Symptom Dynamics and Attention in Depression: Fatigue and Low Positive Affect are Associated With Reduced Orienting Efficiency

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BK developed the study concept, performed data analysis, interpreted results, and wrote the manuscript. NIL, RB, BK, RJ and CH planned and organized the study. BK and RB collected the data. KH provided guidance on data analysis. BK, RB, KH, EK, RJ, CH and NIL interpreted the results. All authors provided critical revisions and approved the final manuscript for submission.

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Materials and analysis code for this study are not available. This study was not preregistered.

Abstract

Depression is a heterogeneous mental disorder involving a complex interplay between potential etiological and maintenance factors. The current study examined how depression heterogeneity is related to attentional functioning. Relying on person-specific network models, we explored the associations between symptom centrality (expected influence) and impairments in attention (orienting, alerting and executive control). Participants (N = 82) with ongoing and remitted depression were enrolled to 13 days of intensive assessment of depression symptoms in their daily life using a smartphone app. Based on these data, person-specific network models were estimated using vector autoregression modelling. Orienting, alerting and executive control were assessed using the Attentional Network Test in the laboratory. Person-specific networks showed large variability in symptom dynamics. Higher centrality for low positive affect and fatigue were associated with reduced orienting efficiency (r = .35, p < .05; r = .30, p < .05, respectively). Results are discussed in relation to anhedonia- and reward-related processes. In conclusion, this study points towards the importance of individual symptom dynamics when considering cognitive functioning in depression.

Keywords: depression, attention, experience sampling methods, ecological momentary assessment, anhedonia, fatigue, network analysis

General Scientific Summary

Attentional problems are common in depression, but we have little specific knowledge for whom this is the case. This study suggests that patients who has a symptom profile which is highly impacted by fatigue and low positive affect tend to orient their attention less efficiently.

Symptom Dynamics and Attention in Depression:

Fatigue and Low Positive Affect are Associated With Reduced Orienting Efficiency

Concentration and attentional impairments are frequently reported by patients with major depression (Gotlib & Joormann, 2010; Hammar & Årdal, 2009; Keller et al., 2019; LeMoult & Gotlib, 2019), although there have been divergent findings with regard to the severity of such impairments (e.g., Ottowitz et al., 2002). Indeed, inability to think and concentrate is a diagnostic criterion for major depressive disorder (MDD; APA, 2013). Reduced attentional functioning negatively impacts daily functioning (Keller et al., 2019), emotion regulation (Koster et al., 2011), has been implicated in the etiology and maintenance of depression (De Raedt et al., 2010), and is increasingly targeted in psychotherapy (Wells, 2009) and computerized training interventions (Koster et al., 2017).

Although, meta-analyses indicate evidence for impaired attentional functioning and executive control (e.g., Snyder, 2013), there is substantial heterogeneity between studies, with several studies reporting no attentional impairments (Ottowitz et al., 2002). This aligns with the fact that depression is a remarkably heterogeneous disorder (Goldberg, 2011) and involves many plausible aetiological and maintaining pathways (e.g., Charney & Manji, 2004; Harrington et al., 1996; Hasler, 2010; Wittenborn et al., 2016). As there is large symptom variation among depressed individuals (Fried & Nesse, 2015), this could potentially explain divergent findings regarding the role of attentional functioning in depression.

Specific depression symptoms differ from each other in their association with other symptoms, risk factors, and underlying biology (Fried, 2015; Fried et al., 2014). Interestingly, functional impairment in daily life depends on which symptoms are present. For example, sad mood explains much more of daily life functioning than for example hypersomnia (Fried & Nesse, 2014). In current network approaches to psychopathology it is argued that we need to study the interactions between depressive symptoms, since depression is the complex and dynamic network of interacting symptoms, not a latent disease entity (Borsboom, 2017). Along these lines, a recent meta-analysis by Malgaroli et al. (2021) examined between-symptom associations in depression which relied on network analysis studies (Borsboom & Cramer, 2013). They found that fatigue and depressed mood were the two most influential symptoms (i.e., had the highest centrality). In contrast, symptoms like weight change emerged as the least influential symptom in the models (Malgaroli et al., 2021). Importantly, centrality of specific depressive symptoms seems to be clinically informative. For example, high symptom centrality of fatigue has been related to non-response, whereas responders where characterized by high centrality of negative mood (McElroy et al., 2019). In patients experiencing recurrence of depression, difficulty concentrating was among the most central symptoms (Lorimer et al., 2019).

