Symptom Network Analysis of Attention-Deficit/Hyperactivity Disorder and Emotional Symptoms in Adults:

Results From the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC)

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Abstract

Objective: The diagnosis of attention-deficit/hyperactivity disorder (ADHD) is based on a set of symptoms and 2 main dimensions (impulsive/hyperactive and attentional). While the relationships between ADHD symptoms and emotional dysregulation (ED) have been widely studied, the interactions between individual symptoms have rarely been examined. The purpose of this study was to assess which symptoms are most influential (central) and which symptoms connect (bridge) the 2 main dimensions of ADHD and ED.

Methods: Data from wave II (2004–2005) of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC-II) were utilized, which included a large, nationally representative sample of the US population (N = 33,546). Eighteen ADHD symptoms were examined based on *DSM-5-TR* criteria, along with 4 variables related to ED. Symptom network analyses were conducted to explore the relationships between ADHD and ED symptoms.

Results: The prevalence of ADHD was found to be 10.12% (N = 3,397). Among all ADHD and ED symptoms, ED symptoms had the lowest influence (centrality) values. In terms of bridging the 2 ADHD dimensions, 2 ED symptoms were among the 4 most influential.

Conclusions: The low centrality of ED symptoms supports the traditional focus on the 2 main dimensions of ADHD. However, the significant role of ED symptoms in connecting the impulsive/hyperactive and attentional dimensions highlights their importance within the ADHD framework. These findings have potential implications for the epidemiology, public health, research, and clinical understanding of ADHD.

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Attention-deficit/hyperactivity disorder (ADHD), the most common neurodevelopmental disorder in children, is a multifactorial and heterogeneous disorder.[1–3] It can persist into adulthood, with a global prevalence between 0.66% and 4.4%,[4–8] constituting an underdiagnosed and undertreated condition in this adult population.[9] Only 1 in 5 adults with ADHD is diagnosed and treated correctly.[4,10] In the *Diagnostic and Statistical Manual of Mental Disorders,* Fifth Edition, Text Revision (*DSM-5-TR*),[11] the diagnosis of ADHD is based on a set of core criteria distinguishing an impulsive/hyperactive and an inattention symptom cluster.[12]

A growing body of research has emphasized the importance of an emotional dimension as a major feature in ADHD in childhood, adolescence, and adulthood.[13–16] The prevalence of emotional dysregulation (ED) in adults with ADHD ranges between 34% and 70%.[17–19] ED is an individual's lack of ability to modify his/her emotional state to support adaptive, goal-oriented behaviors.[20] In recent decades, the potential integration of ED symptoms in the nosographic criteria of ADHD raised great debates.[21]

However, surprisingly, few studies have focused on the precise relationship between ED, inattention, and impulsive/hyperactive symptoms. Network analyses allow to present ADHD as a result of mutually reinforcing symptoms, possibly integrating ED symptoms (eg, sudden mood changes can lead to fidgeting or squirming; this discomfort can then cause a loss of emotional control, making it difficult to organize activities;

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Clinical Points

- Despite extensive research on attention-deficit/hyperactivity disorder (ADHD) and emotional dysregulation (ED), too little is known about the interactions between their constituent symptoms.
- ED symptoms play a significant role in connecting the core ADHD symptoms, particularly those related to the inattention dimension.

consequently, this disorganization can lead to interrupting or intruding on others, which may culminate in explosive anger).[22] Network analysis may suggest hypotheses about how symptoms interrelate and develop, eg, informing about possible causal patterns between inattentive, hyperactive, and emotional symptoms, helping target interventions. More precisely, ED symptoms could prove important in explaining the concomitant presence of the symptoms belonging to the 2 attentional and hyperactive/impulsive dimensions found in ADHD.[16,19,23,24]

Based on symptom network analysis, in a representative population sample, we hypothesize that, although the most central symptoms belong to the attentional and/or hyperactive/impulsive dimensions (ie, that define ADHD), ED symptoms would constitute bridge symptoms connecting the 2 core dimensions of this disorder.

METHODS

Data Analysis

We analyzed cross-sectional data from wave 2 of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC-II). The study protocol obtained full approval from the U.S. Census Bureau and the Office of Management and Budget (Supplementary Methods for details).[25–27]

Assessments

Sociodemographic and socioeconomic characteristics. Sociodemographic characteristics included sex, ethnicity, nativity, age category, and marital status. Socioeconomic characteristics included education, individual income, urbanicity, region of residence, and insurance type. The details of the characteristics of the sample are given in previous works and in Table 1.[28–32]

Diagnostic interview. The diagnostic interview was the Alcohol Use Disorder and Associated Disabilities Interview Schedule—*DSM-IV* Version (AUDADIS-IV)[33] Wave 2 version.[34] The AUDADIS-IV is a valid and reliable fully structured diagnostic interview designed for use by nonclinician's professional interviewers. In this study, we refer to the term *symptom* to designate a diagnostic criterion extracted from the NESARC.

ADHD symptoms. ADHD was assessed at Wave 2 of the NESARC based on *DSM-IV* symptom thresholds and evaluated with the AUDADIS-IV.[35] Twenty symptom items operationalized the 18 ADHD symptoms, with 9 separate questions for inattention and 9 for hyperactivity/impulsivity symptoms. Participants were considered to meet the symptom criteria for ADHD based on these evaluations.

ED symptoms. Second, we extracted 4 main symptoms related to ED. Questions came from the borderline and antisocial personality disorder modules of the AUDADIS-IV, and both have good reliability ($k = 0.71$ and $k = 0.67$, respectively).[36] The choice of these symptoms is justified in Supplementary Methods. These symptoms have a high prevalence in adults meeting criteria for ADHD in NESARC-II, since the symptom of "Lot of sudden mood changes" is present in 68.91% (N = 2,341) of patients with ADHD, the symptom "Outburst angry" in 70.91% (N = 2,409), the symptom "Hit people or thrown things" in 89.52% (N = 3,041), and the symptom "Anger for little things" in 73.82% (N = 2,508) of patients with ADHD. We therefore find an average prevalence of 75.79% of ED symptoms in adults with ADHD.

Statistical Analyses

Weighted prevalence of ADHD symptoms and ED symptoms. Number, percentage, and nonweighted and weighted prevalence are given for each ADHD and ED dimension (Table 2 and Supplementary Table 1).

Symptom network analysis. Three steps were carried out for this network analysis: (1) estimation and regularization of the network (Ising model and representations with the Fruchterman-Reingold algorithm)[37]; (2) network inferences computation, including the centrality (strength) and bridge analysis (reflecting the connection between symptom subgroups); (3) analysis of stability (see Supplementary Methods for more details on symptom network methodology).[38] Two other networks were computed, including only ED symptoms and only ADHD symptoms. Finally, a network of patients only above the ADHD threshold is proposed in Supplementary Materials.

All analyses were performed on R (4.2.3).

RESULTS

Sociodemographic and Socioeconomic Characteristics

After processing the missing data, the analyses were carried out on 33,546 noninstitutionalized U.S. civilian participants, with 47.92% were males and 52.08% females. Table 1 describes their sociodemographic and socioeconomic characteristics. Details on the frequencies and nonweighted percentages of each symptom by dimension are given in Supplementary Table 1.

Table 1.

