Journal of Affective Disorders 296 (2022) 305–308

Contents lists available at ScienceDirect

Journal of Affective Disorders

journal homepage: www.elsevier.com/locate/jad

Short communication

Sleep problems as a transdiagnostic hub bridging impaired attention control, generalized anxiety, and depression

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ARTICLE INFO

Keywords:
Executive control
Generalized anxiety disorder
Major depression disorder
Sleep

ABSTRACT

Background: Major Depression Disorder (MDD) and Generalized Anxiety Disorder (GAD) often co-occur, but uncertainty remains regarding the neurocognitive mechanisms linked to this co-occurrence. In this study, we applied network analytic methods to characterize the associations of the attention control (AC) components, as assessed using laboratory-based measurement tools, with MDD and GAD symptoms. Of critical interest was identifying whether AC components were primarily associated with symptoms unique or common to MDD and GAD.

Methods: We computed a regularized partial correlation network to examine the associations between attention control with symptoms specific to MDD, specific to GAD, and symptoms common to MDD and GAD ($n = 371$).

Results: Symptoms that are common to MDD and GAD emerged as highly influential nodes in the network. In particular, our findings pointed to sleep problems as a hub bridging attention control components to hallmark symptoms of MDD and GAD.

Limitations: The present results should not be interpreted as definitive but instead as hypothesis-generating and highlighting the utility of rethinking the conceptualization of the associations between attention control, MDD, and GAD through the lens of sleep problems. Future studies would especially want to consider the temporal unfolding of the network structure.

Conclusions: To our knowledge, this is the first study to identify sleep problems as a potential pathway bridging together components of attention control with symptoms of GAD and MDD.

Generalized anxiety disorder (GAD) and Major Depressive Disorder (MDD) often co-occur (e.g., Ruscio et al., 2017), and this co-occurrence has severe consequences. For instance, it decreased response to gold-standard pharmacological or psychological treatment options and increased the risk of attempting suicide (e.g., Dold et al., 2017). As a result, clarifying the mechanisms fostering the co-occurrence between symptoms of GAD and MDD has emerged as a hot topic of contemporary affective disorders research (e.g., Dold et al., 2017; Hsu et al., 2015).

Prominent cognitive views of GAD and MDD (i.e., Eysenck and Derakshan, 2011; Hsu et al., 2015) have pointed to attention control (AC)—i.e., the ability to voluntarily regulate the allocation of attentional resources—as a potential neurocognitive mechanism of GAD or MDD, respectively. Many studies have accordingly reported impaired performances of patients with MDD solely, GAD solely, or co-occurring MDD and GAD on various tasks tapping into AC (e.g., Hsu et al., 2015; Lyche et al., 2011). However, these studies have so far relied on comparing groups of patients qualifying for a DSM-5 diagnosis of MDD, GAD, or both, thus precluding any elucidation of the exact symptom-to-symptom pathway bridging AC with these disorders. Particularly, because GAD and MDD diagnoses include overlapping (e.g., sleep problems) and non-overlapping symptoms (e.g., depressed mood, excessive worry), uncertainty remains regarding whether AC is primarily associated with symptoms common or unique to the two disorders.

Moreover, prior research on MDD and GAD has often treated AC as a unitary construct. Yet, prominent contemporary models of attention postulate that AC is a multifaceted construct (e.g., Petersen and Posner, 2012) that includes at least three components: alerting (allowing the

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https://doi.org/10.1016/j.jad.2021.09.092
Received 25 April 2021; Received in revised form 31 August 2021; Accepted 26 September 2021
Available online 1 October 2021

achievement of a state of alertness), orienting (allowing the selection of information from sensory inputs by engaging or disengaging attention to or from one stimulus among others), and executive (allowing conflict resolution among incompatible responses via the top-down control of attention). Inspired by the network approach to mental disorders that conceptualizes comorbidity as a natural consequence of symptom-to-symptom associations between the disorders (Cramer et al., 2010), the main goal of this project was to apply network analytic methods to characterize the associations of AC components with MDD and GAD symptoms. Of critical importance was identifying whether AC components were primarily associated with symptoms unique or common to the disorders.