Recent network studies suggest a link between subjective levels of cognitive functioning, overall depression symptoms, and other vulnerability mechanisms. For example, in a sample of remitted depressed patients, Hoorelbeke et al., (2016) examined links between performance on a cognitive control task (the Paced Auditory Serial Addition task), self-reported executive impairments, and a composite measure of depression symptoms using network analysis. The contribution of the objective measure for cognitive control in the network models was negligible, whereas self-reported executive impairments were linked to emotion regulation processes and depressive symptomatology via resilience. Following up on this, Hoorelbeke et al., (2019) found associations between level of cognitive complaints (subjective experience of executive- and working memory impairments), co-occurrence of depressive symptomatology, as well as other risk factors for depression (e.g., rumination) following remission from depression using time-series data.

Few studies have examined the link between cognitive functioning and *specific* depressive symptoms. Our research group has recently examined the link between executive functioning and depression symptoms in a mixed sample of depressed, previously depressed, and healthy individuals. Results showed that reduced executive functioning was associated with fatigue and anhedonia (Kraft et al., 2022). However, it is unclear whether similar patterns would emerge for attentional functioning. Moreover, when examining associations between cognitive functioning and depressive symptoms it is important to assess depressive symptoms using recent advances in symptoms dynamics.

Estimation of Symptom Dynamics

Symptom dynamics can be estimated using network analysis of intensive time-series data. Data can be gathered by an experience sampling method (ESM) procedure, where participants answer questions several times a day, often by the means of a smartphone app (Trull & Ebner-Priemer, 2009). Using this type of data in combination with multilevel vector auto regressive (VAR) modelling, researchers can provide a window into the temporal order by which symptoms affect one another over time (Epskamp et al., 2018), providing more nuanced information on which symptoms are the most influential. Based on temporally ordered data and network analysis researchers can estimate person-specific networks (Epskamp et al., 2018). This approach, also called idiographic network analysis, estimates symptom networks per subject and highlights which symptoms are most influential (i.e., central) in a each subject’s symptom profile. Several studies have used this approach to examine individual symptom dynamics, and demonstrate large variability in symptom profiles (see for example Fisher et al., 2017; Levinson et al., 2020; Reeves & Fisher, 2020).

Current Study

The current study examines the impact of depression heterogeneity on attentional functioning in depression.

First, we estimate person-specific networks based on ESM data using an idiographic network analytical approach. This allows us to model the extent to which specific symptoms appear to play a more central role in each individual's symptom dynamics in daily life.

Secondly, we measure attentional functioning in line with the seminal work by Posner and Petersen (1990) on attentional networks in the brain, where attention can be decomposed into three main functions. *Orienting* selects information from the sensory input; *alerting* maintains an alert state; *executive control* resolves conflict among possible responses (Fan et al., 2002). Findings regarding these attentional functions in depression are mixed. For instance, Lyche et al. (2011) reported reduced alerting in patients suffering from ongoing major depression disorder. Impairments in all three functions have been reported in remitted depression (Paelecke-Habermann et al., 2005). However, other studies have shown no association between orienting, alerting, and executive control in remitted and subclinical depression (Preiss et al., 2010; Yang & Xiang, 2019).

Finally, we examine associations between symptom centrality and attentional functioning. In this way the current study may clarify inconsistencies in the literature regarding the relationship between depressive symptomatology and attentional functioning.

Method

Sample and Procedure

Individuals with depressive complaints with or without comorbid mental disorders were recruited by advertisement. Inclusion criteria were age 18 - 65 years and fluency in Norwegian. Exclusion criteria were manic episodes, psychosis, and neurological disorders. Diagnostic status was assessed by psychologists and trained psychology students using the *MINI International Neuropsychiatric Interview* (Sheehan et al., 1998). All participants provided written informed consent in accordance with the Declaration of Helsinki, and the study was carried out in accordance with the recommendations of the Regional Committee for

Medical and Health Research Ethics in Norway (2019/330) and the Norwegian Social Science Data Services.