Sociodemographic and Socioeconomic Characteristics of the NESARC Participants (N = 33,546 of Noninstitutionalized US Civilian Participants After Processing the Missing Data on 34,653 Participants)

	% (SE)
Sex	
Male	47.92 (0.34)
Female	52.08 (034)
Ethnicity	
White	70.91 (1.54)
Black American	11.05 (0.66)
Native American	2.19 (0.18)
Asian	4.27 (0.52)
Hispanic	11.58 (1.19)
Nativity	
US born	86.13 (1.38)
Foreign born	13.87 (1.38)
Age category	
18–29 y	16.34 (0.31)
30–44 y	29.74 (0.36)
45–64 y	34.61 (0.32)
65+ y	19.31 (0.34)
Education	
Less than high school	5.56 (0.29)
High school graduate	35.94 (0.57)
Some college or higher	58.50 (0.63)
Individual income	
$0-$19,999	39.40 (0.58)
$20,000–$34,999	24.23 (0.36)
$35,000–$69,999	25.47 (0.40)
>$70,000	10.91 (0.46)
Marital status	
Married, living common law	63.79 (0.48)
Widowed/divorced/separated	18.86 (0.26)
Never married	17.35 (0.45)
Urbanicity	
Urban	83.69 (0.55)
Rural	16.31 (055)
Region of residence	
Northwest	17.78 (1.17)
Midwest	18.48 (1.10)
South	38.44 (1.56)
West	25.30 (0.94)
Insurance	
Public	11.12 (0.33)
Private	77.19 (0.57)
None	11.70 (0.39)

Abbreviations: NESARC = National Epidemiologic Survey on Alcohol and Related Conditions, SE = standard error.

Weighted Prevalence of ADHD Symptoms and ED Symptoms

The prevalence of ADHD in the cohort of 33,546 participants was 3,397 (10.12%). We found 1,607 (47.31%) individuals fulfilling the criteria of inattention and 1,790 (52.70%) fulfilling the criteria of hyperactivity/impulsivity. We found 668 individuals who met the criteria of both dimensions (representing 1.99% of the total number of participants and 19.66% of the 3,397 individuals meeting criteria of ADHD), 832 (2.48%) who met the criteria of inattention with at least 1 symptom of hyperactivity/impulsivity, and 876 patients (2.60%) who met the criteria of hyperactivity/impulsivity with at least 1 symptom of inattention. Supplementary Results details Table 2.

Estimation of the Symptom Network

A correlation matrix, based on each pair of variables, is presented in Supplementary Figure 1. The symptom network of ADHD and ED symptoms, based on partial correlations, is presented in Figure 1.

The highest correlations between 2 symptoms were found between "Blurts out answers" and "Interrupts or intrudes on others" ($r = 0.85$), belonging to the hyperactive/impulsive symptom cluster. "Trouble keeping attention" was also strongly positively correlated with "Often easily distracted," and "No attention to details or careless mistakes" with "Often forgetful in daily activities" (both at $r = 0.84$), belonging to inattention. Finally, "No attention to details or careless mistakes" was also strongly correlated with "Often does not seem to listen," which was itself strongly correlated to "Often forgetful in daily activities" (both at $r = 0.82$), also belonging to the inattention symptom cluster. All these pairwise correlations were intrinsic to each dimension. Interestingly, the pairwise correlations are approximately the same in the network considering only individuals meeting symptom criteria for ADHD (Supplementary Figure 2).

Regarding ED, the symptoms of "Outburst angry loss control" and "Hit people or thrown things" were the most strongly related ($r = 0.73$), like those of "Outburst angry loss control" and "Little things angry" ($r = 0.74$). In the network represented in Figure 1, the emotional symptom of "Lot of sudden mood changes" was not strongly related to the other 3 symptoms of the ED dimension. However, this symptom had the highest value of centrality within the network consisting only of ED symptoms (Supplementary Figure 3—at 0.77, vs values at 1.35 for the symptom of "Outburst angry loss control," at 0.73 for "Hit people or thrown things," and at 0.16 for "Little things angry").

Interestingly, the predictability of most symptoms was significant, with average predictability to 0.74 (SD = 0.14).

Centrality and Bridge Analysis

Strength-type centrality is described in Figure 2. The 4 measures of centrality (strength, closeness, betweenness, and expected influence) are given in Supplementary Figure 4. The symptoms of "Often does not seem to listen" and "Often easily distracted" constituted the 2 symptoms with the highest centrality in terms of strength (Figure 2). ED symptoms have a

Table 2.

Weighted Prevalence of ADHD Symptoms (Belonging to the Attentional and/or Hyperactive/Impulsive Dimensions) and Emotional Dysregulation (ED) Symptoms (Belonging to the ED Dimension) on the 33,546 Noninstitutionalized US Civilian Participants of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC-II)

Symptoms	% (SE)
Attentional dimension	
Often does not give close attention to details or makes careless mistakes in schoolwork, work, or other activities	9.92 (0.25)
Often has trouble keeping attention on tasks or play activities	7.17 (0.20)
Often does not seem to listen when spoken directly	12.82 (0.31)
Often does not follow through on instructions and fails to finish schoolwork, chores, or duties in the workplace	16.84 (0.37)
Often has trouble organizing activities	5.93 (0.16)
Often avoids, dislikes, or does not want to do things that take a lot of mental effort for a long period of time	13.58 (0.29)
Often loses things needed for tasks and activities	6.56 (0.18)
Is often easily distracted	11.92 (0.29)
Is often forgetful in daily activities	6.25 (0.19)
Hyperactive/Impulsive dimension	
Often fidgets with hands or feet or squirms in seat when sitting still is expected	14.03 (0.32)
Often gets up from seat when remaining in seat is expected	7.06 (0.21)
Often excessively runs about or climbs when and where it is not appropriate (restless)	20.38 (0.38)
Often has trouble playing or doing leisure activities quietly	8.70 (0.23)
Is often "on the go" or often acts as if "driven by a motor"	30.49 (0.58)
Often talks excessively	20.18 (0.30)
Often blurts out answers before questions have been finished	12.16 (0.28)
Often has trouble waiting one's turn	5.92 (0.18)
Often interrupts or intrudes on others	11.92 (0.25)
Emotional dysregulation dimension	
Lot of sudden mood changes	33.46 (1.94)
Outburst angry	31.08 (1.90
Hit people or thrown things	28.94 (1.97)
Anger for little things	28.34 (1.84)

Abbreviation: SE = standard error.

relatively low centrality on all 4 measures of centrality (Figure 2); the 4 ED symptoms ranked among the 5 least central symptoms on all the centrality measures in the general population (Supplementary Figure 4) as well as in individuals above the ADHD threshold (Supplementary Figure 5).

Bridge analysis is described in Figure 3. The most important bridge symptom in terms of strength is the symptom of "Gets up unexpectedly," belonging to hyperactivity/impulsivity and constituting a bridge between inattention and hyperactivity/impulsivity ($r = 6.83$). The second most important bridge symptom in terms of strength is "Lots of sudden mood changes," belonging to ED, and constituting a bridge between ED and inattention ($r = 6.80$). The third most important bridge symptom in terms of strength is "Often does not seem to listen," belonging to inattention and constituting a bridge between inattention and hyperactivity/impulsivity ($r = 6.65$). The fourth most important bridge symptom in terms of strength is "Outburst angry loss control," belonging to the ED and constituting a bridge between inattention and ED ($r = 6.63$).

Finally, the small-world analysis offers a Small World Index (SWI) of 1.388 for the ADHD and ED network (see Supplementary Methods), 1.393 for the ADHD without ED network, and 1.648 for the ED network (these networks are represented in Supplementary Figure 2). The small-worldness (and more precisely, the average short path lengths) is numerically lower in magnitude in the ADHD and ED network than in the other 2 networks.

Analysis of Stability

The stability of the centrality, based on bootstrap analysis, is questionable (Supplementary Figure 6).