1. Method

1.1. Participants

We relied on an unselected sample of 371 Belgian French-speaking participants (75.7% women) from the general community and the Belgian "Beau Vallon" Psychiatric Hospital. Following guidelines for network analysis in psychopathology (Fried, 2016), we opted for an unselected sampling approach to avoid potential problems of range restriction that are likely among samples comprising only clinical or healthy volunteers. Participants were between the ages of 18 and 63 (M = 26.89, SD=10.84). Their years of education completed since primary school ranged from 3 to 25 (M = 14.21, SD=2.60). The study was approved by the local Institutional Review Board. Each participant provided signed informed consent and was tested individually in a dim-lit laboratory setting.

1.2. Materials and measures

1.2.1. Symptoms measurement

We assessed MDD and GAD symptoms using the validated French version the 21-item Beck Depression Inventory (BDI-II; Beck et al., 1998) and the Generalized Anxiety Disorder 7-item (GAD-7; Micoulaud-Franchi et al., 2016). Their internal reliability was high in the present sample, with Cronbach's alphas of 0.95 and 0.91, respectively, for the BDI-II and GAD-7.

1.2.2. Neuropsychological assessment of AC components

We assessed the alerting, orienting, and executive components of AC via the Attention Network Task (Fan et al., 2002), a highly validated and commonly-used tool in attention research. A complete description of the task is available in the supplementary materials.

1.3. Data analysis plan

1.3.1. Data preparation

Symptoms corresponding to the DSM-5 criteria unique to MDD, unique to GAD, and common to MDD and GAD were respectively estimated from the BDI-II and GAD-7 by aggregating items reflecting the same corresponding criterion (for a complete description of the procedure, see the supplementary materials). The alerting, orienting, and executive indices of the ANT were computed as in Fan et al. (2002). For both the alerting and orienting components, greater values reflect greater efficiency, whereas greater values for the executive component indicate increased difficulty with executive control of attention. A full description of the computational approach is provided in the supplementary materials.

This data preparation resulted in 16 variables (see Fig. 1), each belonging to one of the four following categories: AC components, symptoms specific to MDD, symptoms specific to GAD, or symptoms common to MDD and GAD.

1.3.2. Network estimation

We estimated the network using a sparse Gaussian graphical model (GGM), which applies a graphical LASSO regularization (Epskamp et al., 2018) and the corresponding tuning parameter selected by minimizing the Extended Bayesian Information Criterion. We nonparanormally transformed all variables using the R package *huge* (Jiang et al., 2019). This ensured that the data met the assumption of multivariate normality required by the GGM. In our GGM, nodes represented our 16 variables of interest and edges the regularized partial correlations between them. To