After diagnostic assessment and inclusion in the study, participants (N = 82) were enrolled to 13 days of ESM assessment of depression symptoms and carried out their daily life as normal (for details, see below). At day 14, 76 participants returned to the lab for assessment of attentional functioning and depression symptoms (*Beck's Depression Inventory II* [BDI]; Beck et al., 1996). Data collection was performed from February 5, 2020 to August 31, 2021. Administrators were clinical psychologists and psychology students.

ESM

ESM data was collected using an app (PsyMate) installed on participants' smartphones. The app notified participants to report depression symptoms five times per day at random intervals between 8 AM and 10 PM (total number of measurements = 65). At each measurement participants were asked to complete a short questionnaire introduced by the sentence: "How have you been the last hour?". The questionnaire had to be completed within 30 minutes, or else a non-response was recorded.

The questionnaire consisted of eight items measuring specific depression symptoms using a slider scale with values going from 0 (nothing) to 100 (very much). When notified, participants were instructed to use approximately one minute to answer the questionnaire. Participants received in-person demonstration of the app and received information on how to understand the items of the questionnaire.

Items were generated by B. Kraft and R. Bø based on the DSM-5 (APA, 2013). The items cover five depression criteria, as well as rumination and activity level (which are often highlighted in research and targeted in clinical interventions). The items were as follows: sadness ("How sad have you been?"), fatigue ("How tired have you been?"), interest ("How interested have you been in what you have been doing?", positive affect ("How happy have you been?”), negative thoughts (“How much negative thoughts have you had?”), concentration problems (“How great difficulties have you had concentrating?”, ruminating (“How much have you been ruminating?”, and activity (“How active have you been (physical/ mentally/socially)? Overall depression symptoms were also assessed (“How depressed have you been”), but not included in the analysis given the level of content overlap with the other items.

Several DSM-5 criteria were not assessed to reduce load on participants and keep well below the recommended number nodes in the network analysis (Epskamp, 2015). These were depression symptoms which are less common and involve both increased or decreased symptom quality (e.g., decreased, or increased appetite). We did not assess suicidal thoughts, as it might be disturbing for participants to answer this item repeatedly throughout the day.

Attentional Functioning

The Attentional Network Test (ANT; Fan et al., 2002) is a computerized task which measures the efficiency of the attentional networks involved in alerting, orienting, and executive attention. In each trial, five arrows pointing left or right are presented either above or below a fixation cross. The target is the arrow at the center. By using two buttons on the keyboard, participants are asked to respond as quickly and accurate as possible to which direction the target arrow points. The target can be flanked by distractors which are either congruent (pointing in the same direction as the target) or incongruent, or by no distractors (neutral). Before each trial, one of four cues is presented: a spatial cue which indicate where the arrows will appear, and three cues which do not provide information about the location of the arrows (no-cue, center-cue, and double-cue). See Fan et al. (2002) for further details.

Calculation of attentional functioning measures are based on mean reaction time (RT) on correct trials (excluding RTs above and below 3 *SD).* Three estimates of attentional functioning are computed as follows: Alerting = mean $RT_{no\text{-}cue}$ – mean $RT_{double\text{-}cue;}$ Orienting =

mean $RT_{center\text{-}cue}$ – mean $RT_{spatial\text{-}cue;}$ Executive = mean $RT_{incongruent}$ – mean $RT_{congruent}$. Note that lower alerting and orienting scores indicate poorer performance, while higher executive scores indicate poorer conflict resolution.

Statistical Analyses

Analyses involved four steps: 1) pre-processing of ESM-data, 2) estimation of person-specific networks, 3) calculation of centrality indices, and 4) examination of correlations between centrality indices and attentional functioning measures.

Interest, positive affect, and activity items were reverse coded, and are therefore hereby referred to as "interest loss", "low positive affect", and "passivity", respectively. Pre-processing of ESM-data started by excluding participants who responded to less than 30 measurements (Epskamp, 2015). We removed the linear trend of variables that showed a significant linear trend over time (Fisher et al., 2017). Following this, we examined the overall correlations between the eight items measuring specific depression symptoms. One variable pair was highly correlated: ruminating - negative thoughts (r = .74), likely driven by overlap between constructs. Given that network analysis assumes that each symptom represents distinct constructs, we included 'ruminating' (and excluded 'negative thoughts') for further analyses. Correlations between the remaining variables ranged from .04 to .58. To check whether results were sensitive to this item selection, we conducted sensitivity analyses where 'negative thoughts' was included in the network models instead of 'ruminating'.