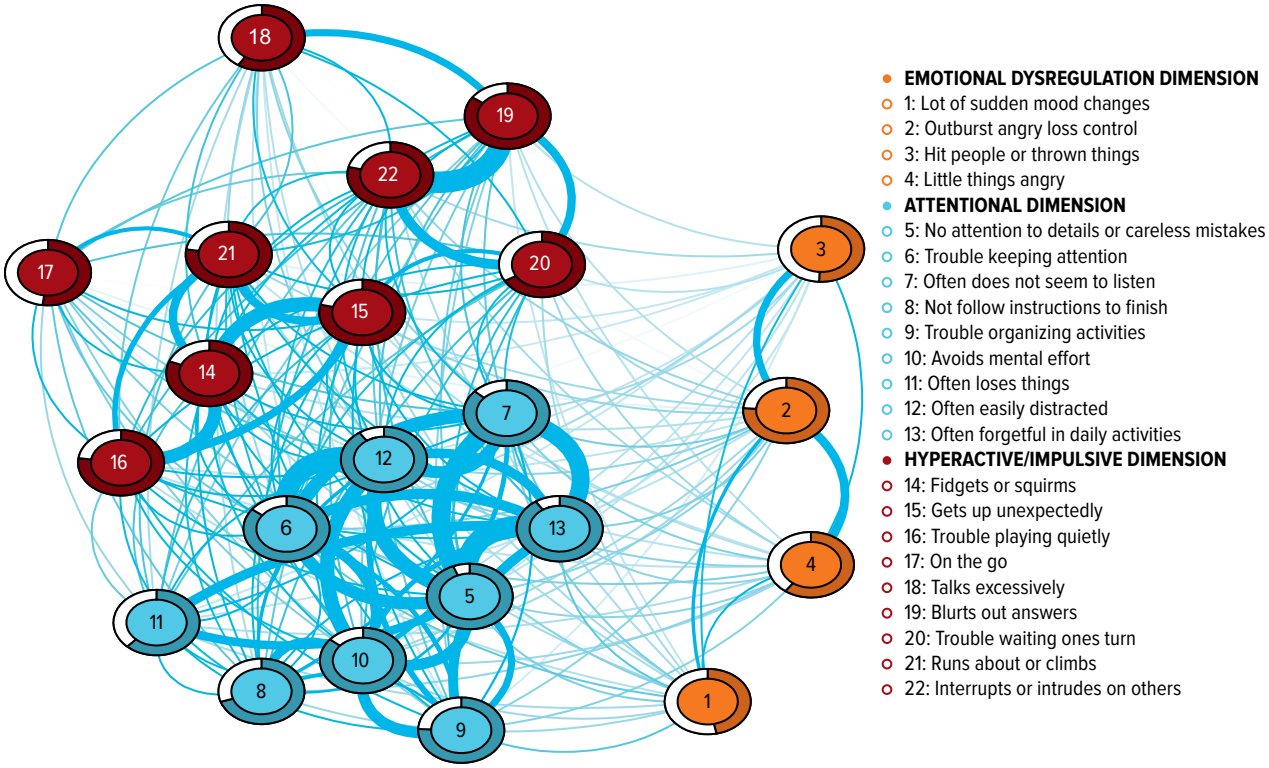
DISCUSSION

In this discussion, we first address 4 key points regarding the relevance of symptom networks in ADHD and ED (importance of pairwise relationships, noncentrality of ED symptoms, small-worldness, and bridge analysis). In the second part, we explore different models explaining the association between ED and ADHD symptoms. The third part focuses on the clinical implications of such a network modelization. We finally discuss the limitations of this study.

First, symptom networks allow to find the most relevant symptoms among a set of interacting elements.

Figure 1.

Symptom Network of the ADHD Symptoms and Emotional Dysregulation (ED) Symptoms on the 33,546 Noninstitutionalized US Civilian Participants of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC-II)[a]



[a]The thickness of the lines (edges) represents the level of correlation between 2 symptoms. Positive correlations are represented in blue. The 3 dimensions are presented: attentional dimension, hyperactive/impulsive dimension, and ED dimension. Predictability of a node is depicted as a pie chart in the rings around nodes: the area in the outer ring of nodes represents the percentage of variance of the node that is explained by all neighboring nodes.

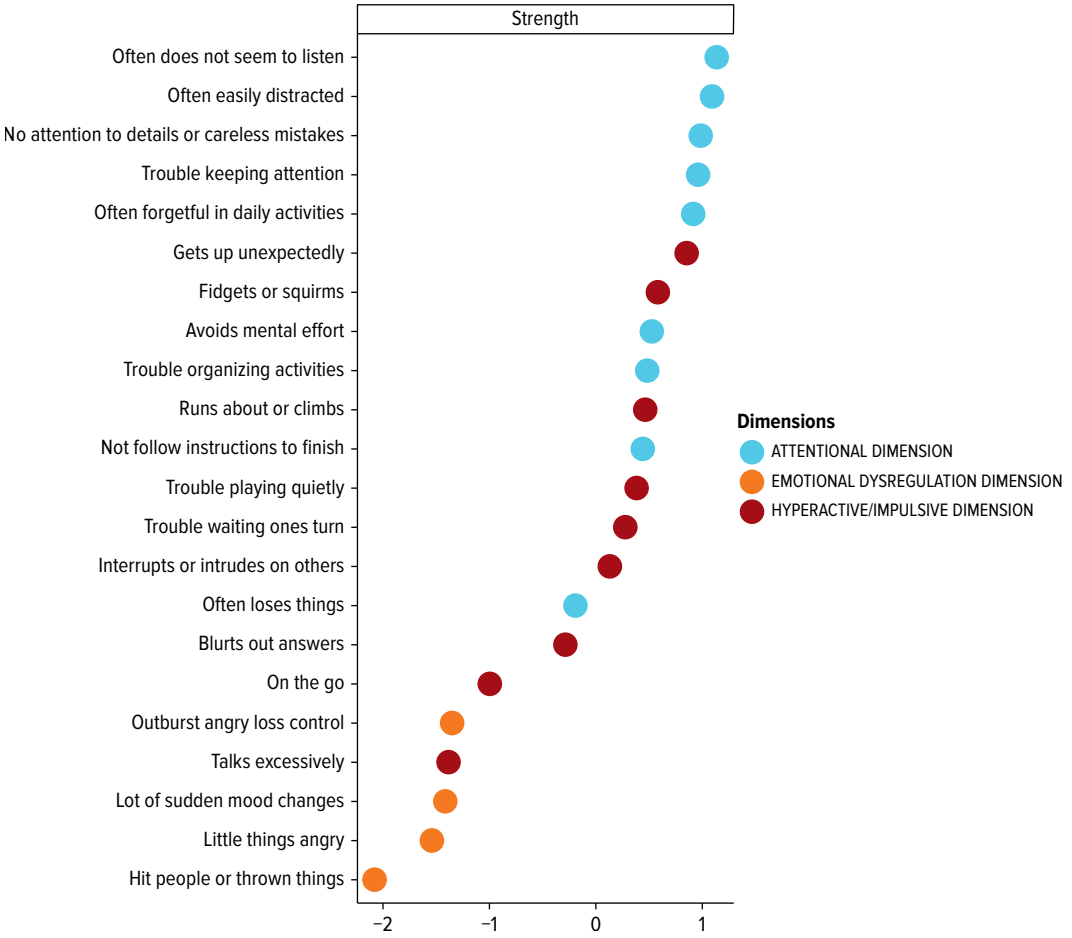
Regarding the local analysis, our network shows that the strongest pairwise correlations are intrinsic to each ADHD symptom cluster (eg, "Blurts out answers" belonging to hyperactivity/impulsivity, or "Trouble keeping attention" belonging to inattention), consistent with ADHD models showing the importance of a clinical distinction between the inattention and impulsivity/hyperactivity core constructs within ADHD.[12] This result highlights the importance of pairwise relationships between symptoms of the same cluster.[39–42]

A second result refers to the noncentrality of ED symptoms in our network which includes both ADHD and ED symptoms. This indicates that ADHD symptoms (symptoms belonging to the inattention and hyperactivity/impulsivity symptoms presented in international classifications) were generally central, while ED symptoms were not. Interestingly, this lack of centrality for ED symptoms aligns with the approach taken during the development of the *DSM-III*. In the early conceptualization of ADHD, reflecting "minimal brain damage," ED was considered more important than inattention among the cardinal symptoms.[16] In the *DSM-III*, ADHD was termed attention deficit disorder with or without hyperactivity (ADD/H), and these ED symptoms were reclassified as "associated features" rather than diagnostic criteria for ADHD (termed ADD/H).[39] The ability to consider the mutual influences between ADHD and ED symptoms within such a network model can support the clinician's reasoning, because this approach aligns with how mutual influences between these symptoms are typically considered in clinical practice. For instance, it allows for comparing ADHD with disorders characterized by severe temper outbursts or irritability, such as disruptive mood dysregulation disorder (DMDD).