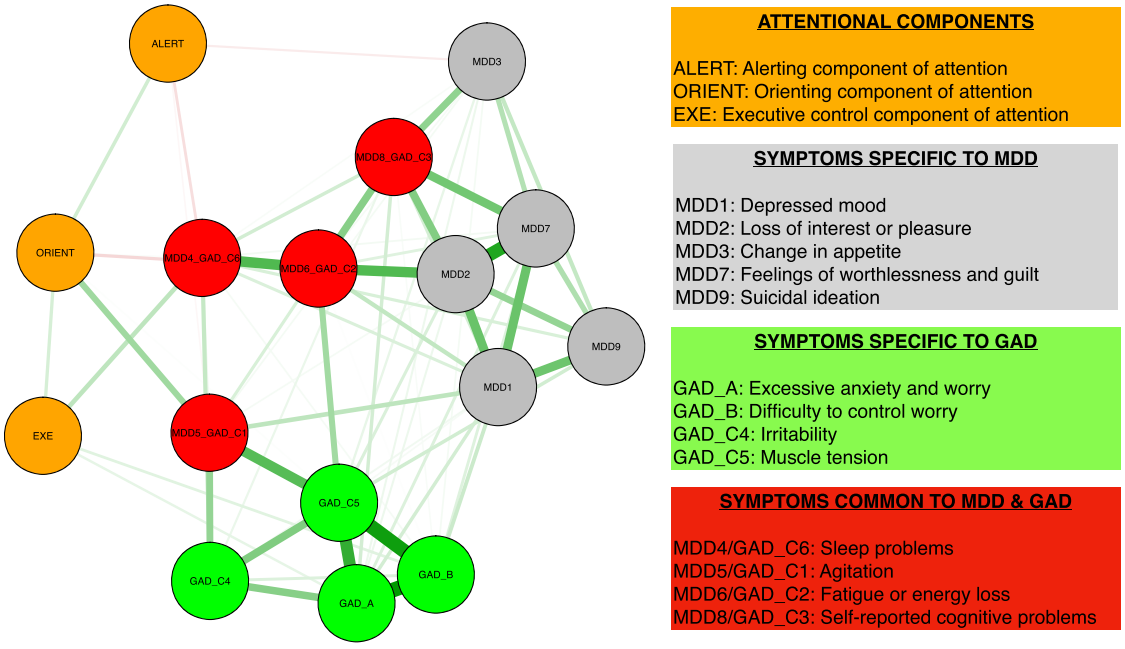

Fig. 1. Gaussian Graphical Model of the associations between components of attention control, symptoms specific to MDD, symptoms specific to GAD, and symptoms common to MDD and GAD.
Note. Nodes are labelled according to the corresponding DSM-5 criteria. Green edges represent positive regularized partial correlations, whereas red ones represent negative regularized partial correlations.

quantify the importance of the cross-associations between nodes belonging to our four clusters of interest, we estimated the bridge expected influence of each node, which is the sum of the edge-weight values connecting a given node to all nodes in the other clusters. We assessed the stability and the accuracy of the edge-weight and bridge centrality estimates using 1000-iterations bootstrap methods. De-identified data and R script are publicly available via the Open Science Framework at https://osf.io/fm9x7/.

2. Results

Fig. 1 shows the GGM network, which was highly stable and robust (see the supplementary material). The thickness of the edge denotes the strength of the association, with a thicker edge indicating a larger association. We used the Fruchterman-Reingold layout algorithm to determine node placement so that nodes closer to the center of the network tend to yield the strongest associations with other nodes.

Although there were strong associations between nodes belonging to the same category, a few strong cross-category associations stood out. First, AC components were strongly associated with symptoms common to MDD and GAD, while hardly connected to symptoms specific to either MDD or GAD. In particular, sleep problems was positively associated with poor executive control and negatively associated with the orienting and alerting components of AC. Agitation was also positively associated with the orienting component of AC. Second, nodes denoting symptoms shared by MDD and GAD exhibited the highest bridge expected values (the bridge centrality estimates are available in the supplementary materials). Finally, there were only a few connections between AC and symptoms specific to one of the two disorders. For GAD, poor executive AC was associated with excessive worry and difficulty to control worry, dovetailng with previous research (e.g., Eysenck and Derakshan, 2011). For MDD, there was only a very thin negative association between alerting and change in appetite.

3. Discussion

Many people with MDD also suffer from GAD, and vice versa. Prominent cognitive models of GAD and MDD have pointed to AC as a potent neurocognitive mechanism of these disorders. To our knowledge, this is the first study to examine the network structure of the cross-associations between AC components with symptoms specific to either MDD or GAD and common to MDD and GAD.

Perhaps the most striking result was the observation that symptoms common to MDD and GAD emerged as highly influential nodes, sharing many strong associations with other nodes. In particular, our results pointed to sleep problems as a potential hub bridging AC components to symptoms of MDD and GAD.