Person-specific networks were estimated using the var1-function in the *R* package *psychonetrics*, with full-information maximum likelihood estimator and default settings. For each participant, we estimated a temporal network (in which symptoms predict one another over time) and a contemporaneous network (in which symptoms predict one another in the same measurement window). We used *qgraph* to plot two sample participant's symptom networks for illustration, where symptoms are depicted as nodes, and associations between symptoms are depicted as edges. The temporal networks were estimated using lag-1 vector autoregression (VAR) modelling, where one variable predicts another in the next window of measurement (represented in the network as an edge with an arrowhead). We specified the model so that the first response of the day was not regressed on the last response of the previous day. The contemporaneous network was estimated from the residuals of the lag-1 VAR model. Here, associations represent partial correlations controlled for temporal effects and all other variables in the same window of measurement (thus represented in the network as edges without arrowheads).

We used qgraph to calculate standardized expected influence centrality indices based on the contemporaneous networks, and standardized outgoing expected influence centrality based on the temporal networks. Expected influence reflects a node's cumulative influence within a network, and outgoing expected influence reflects the influence a node has on other nodes in the network (Robinaugh et al., 2016).

Finally, bivariate correlations between centrality indices and attentional functions were calculated.

Results

Sample Characteristics

Six participants were excluded from further analyses because they did not return for assessment of attentional functioning, and thirty participants were excluded because they responded to fewer than 30 ESM measurements. The final sample (n = 46) answered in total 2 072 of 2 990 ESM measurements (69 %). The sample consisted of 33 (72 %) women and 12 (26 %) men. Mean age was 44.5 years (SD = 11.2). Thirty-nine (85 %) had an educational level comparable to bachelor's level or above. Forty-four (92 %) fulfilled criteria for previous MDD, 22 (48 %) for ongoing MDD, and 33 (72 %) for on-going anxiety disorder. Mean BDI score was 23.7 (range = 3-53; SD = 11.4). Twenty-seven participants (59 %) used psychotropic medication. Means for attentional control measures were as follows: alerting = 30.2 (*SD* = 28.9); orienting = 62.7 (*SD* = 42.3); executive control = 138.0 (*SD* = 64.9).

Person-specific Networks

Visual inspection of person-specific networks showed large variability in symptom networks. The networks for two sample participants are presented in Figure 1. Edge thickness corresponds to the association strength. Blue edges represent positive associations between two given nodes, whereas red edges represent negative associations.

In sample participant #1's contemporaneous network we see that sadness is strongly connected with both fatigue and rumination. That is, when this participant reported being sad, higher levels of fatigue and rumination were also reported during the same window of measurement. These symptoms were also the most influential symptoms deemed by expected influence indices, ranging from 0.4 (rumination) to 1.4 (fatigue). For instance, there were strong edges between the same symptoms in the temporal network. Notably, these edges represent cross-lagged associations: being sad predicts rumination and low positive affect in the next measurement. The most influential symptom in the temporal network was sadness (outgoing expected influence = 1.4).

Sample participant #2's contemporaneous network showed that strong associations emerged between interest loss, concentration problems, rumination, and passivity. The most influential symptom was interest loss (expected influence = 1.1). The temporal network showed, for instance, that interest loss predicted rumination and low positive affect in the next time window. The most influential symptom in the temporal network was passivity (outgoing expected influence = 0.5).