Third, our results also report that small-worldness is numerically lower in magnitude in the ADHD and ED network (1.388) than in the other 2 networks (1.393 for the ADHD without ED network and 1.648 for the ED network). The ADHD and ED network is, therefore, less "compact," ie, a point is less easily reached from another point. Interpreting this lower small-worldness as indicative of reduced overall network consistency suggests that the integration of ED into the ADHD

Figure 2.

Strength-Type Centrality of the ADHD Symptoms and ED Symptom Network on the 33,546 Noninstitutionalized US Civilian Participants of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC-II)[a]



[a]The rightmost symptom is the most central. Centrality numbers at the bottom of the figure, on the x-axis, show standardized z-scores (ie, standardized coefficients, calculated by subtracting the mean and dividing by the SD for each observation). A z-score at ~[−2] on the x-axis for Strength (eg, "Hit people or throw things") indicates that that node has the least strength on the network.

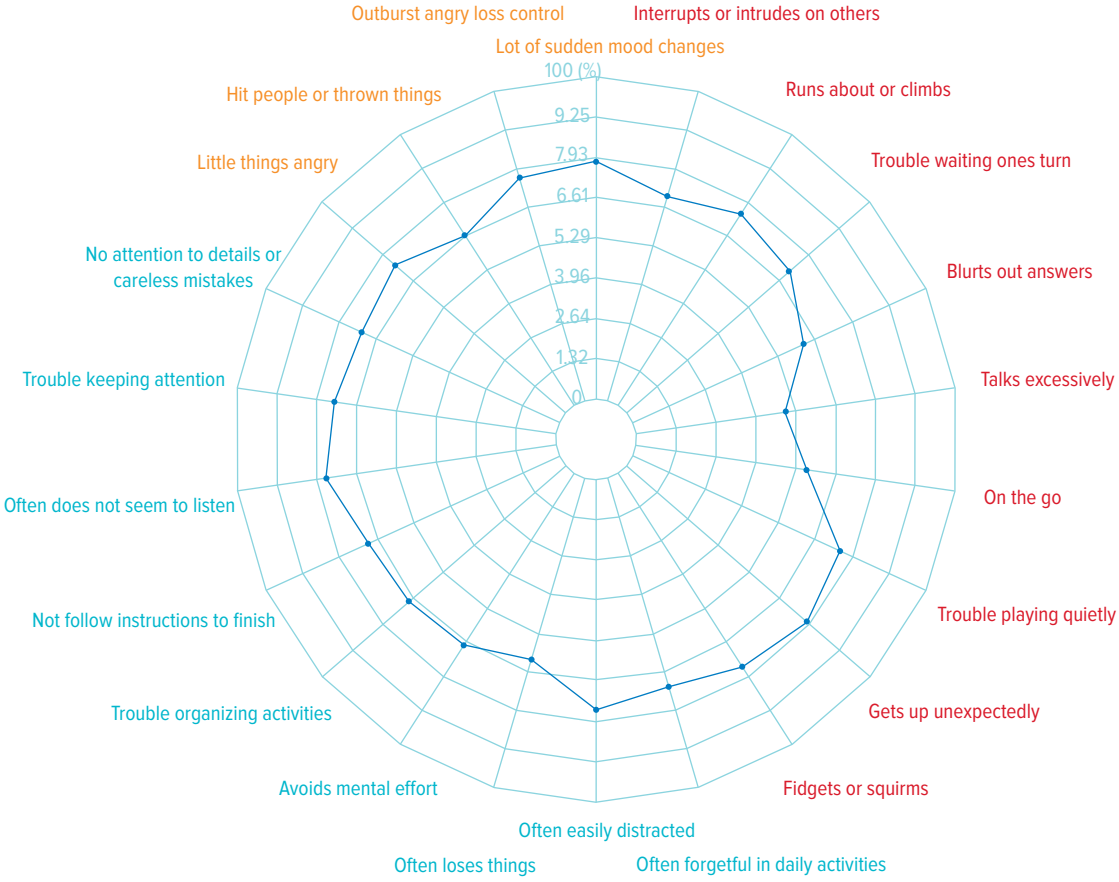
network may weaken its structural coherence. This reduction in consistency could be seen as a potential argument for maintaining the distinction between ADHD and ED as relatively independent constructs. Moreover, this result could align with the high predictability of ADHD symptoms, highlighting the importance of considering these more predictable symptoms to guide targeted interventions, whether focused directly on the core symptoms or on those closely related to them.[43]

Fourth, bridge analysis, exploring the connection between different clusters of symptoms (eg, ADHD core symptom clusters and ED), is particularly interesting because it shows that 2 of the 4 most important bridge symptoms are emotional ("Lots of sudden mood changes" and "Outburst angry loss control," between ED and attentional dimensions), in addition to an attentional symptom ("Often does not seem to listen") and a hyperactivity/impulsivity symptom ("Gets up unexpectedly") (Supplementary Materials give details on the precaution of interpreting bridge symptoms). This strong bridgeness also allows the advancement of the understanding of the hypotheses explaining the presence of ED symptoms within/co-occurring with ADHD.[44,45]

These various delineations provide a clearer basis for explaining the association between ED and ADHD symptoms. At least 3 models aim to explain this association: (1) ED is a dimensional entity that co-occurs with ADHD, but they are ultimately dissociable dimensions (the "diplomat model"),[46–49] (2) ADHD with ED is a separate nosological entity from ADHD without ED (the "split model"),[50,51] (3) or ED is a core-symptom of ADHD (the "lumping model").[16,52] The diplomat model is

Figure 3.

Radar Plot of the Bridge Analysis of the ADHD Symptom and ED Symptom Network on the 33,546 Noninstitutionalized US Civilian Participants of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC-II)[a]



[a]The rightmost symptom is the most central ("Gets up unexpectedly"). Centrality numbers at the bottom of the figure, on the x-axis, show standardized z-scores (ie, standardized coefficients, calculated by subtracting the mean and dividing by the SD for each observation). A z-score at ~[−2] on the x-axis for Strength (eg, "Hit people or throw things") indicates that that node has the least strength on the network.

supported by (modest) significant correlations between ADHD symptoms and ED. Partially superimposed but dissociable neurocognitive deficits could underpin it.[46] This model presents challenges due to the lack of integration of a diagnosis for individuals with ED without ADHD, leading to practical consequences such as issues with administration, reimbursement, and medical recognition.[46–49] It is also in this model that categories such as DMDD or intermittent explosive disorder have been proposed, to provide access to care and reimbursement. The split model came primarily from genetic findings of familial cosegregation of ADHD and ED; it might imply both a distinct neurocognitive etiology and clinical course for people with both ADHD and ED symptoms.[50] Finally, the lumping model recognizes the close associations between cognitive and emotional regulation systems and seeks to remain parsimonious by considering primarily a hybrid entity; it is supported by the expression of the same neurocognitive deficits that underlie ADHD, eg, the expression of a purely cortico-striato-cerebellar dysfunction or more subtly of a (para)limbic dysfunction.[53]