Although our findings may seem at odds with prominent neurocognitive models pointing to AC as core processes common to MDD and GAD, they align with recent but empirically sound research viewing sleep problems as a transdiagnostic pathway at play in the onset of depression and anxiety-related psychopathology (e.g., Cox and Olatunji, 2020; Freeman et al., 2020). Likewise, numerous studies have linked sleep problems and AC, particularly with impairments in the executive control of attention (e.g., Kuula et al., 2018). To our knowledge, this is the first study to identify sleep problems as potent pathways bridging together AC components and hallmark symptoms of MDD and GAD. Interestingly, the node denoting sleep problems was also strongly associated with fatigue/energy loss, another symptom shared by MDD and GAD emerging as a hub bridging the symptoms common to MDD and GAD to the specific ones, like muscle tension, loss of interest, or depressed mood. Given the strong association between sleep problems and fatigue/energy loss, our findings invite the hypothesis that sleep problems may trigger symptoms specific to GAD or MDD via fatigue and energy loss. However, the cross-sectional nature of our data precludes any definite conclusion regarding the cause-effect relationship between our variables of interest, and further research is required to confirm our prediction.

Moreover, regarding whether AC is primarily associated with symptoms common or unique to the two disorders, we found that the strongest associations between AC components and hallmark symptoms of MDD and GAD involved symptoms common to MDD and GAD, primarily via sleep problems. This set of findings dovetails with prominent neurocognitive models pointing to AC as a potent mechanism of GAD and MDD (e.g., Eysenck and Derakshan, 2011; Hsu et al., 2015) and invite to the hypothesis of sleep problems as a potent process bridging AC to the disorders. Interestingly, the orienting component of AC was also highly related to agitation—another symptom common to MDD and GAD. Although the orienting component of AC did not emerge as a bridge per se, this observation lends some support to a shred of small but mounting evidence pointing to the orienting component of AC as predictive of emotion regulation problems and psychopathology (e.g., Heeren and McNally, 2016; Rothbart et al., 2011).

While the evidence requires further advancement, especially regarding the temporal unfolding of the network structure and the assessment of sleep problems via multi-item self-report or more objective measures (e.g., actigraphy, polysomnography), this study provides insight into how AC, MDD, and GAD bridge, which may help to guide future experimental and translational research forward. In particular, the network approach to psychopathology posits that deactivating nodes serving as hubs in the network should foster a downstream beneficial cascade (e.g., Blanchard and Heeren, 2020; Cramer et al., 2010). Consequently, if it holds for the variables investigated here, interventions directly targeting sleep should alter the interlock between AC, MDD, and GAD. Of note, recent treatment efforts have recently shed light on the benefit of treating sleep problems before other symptoms among patients with various psychiatric disorders (Freeman et al., 2020). Network theories also speculate that nodes serving as bridges might be more likely to propagate activation through the entire network when re-activated after treatment (e.g., Cramer et al., 2010). Thus, a next step would be to examine whether sleep problems constitute harbingers of relapse, deserving careful audit during follow-up.

In conclusion, although one should not interpret the present results as definitive before replications in larger and more diverse samples (e.g., less predominantly female, more geographically diverse), this study highlights the relevance of rethinking the conceptualization of the associations between AC, MDD, and GAD through the lens of sleep problems.

Funding sources

This research was funded by a research grant (Grant "1.C.059.18F") awarded to AH by the FRS-FNRS Belgian Science Foundation and a research fellowship award (Grant "G0118001") to CC by the Beau Vallon Psychiatric Hospital.

CRediT authorship contribution statement

Charlotte Coussement: Conceptualization, Data curation, Funding acquisition, Investigation, Methodology, Project administration, Writing – original draft. **Alexandre Heeren:** Conceptualization, Formal analysis, Supervision, Project administration, Visualization, Writing – original draft, Funding acquisition.

Declaration of Competing Interest

The authors have no known conflict of interest to disclose.

Acknowledgement

The authors are thankful to Yorgo Hoebeke, David Gamero, and Mónica Riesco de Vega for their help in the data collection.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jad.2021.09.092.

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