making process in obsessive-compulsive disorder. *Medical hypotheses.* 2016;96:1-4.
48. Gangemi A, Mancini F, Dar R. An experimental re-examination of the inferential confusion hypothesis of obsessive-compulsive doubt. *Journal of behavior therapy and experimental psychiatry.* 2015;48:90-97.
49. Fried EI, van Borkulo CD, Epskamp S, Schoevers RA, Tuerlinckx F, Borsboom D. Measuring depression over time... Or not? Lack of unidimensionality and longitudinal measurement invariance in four common rating scales of depression. *Psychological Assessment.* 2016;28(11):1354.
50. Taylor S. Early versus late onset obsessive-compulsive disorder: evidence for distinct subtypes. *Clinical psychology review.* 2011;31(7):1083-1100.
51. Hashimoto N, Nakaaki S, Omori IM, et al. Distinct neuropsychological profiles of three major symptom dimensions in obsessive-compulsive disorder. *Psychiatry research.* 2011;187(1-2):166-173.

Table 1

Demographic and Clinical Characteristics of the School-Based and Clinic-Based Samples

	Age <i>M (SD)</i>	Girls (%)	Missing data (%)	CY-BOCS <i>M (SD)</i>
School samples				
Chile (<i>n</i> = 939)	14.77 (2.13)	38.1	0.00	-
Italy (<i>n</i> = 1959)	12.78 (3.02)	57.7	0.29	-
Spain (<i>n</i> = 3013)	13.72 (2.04)	48.6	0.38	-
Turkey (<i>n</i> = 1111)	15.26 (1.30)	45.5	0.31	-
Clinical samples				
Italy (<i>n</i> = 7)	14.29 (2.69)	14.3	0.00	-
Spain (<i>n</i> = 78)	15.07 (2.70)	50.0	0.00	21.73 (5.50)
Sweden (<i>n</i> = 432)	13.86 (2.53)	57.0	0.11	22.96 (4.48)
USA (<i>n</i> = 187)	12.26 (3.13)	46.0	0.92	24.61 (5.56)

Note. CY-BOCS = Children's Yale-Brown Obsessive-Compulsive Scale.

Table 2

Predictability Estimates Across School-Based Subsamples for the Obsessive-Compulsive Inventory - Child Version (OCI-CV) Symptom Dimensions

	<13 years	>12 years	Boys	Girls	Chile	Italy	Spain	Turkey
Doubting/checking	0.33	0.47	0.42	0.45	0.41	0.41	0.35	0.50
Obsessing	0.22	0.36	0.32	0.33	0.27	0.30	0.24	0.34
Washing	0.21	0.34	0.32	0.31	0.28	0.23	0.27	0.45
Hoarding	0.17	0.23	0.23	0.19	0.24	0.20	0.18	0.39
Ordering	0.25	0.33	0.32	0.30	0.34	0.30	0.27	0.35
Neutralizing	0.17	0.35	0.30	0.31	0.26	0.25	0.19	0.35

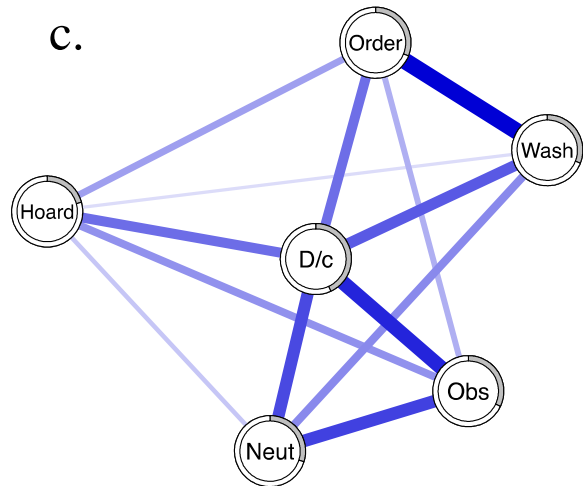
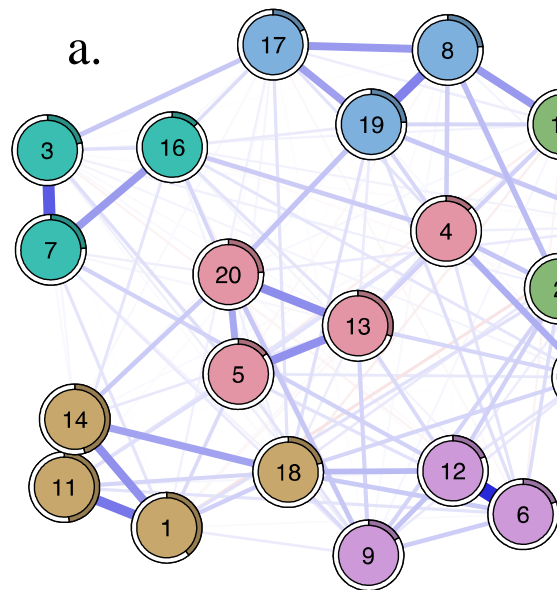
Note. OCD = Obsessive-compulsive disorder. OCI-CV = Obsessive Compulsive Inventory-Child Version.

Figure 1. Network Structure for School- and Clinic-Based Samples

Note: The individual (a) and factor-analysis derived (c) symptom network of schoolchildren and of children with obsessive-compulsive disorder (OCD) (b) and (d). Solid edges represent a positive interconnection, dashed edges a negative interconnection. The width of edges represents the strength of an edge. The node circle depicts predictability of that specific node.

Figure 2. Centrality Estimates for School- and Clinic-Based Dimension Networks

Note: Centrality estimates for the symptom dimension network of schoolchildren (a) and of children with obsessive-compulsive disorder (b).



Doubting/checking

- 4: Checking things
- 5: Doubting if I did things
- 13: Worry I didn't finish things
- 15: Checking doors, windows, etc.
- 20: Doubting if I did something right

Obsessing

- 1: Can't stop bad thoughts
- 11: Upset by bad thoughts
- 14: Upset by intrusive bad thoughts
- 18: Saying things in response to bad thoughts

Washing

- 2: Compulsive washing
- 10: Worry about cleanliness
- 21: Wash more than others

Hoarding

- 3: Collect things that get in the way
- 7: Collecting things I don't need
- 16: Difficulty discarding things

Ordering

- 8: Upset if things not in order
- 17: Upset if people move things
- 19: Need for order

D/c: Doubting/checking
 Obs: Obsessing
 Wash: Washing
 Hoard: Hoarding
 Order: Ordering
 Neut: Neutralizing

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