The interpretation of the bridgeness of ED symptoms in our ADHD network within the adult population highlights the importance of considering these ED symptoms as being primarily related to the inattention dimension, rather than the hyperactivity/impulsivity dimension. With due caution and necessary modesty in this highly complex debate, these results could rather support the lumping model (considering ED as a core symptom of ADHD) or the diplomat model (where ED is seen as a dimensional entity co-occurring with ADHD). Whatever the model supported, these results, based on a conception of ADHD with ED as a unified nosological entity supported by symptom networks, seem important to identify etiologies and therapeutic targets for future studies. ED symptoms are consistent with the Research

Domain Criteria project launched by the National Institute of Mental Health[54,55] and constitute a clinical construct more readily tied to underlying neurobiological mechanisms. The investigations developed in such a network study sustain the important role of ED as a fundamental mechanism potentially useful in the development of therapeutics for ADHD.[16,18,56]

These findings offer several practical implications for clinicians. First, recognizing the high prevalence and significant impact of ED symptoms within the population with ADHD can guide more comprehensive assessment and diagnostic practices. Moreover, understanding that ED symptoms can serve as a bridge between the core symptom clusters of ADHD highlights the necessity of addressing ED not merely as a comorbidity but as a critical component of the disorder itself. Although this study cannot establish causality, the relationships between inattention and ED symptoms support the need to investigate one when the other is found. In this way, the data supporting the diplomat and lumping models suggest that interventions targeting ED symptoms might simultaneously reduce ADHD symptoms, particularly those related to inattention. For instance, incorporating behavioral strategies and other therapeutic modalities to improve emotional regulation could complement pharmacologic treatments. More generally, any therapeutic intervention tested in a clinical trial for populations with ADHD should ideally include a more systematic evaluation of ED symptoms. This integrated perspective can also facilitate more informed discussions with patients and their families.

Several limitations should be acknowledged regarding this network analysis. First, how ADHD symptoms are measured should be discussed, particularly because ADHD symptoms and ED symptoms are present in patients over 2 different periods: ADHD symptoms are measured retrospectively "before the age of 18," while ED symptoms are present at the time of collection. The generalization of the results according to the target population (childhood, adolescence, or adulthood) should therefore be particularly cautious. Second, network centrality should be interpreted with great caution, with regard to its clinical relevance, but also due to the post hoc analysis of robustness.[57] Third, regarding their nature, ED symptoms depend on the choice of the questionable ED definition (eg, other ED symptoms could have been added in the network analysis, like tonic irritability, defined as persistently angry or grumpy mood). However, this choice allows manipulable data and clinically relevant results, while guaranteeing, with the 4 ED symptoms chosen, to consider the entire NESARC population (unlike the symptom screeners in the mood disorder section which are not systematically searched for). Moreover, this limit can be nuanced due to the relative high prevalence of ED symptoms in ADHD (75.79% [68.9%–89.52%]). Different results might have been obtained if other ED symptoms, such as emotion-related impulsivity (ERI), had been included. While ED reflects difficulty in downregulating emotions after affective arousal, ERI involves challenges in controlling reactions to emotional stimuli,[24,58] often leading to impulsive speech, behavior, and thoughts during emotional states.[14,59,60] Some studies suggest that hyperactivity/impulsivity is more closely linked to ERI, while inattention is more associated with ED.

To conclude, this network analysis revealed, for the first time to our knowledge, the significance of ED symptoms as bridges in ADHD, particularly their strong association with the inattention dimension rather than the hyperactivity/impulsivity dimension. Our results suggest that ED symptoms may serve as diagnostic core—or gateway—markers of ADHD, supporting the hypothesis that they could be major targets for both diagnosis and treatment in this neurodevelopmental disorder.

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Supplementary Material: Available at Psychiatrist.com.

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Supplementary Material

Article Title: Symptom Network Analysis of Attention-Deficit/Hyperactivity Disorder and Emotional Symptoms in Adults: Results From the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC)

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LIST OF SUPPLEMENTARY MATERIAL FOR THE ARTICLE

The Journal of Clinical Psychiatry

	Institutionalized U.S. Civilian Participants of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC-II)
8. **Figure 6**	Stability Analysis Based on the Bootstrap on the Strength for the Attention Deficit Hyperactivity Disorder (ADHD) and Emotional Dysregulation (ED) Network on the 33,546 Non-Institutionalized U.S. Civilian Participants of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC-II)
9. **Supplementary Results**	

DISCLAIMER

Supplementary Material: Methods

Details on the NESARC

The NESARC-II is a representative sample collected in 2004-2005 on the non-institutionalized U.S. population, consisting of 34,653 civilian participants over the age of 18, with 86.7% response rate. Trained members of the U.S. Census Bureau conducted face-to-face interviews. The study protocol, which included written informed consent procedures, obtained full approval from the U.S. Census Bureau and the Office of Management and Budget. Sampling weights were employed to ensure that the sample reflected the U.S. population and accounted for nonresponse and sample attrition, regarding socioeconomic variables based on the 2000 Decennial Census [1]. Detailed information regarding the sampling and weighting procedures are given in [2,3]. Missing data is processed by deleting individuals with at least one missing value.

AUDADIS-IV

The AUDADIS-IV methods to diagnose ADHD are detailed elsewhere [4–6]. To summarize, in these different validation and reliability studies, Wave 2 NESARC respondents who completed the entire Alcohol Use Disorder and Associated Disabilities Interview Schedule-IV (AUDADIS-IV) interview were randomly selected for a retest interview at one of four Census Bureau regional offices. Each office conducted in-person reinterviews within 10 weeks of the initial survey. In Boston, sections on acculturation, discrimination, stress, social networks, support, adverse childhood experiences, and abuse were tested with a 91.9% response rate (518 initial, 476 interviewed). Philadelphia tested DSM-IV personality disorders with an 87.9% response rate (552 initial, 485 interviewed). Detroit focused on DSM-IV PTSD and discrimination with a 92.8% response rate (526 initial, 488 interviewed). Denver tested ADHD, sexual orientation and behavior, intimate partner violence, and sexual orientation discrimination with a 93.7% response rate (480 initial, 450 interviewed).

Regarding ADHD, the test–retests concentrated on five DSM-IV diagnoses, including two Axis I disorders: PTSD and ADHD. The test–retest statistics cover 12-month and lifetime diagnoses of PTSD, as well as ADHD diagnoses during childhood (before age 18) and adulthood (since age 18). Additionally, the reliability of DSM-IV lifetime diagnoses of Axis II disorders, specifically borderline, schizotypal, and narcissistic personality disorders (PDs), was assessed. For each DSM-IV disorder, intraclass correlation coefficients were calculated based on scales constructed from the associated diagnostic symptom items, such as symptom counts. For ADHD, the test-retest reliability showed a kappa of 0.71 (SE = 0.12) for childhood diagnoses and 0.63 (SE = 0.09) for adult diagnoses, with prevalence rates of 0.05/0.06 and 0.03/0.02 respectively, and an intraclass correlation coefficient (ICC) of 0.75 (95% CI: 0.71, 0.78) for adult ADHD symptom scales, with an alpha of 0.89 [4–6].

ADHD symptoms

These symptoms had to be present for at least 6 months, have onset before the age of 18 and significantly interfere with social, school, or work functioning. The age of onset criterion was increased to 18 years old, with a diagnosis in adults which is made if the symptoms began before the age of 12, as endorsed by the DSM-5 ADHD committee [7,8]. Test-retest reliability for ADHD was good (k=0.71) [9]. Internal consistency reliability of the ADHD symptom items (Cronbach's α= 0.89) was excellent [9].