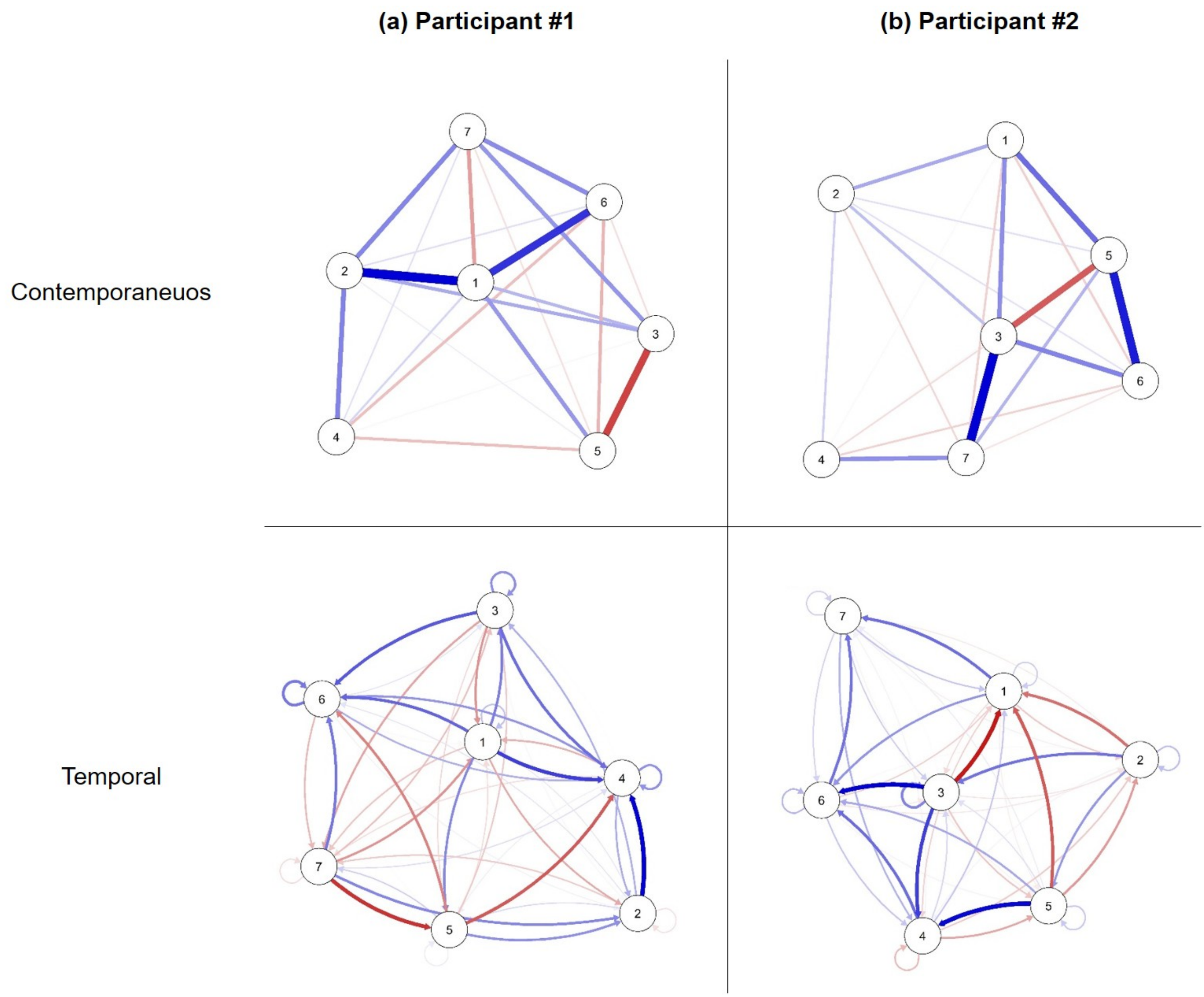

Figure 1

Contemporaneous and Temporal Networks for Two Sample Participants.

Note. Edge thickness reflects the magnitude of the association (blue = positive, red = negative).1 = Sadness; 2 = Fatigue; 3 = Interest loss; 4 = Low positive affect; 5 = Concentration problems; 6 = Ruminating; 7 = Passivity.

Associations Between Symptom Centrality and Attentional Functioning

Correlations between symptom centralities and attentional functioning are presented in Table 1. Based on contemporaneous networks, results showed significant correlations between fatigue and orienting (r = -.30, $p < .05$), and interest loss and alerting (r = -.32, $p < .05$). Based on temporal networks, results showed a correlation between low positive affect and orienting (r = -.35, $p < .05$).

Sensitivity Analysis

Correlations based on network models where ‘negative thoughts’ was included instead of ‘ruminating’ were examined. Based on contemporaneous networks, results showed that fatigue and orienting were still correlated (r = -.32, $p < .05$). However, the correlation between interest loss and alerting was non-significant (r = -.20, p = .17). Based on temporal networks, low positive affect and orienting were still correlated (r = -.31, $p < .05$). There were no other statistically significant correlations between attentional functioning and depressions symptoms.