ED symptoms

ED encompasses emotional experiences and expressions that are: i) excessive and context-inappropriate as regards social norms, ii) rapid, poorly controlled shifts in emotion (i.e., "emotional lability"), iii) characterized by an anomalous allocation of attention to emotional stimuli [10]. ED-related symptoms comprise sudden mood changes or loss of emotional control, as well as explosive anger or anger related to minor events, e.g., leading individuals with ADHD to engage in aggressive behaviour towards objects, themselves or others [11–13].

The ED dimension showed satisfactory reliability and validity [14,15], an independent effect on the functional consequences of ADHD (e.g., in social relationships, comorbidities or quality of life) [12,13,16–18] and constitutes a potential pharmacological and psychotherapeutic lever [19,20].

In this study, participants were asked if they "had a lot of sudden mood changes", if they "often had temper outbursts or gotten so angry that [they] lose control", if they have "hit people or thrown things when [they] got angry" and if "even little things made [them)] angry or have [them] had difficulty controlling [their] anger". Participants reporting at least one of these reactions and who did not fulfill all of the criteria for borderline personality disorder were considered as presenting ED. We did not include patients with this disorder because our focus is on emotional symptoms rather than the singular construct of borderline personality disorder, which have to be diagnosed based on a certain threshold of symptoms. We aim to compare emotional symptoms with ADHD symptoms, rather than comparing the "construct of borderline disorder" with the "construct of ADHD".

The choice of the ED symptoms in this study was based on the definition of ED [10] and justified as follows:

1) One symptom is related to sudden mood changes (here referred to as "Lot of sudden mood changes"), related to emotional lability and poor control shift in emotions.
2) Two symptoms are related to explosive anger and anger related to minor events (here referred to as "Anger for little things" and "Outburst angry"), related to excessiveness in relation to social norms and context-inappropriate.
3) One symptom is related to the functional impact of relationship difficulties, leading individuals with ADHD to potentially engage in aggressive behavior with others (here referred to as "Hit people or thrown things"), related to the inability to promote adaptive and goal-oriented behaviors.

Test-retest, as well as convergent, discriminant or construct validity could not be specifically tested for this set of symptoms.

Weighted prevalence of ADHD symptoms and ED symptoms

We provide the number and percentage of patients meeting ADHD criteria (≥ 6 symptoms in at least one dimension), and the number of patients who have more than 6 symptoms in both dimensions. Regarding the diagnosis of ADHD symptoms and ED symptoms, separately, weighted prevalence of estimates with standard errors (SEs) and adjusted odds-ratio (aOR) estimates and 95% confidence intervals (95% CI) were computed (using multiple logistic regressions). Weighted prevalence, given in a specific table (**Table 1**), refer to an adjustment of the frequencies to the total number of symptoms for each individual. Percentage of each symptom by dimension is also given in **Supplementary Table 1**.

Network estimation and visualization

Network analysis characterizes structures of a system, in terms of nodes (aka "symptoms" or "diagnostic criteria") and edges which connect the nodes (aka correlation coefficients). The focus on symptoms rather than factorial analysis allows to avoid using the notion of latent variable, which are entities, by definition, not directly observed in clinical practice. A latent variable like the "ADHD category" is never directly observed by clinicians; it is inferred based on a collection of symptoms that are clinically measured. The significance for clinical practice is that it enables direct measurement of what clinicians observe during consultations, rather than relying on a theoretical, inferred diagnosis that exists independently of the symptoms.

In this study, symptom networks consist of nodes built on symptoms of the DSM-5 ADHD, belonging to the attentional and/or impulsive/hyperactive dimension, and ED symptoms, belonging to the ED dimension) and edges (the connections between these symptoms), which represent the conditional pairwise relations between two symptoms, controlling for all other symptoms in the network [21].

A computational network analysis was conducted according to the network guidelines for the computational analysis of network properties [21(p20)]. The estimation of pairwise relationships between criteria can be seen as conditional dependence relations. With such partial correlations, association between two diagnostic criteria means that they remain conditionally dependent after controlling for all other associations among criteria in the global network. Conversely, if no edge emerges between two criteria, they are conditionally independent after controlling for the associations among all other criteria. In parallel, a correlation matrix was provided to visualize the pairwise correlations, based on simple correlations between each pair of variables. In the network, based on partial correlations, these direct negative relationships may be attenuated or disappear because partial correlations control for the influence of other variables in the model. For instance, a negative relationship observed in simple correlations might be due to the influence of a third variable, which is accounted for in partial correlations.

The criteria network of the two scales are graphically represented according to a Fruchterman-Reingold algorithm. In this representation, the weight of the connection between two nodes is proportional to the correlation measure, and the place of the node is positioned according to a force-directed graph measure, so that criterion with stronger and/or more connections are placed closer to each other. Nodes that are nearer to the center of the graph have the strongest connections to other nodes.

We estimated a network via an Ising model whereby edges signify conditional independence relationships among the nodes (i.e., partial correlations between pairs of nodes controlling for the influence of all other nodes).

We regularized our model by running the graphical LASSO (Least Absolute Shrinkage and Selection Operator) [22] to avoid false-positive edges. The aims of this regularization are to compute (regularized) partial correlations between pairs of criteria (thereby eliminating spurious associations attributable to the influence of other criteria in the network), and to shrink trivially small associations to zero, removing them from the graph as potentially "false positive" edges (thereby returning a sparse graph comprising only the strongest edges).

Additionally, we use extended Bayesian Information Criterion (EBIC) model selection [23] in a two-step procedure: 100 different network models with different degrees of sparsity are estimated, and then the model with the lowest EBIC is selected, given a certain value on the hyperparameter gamma (γ), which controls the trade-off between including false-positive edges and removing true edges. The hyperparameter γ is usually set between zero and 0.5 [24]. We opted to set γ to 0.5 to be confident that our edges are truly authentic, given that the closer one chooses a value of γ near 0.5, the more the EBIC will favor a simpler model containing fewer edges, whereas the closer one chooses a value of γ near zero, the more the EBIC will favor a model with more edges.

Nodal predictability was calculated based on models derived from Mixed Graphical Models (MGM) [25] and graphically represented as a pie chart in the ring around each variable. Predictability has a value between 0 and 1, provided on the basis of the variance of the prediction error calculated according to the R^2 of the MGM. It refers to how well a given node in the network can be predicted by all remaining nodes. It thus shows how relevant edges are, e.g., a node may be connected to many other nodes but if these only explain only 1% of its variance, it is unlikely that this node is very relevant. This has further implications: for example, designing an intervention to affect certain nodes, or detecting where data is lacking (e.g., when parts of the network are little influenced by related nodes and thus must depend on external factors). In clinical practice, predictability of a symptom indicates "whether an intervention on that symptom through the symptom network is promising" [25].

Concerning the computational analysis, processing and graphical visualizations used the R (4.2.3) package *bootnet* (version 1.2.3) [24], which leads more strongly connected sets of nodes to cluster closer together than the R-packages *IsingFit* (version 0.3.1) [26(p201)], Pearson correlations for the binary data in our dataset and with the *qgraph* package for visualization (version 1.6.3) [27]. Expected influence and bridge symptoms (see below) were calculated with the *networktools* R package.

Network inferences: centrality and bridge measures

Network analysis provides interesting inferences, both qualitative (visual) and quantitative (statistically determined). Concerning these network inferences, the clustering coefficient can be approximated to three times the number of triangles divided by the number of connected triples of vertices (Newman, 2001; Newman et al., 2002). The shortest path length between two nodes equals the minimum number of edges that must be passed over to get from one to the other. The average shortest path length is the average over the shortest path lengths of all node pairs.

The local measures of a network are related to centrality measures. Centrality measures play a crucial role in connecting two or more nodes (Cramer et al., 2010; Jones et al., 2018). Nodes with high centrality index measures represent criteria that are highly connected to other criteria. In a nutshell, centrality can be understood to reflect how connected and thus potentially clinically relevant a diagnostic criterion is in a network (via paths through other diagnostic symptoms, intervening on a highly central diagnostic criterion, other nodes will be both directly and indirectly affected). Measures of centrality are given with standardized z-scores, i.e., standardized coefficients calculated by subtracting the mean and dividing by the standard deviation for each observation. The correlations between criteria may be considered as stronger when the nodes have higher centrality. In the network graph based on a Fruchterman-Reingold algorithm, central nodes often end up in the center of the graph and nodes with low centrality in the periphery. Four centrality measures are classically given in network studies of symptoms of psychopathology: *Strength*, *Closeness*, *Betweenness* and *Expected Influence*. To help understand these measures, by analogy, the ADHD network can be considered like a railroad network map, with the city being considered as a node, and the railroad between two cities as a connection.

Node strength is the sum of the weights of the edges attached to that node. The weighted number of connections for a given node, and the degree to which it is connected with all the other nodes of the network can be computed (Barrat et al., 2004). A criterion has high strength centrality if this criterion is highly connected to all the other criteria. In the rail network metaphor, a city has high strength if it is connected to an extremely large number of other cities, e.g., Washington in the USA.

The closeness of a node is computed according to the shortest path length measure and is inversely proportional to the shortest mean distance from all the other nodes (Boccaletti et al., 2006). Closeness centrality indicates the average distance of a node from all other nodes in the network and is computed as the inverse of the weighted sum of shortest path lengths to a given node from all other nodes in the network. A criterion has high closeness centrality if the criterion can be connected shortly to other criteria (Bringmann et al., 2019; Richetin et al., 2017; Smith et al., 2017). Using the rail network metaphor, a city has high closeness if it is central compared to many other cities, i.e., it is "close" to many others, e.g., like Kansas City which is geographically central on the map of the USA.

The betweenness of a node computes the degree to which a given node connect different parts of the network, thus reflecting the degree to which it controls the flow of information across the network. The betweenness centrality of a node equals the number of times that it lies on the shortest path length between any pair of other nodes. A criterion has high betweenness centrality if the criterion can influence the connection between non-adjacent (i.e., not directly connected) criteria, thus acting as gatekeeper (Bringmann et al., 2019; Bringmann et al., 2013). In the railroad network metaphor, a city has high betweenness if it is necessary to transit through that city to reach other cities, like Las Vegas, which should be passed through on the route between San Francisco and New York City.

Finally, the expected influence of a node is computed to improve the measurement of centrality of the nodes in a network (Robinaugh et al., 2016). It is computed as the sum of all edges which extend from a given node, accounting for both positive and negative correlation values with regard to the entire network. A criterion with high Expected Influence has an influence on the criteria network based on its positive correlations, negative correlations being corrected by this centrality measure. In the railroad network metaphor, a city has a high expected influence if it is connected to an extremely large number of connected neighboring cities, considering possible negative correlation values between cities.

Centrality measures are differentiated from bridge measures, which can be assessed by using bridge centrality statistics (Heeren et al., 2018; Jones et al., 2018; Opsahl et al., 2010). Bridge symptoms connect different clusters of symptoms [28]. They can specifically be used to detect and quantify interacting symptoms between "modules" [29], aka ADHD dimensions. They can specifically be used to detect and quantify interacting symptoms between "modules" [29], herein ADHD attentional and hyperactive/impulsive dimensions. Two conceptions of bridge symptoms should be distinguished [28]: either there are symptoms belonging to two or more clusters/disorders and allow an overlap between them; either these symptoms belong to just one cluster/disorder, or alternatively are not specific symptoms of a cluster/disorder, and play an important role in connecting different clusters/disorders. In this article, we refer to the second conception: bridge symptoms account for the connection between clusters of symptoms (of ADHD). In this study, we provide bridgeness in terms of strength (defined as the sum of the absolute value of all edges that exist between a specific node and all nodes that are not in the same community as this specific node). This comparison is completed with the calculation of the small-worldness, measured using clustering coefficient (degree to which nodes in a graph tends to cluster together) and the average shortest path length between two nodes (the average over the shortest path lengths of all node pairs) relatively to a random network.

Network robustness (stability)

Concerning the robustness, we refined the analyzes based on the classical bootstrap methods used in the literature on symptom networks, to provide a more precise approach. Two steps were conducted to assess the accuracy of symptom network structures: i) estimating the confidence intervals on the edge-weights; ii) assessing the stability of centrality indices under observing subsets of cases. Network robustness was calculated by the analysis of the centrality stability, with the use of a correlation coefficient (CS-coefficient). The CS-coefficient represents the maximum proportion of participants that can be dropped while maintaining 95% probability that the correlation between centrality metrics from the full data set and the subset data are at least 0.70. Based on a simulation study (Epskamp et al.,

2017), a minimum CS-coefficient of 0.25 is recommended for interpreting centrality indices.

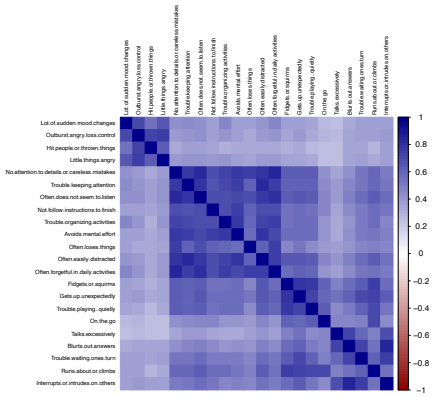
Small-worldness

We provide a small-world measure for the network. Small-worldness is measured using clustering coefficient (degree to which nodes in a graph tend to cluster together), the average shortest path length (APL – the average over the shortest path lengths of all node pairs), relatively to a random network (i.e., a network whose distribution can be described by a random process). Thus, the ADHD-ED network small-worldness index (SWI) is calculated according to the following formula: SWI = (Clustering-ADHD-ED / Clustering-Random) / (APL-ADHD-ED / APL-Random). Small-world measures for the ADHD and emotional symptoms network may be used to evaluate the degree of association between symptoms in this network. This helps clinicians to rapidly look for the other symptoms of such a syndrome (known in network theory as "high signal-propagation speed"), and the global consistency and manipulability of these disorders for clinicians. A network can be called a small-world if its index is higher than 1 [30].

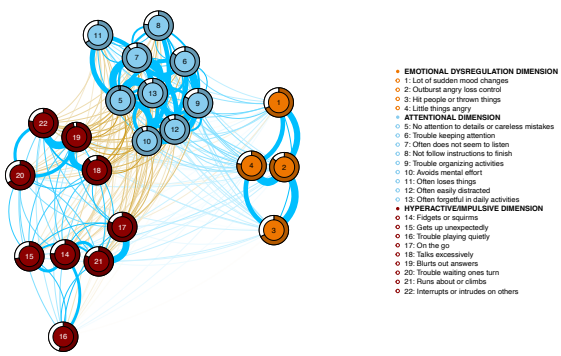
Supplementary Materials: Results

Supplementary Table 1. Number and non-weighted percentages of symptoms on the 33,546 non-institutionalized U.S. civilian participants of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC-II). ED: emotion dysregulation. It is interesting to note that the prevalence of the hyperactive/impulsive dimension is relatively high in our sample. In the literature, the prevalences relating to the dimensions of ADHD differ widely depending on the cohorts studied.[31]

Dimensions	Name of the symptoms	Number of symptoms (N = 33,546)	Percentage of symptoms
Hyperactive/impulsive	On the go	9884	29%
Hyperactive/impulsive	Talks excessively	6994	21%
Hyperactive/impulsive	Runs about or climbs	6771	20%
Attention	Not follow instructions to finish	5440	16%
Attention	Avoids mental effort	4504	13%
Hyperactive/impulsive	Fidgets or squirms	4378	13%
Hyperactive/impulsive	Blurts out answers	4184	12%
Attention	Often does not seem to listen	4170	12%
Attention	Often easily distracted	3833	11%
Hyperactive/impulsive	Interrupts or intrudes on others	3667	11%
	No attention to details or careless mistake	3157	9%
ED	Hit people or thrown things	3041	9%
Hyperactive/impulsive	Trouble playing quietly	2717	8%
ED	Little things angry	2508	7%
ED	Outburst angry loss control	2409	7%
Attention	Trouble keeping attention	2377	7%
Hyperactive/impulsive	Gets up unexpectedly	2350	7%
ED	Lot of sudden mood changes	2341	7%
Attention	Often loses things	2178	6%
Attention	Often forgetful in daily activities	2096	6%
Attention	Trouble organizing activities	2079	6%
Hyperactive/impulsive	Trouble waiting ones turn	2030	6%

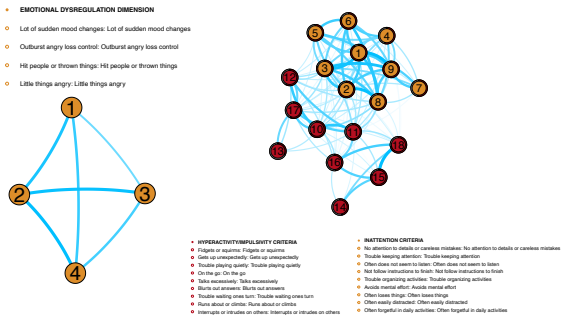


Supplementary Figure 1. Correlation matrix of Attention Deficit Hyperactivity Disorder (ADHD) symptoms and Emotional Dysregulation (ED) symptoms on the 33,546 non-institutionalized U.S. civilian participants of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC-II). Regarding differences in negative relationships, the correlation matrix shows direct negative relationships between variables, indicating that an increase in one variable is associated with a decrease in another, without considering other variables.

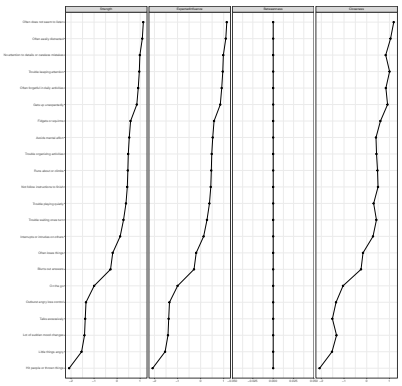


Supplementary Figure 2. Symptom network of the ADHD symptoms and emotional dysregulation (ED) symptoms in patients exceeding ADHD

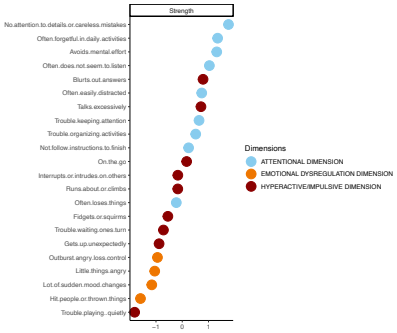
threshold (N= 3397), in non-institutionalized U.S. civilian participants of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC-II). The thickness of the lines (edges) represents the level of correlation between two symptoms. Positive correlations are represented in blue. The three dimensions are presented: attentional dimension, hyperactive/impulsive dimension and ED dimension. Predictability of a node is depicted as a pie chart in the rings around nodes: the area in the outer ring of nodes represents the percentage of variance of the node that is explained by all neighboring nodes.



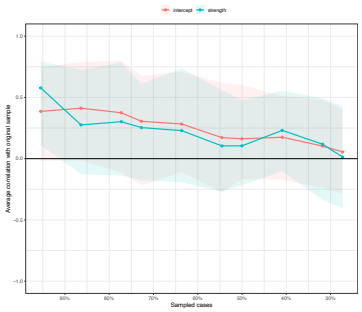
Supplementary Figure 3. **Left**: Symptom network of the Emotional Dysregulation (ED) symptoms. **Right**: Symptom network of the Attention Deficit Hyperactivity Disorder (ADHD) symptoms, based on the 33,546 non-institutionalized U.S. civilian participants of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC-II). The thickness of the lines (edges) represents the level of correlation between two symptoms. Positive correlations are represented in blue.



Supplementary Figure 4. The four measures of centrality (Strength, Closeness, Betweenness and Expected influence) of the Attention Deficit Hyperactivity Disorder (ADHD) and Emotional Dysregulation (ED) symptom network on the 33,546 non-institutionalized U.S. civilian participants of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC-II). Each of the four vertical tables corresponds to a measure of centrality. Within each table, the highest centrality is on the right, the lowest is on the left. Thus, the rightmost symptoms are the most central. All the tables are classified according to the decrease in centrality of the Strength (from top to bottom). Centrality numbers at the bottom of each vertical table, on the x-axis, show standardized z-scores (i.e., standardized coefficients, calculated by subtracting the mean and dividing by the standard deviation for each observation). A z-score at ~[-2] on the x-axis for Strength (e.g., "Hit people or throw things") indicates that that node has the least strength on the network.



Supplementary Figure 5. Strength-type centrality of the ADHD symptoms and ED symptom network in patients exceeding ADHD threshold (N= 3397), in non-institutionalized U.S. civilian participants of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC-II). The rightmost symptom is the most central. Centrality numbers at the bottom of the figure, on the x-axis, show standardized z-scores (i.e., standardized coefficients, calculated by subtracting the mean and dividing by the standard deviation for each observation).



Supplementary Figure 6. Stability analysis based on the bootstrap on the Strength for the Attention Deficit Hyperactivity Disorder (ADHD) and Emotional Dysregulation (ED) network on the 33,546 non-institutionalized U.S. civilian participants of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC-II). More precisely, the red curve, read from left to right, corresponds to the modification of the centrality relations (Strength) of the network as the participants are dropped (in %). Thus, if the red curve falls rapidly according to the average correlation with the original sample, the stability of the network is lower than if the curve remains more horizontal. The robustness is low for this model.

Supplementary Materials: Results

Details on the weighted prevalence of ADHD symptoms (Table 2)

The prevalence of attention symptoms varied from 5.93% ("Trouble organizing activities") to 16.84% ("Does not follow instructions"). For hyperactive/impulsive symptoms, the prevalence ranged from 5.92% ("Trouble waiting one's turn") to 30.49% ("Often on the go"). In the ED dimension, the prevalence of symptoms spanned from 28.34% ("Anger for little things") to 33.46% ("Lots of sudden mood changes") (**Table 2**).

On the precaution of interpreting bridge symptoms

This result should be interpreted with great caution regarding its potential for refining phenotypes. The symptoms "Lots of sudden mood changes" and "Outburst angry loss control" certainly appear to act as bridges between the ED dimension and at least one dimension of ADHD, specifically the attentional dimension. However, other symptoms, not necessarily related to ED, could also have been added to the network and potentially functioned similarly as bridges. Therefore, the importance of ED symptoms as bridge symptoms does not imply that they are specific to the ADHD construct. This finding highlights the bridging role of ED symptoms but does not suggest that these symptoms are unique to ADHD or necessarily refine its phenotype.

Such a result should therefore not be interpreted as a need to include ED symptoms in ADHD with a view to nosological refinement. ED symptoms could serve as red flags, acting as warning signs that can support the diagnosis of ADHD, particularly when other symptoms, such as those from the inattention dimension, are more difficult to identify. As bridges, ED symptoms reinforce the possibility to clinically identify ADHD symptoms (and especially of the attentional dimension).