Table 1

Correlations Between Symptoms and Attentional Functioning

Variable	1	2	3
1. Alerting			
2. Orienting	-.10		
3. Executive	.05	-.30*	
Contemporaneous networks			
Sadness	-.12	-.08	-.02
Fatigue	.25	**-.30***	.04
Interest loss	**-.32***	.09	-.06
Low positive affect	-.16	.11	-.06
Concentration problems	.25	-.15	-.13
Ruminating	-.21	.26	-.22
Passivity	.22	.04	.22
Temporal Networks			
Sadness	-.06	-.12	.21
Fatigue	-.06	-.02	.18
Interest loss	-.24	-.27	.02
Low positive affect	-.04	**-.35***	.01
Concentration problems	.23	-.12	.11
Ruminating	-.17	.22	.14
Passivity	-.19	-.16	.12

Note. Significant correlations in boldface. * indicates $p < .05$

Discussion

Theoretical models have postulated that attentional impairments play an important role in depression vulnerability. Unfortunately, most extant research is done at the group level and has mainly considered depression as a singular disease entity. Our study set out to examine the association between individuals' depressive symptom profiles, meaning the extent to which specific symptoms appear to play a more central role in individual symptom dynamics in daily life, and objective indicators of attentional functioning.

Results showed that higher centrality for low positive affect and fatigue was related to reduced orienting efficiency. Regarding low positive affect, this finding was observed based on temporal networks, reflecting symptom dynamics over time, suggesting that individuals whose daily symptom dynamics are highly influenced by low positive affect have reduced orienting efficiency. Regarding fatigue, this finding was observed based on contemporaneous networks. Contemporaneous networks reflect co-occurring symptom dynamics. This suggests orienting efficiency is reduced when fast-paced symptom dynamics is highly influenced by fatigue. Higher centrality for interest loss was associated with reduced alerting efficiency (contemporaneous networks), but this finding was not statistically significant in the sensitivity analysis. We therefore limit our discussion to the associations involving orienting.

Low positive affect is a core aspect of what has been termed anhedonia in depression (i.e., a reduced ability to experience pleasure; Treadway & Zald, 2011). Depression in general is associated with blunted sensitivity to rewards (Anderson et al., 2014; Pechtel et al., 2013). Anhedonia, specifically, involves reduced willingness to modify behavior to obtain rewards, impaired ability to learn from obtaining rewards, and a dissociation between experienced pleasure and willingness to invest effort into achieving pleasure (Grahek et al., 2018). This is relevant as control of attentional resources is guided by reward-processing, both directly through associative learning, and indirectly by modulating goals and motivation (Anderson, 2016). This may explain the link between low positive affect and reduced orienting.

Our findings are consistent with prior studies in which low levels of positive affect in daily life have shown to predict an increase in self-reported cognitive complaints in remitted depressed patients (Hoorelbeke et al., 2019). Relatedly, building on prior contemporaneous network models, low levels of positive affect have been associated with poorer cognitive functioning in patients with a history of depression.

Interestingly, fatigue may in many ways be considered indistinguishable from anhedonia (Billones et al., 2020). Fatigue may reduce the ability to allocate attention efficiently (Boksem et al., 2005), and is associated with reduced orienting efficiency (Feltmate et al., 2020). Orienting is an active process which aligns "attention with a source of sensory input" (Posner, 1980, p. 4), and this process may be hampered by fatigue. For example by increasing distractibility and decreasing flexibility (Müller & Apps, 2019), which might lead to an increased threshold of responding, and increased response times (Posner & Petersen, 1990).

Studies emphasizing anhedonia and fatigue as indistinguishable have pointed to reward-processing as the common mechanism (Billones et al., 2020). Early studies argued that fatigue can be "traced to neural systems that block reward reinforcement from the source of pleasurable stimuli" (Billones et al., 2020, p. 8). According to contemporary models, the neural "block" seems to involve functional changes in frontal cortex and the insula, as well as in subcortical areas related to motivation, such as the nucleus accumbens (Boksem & Tops, 2008; Müller & Apps, 2019). Changes in these areas correspond with a behavioral shift in the weighing of costs and rewards. As attention is a behavior which is responsive to rewards and effort (Kahneman, 1973), fatigue may modulate orienting by increasing the perceived costs of a being attentive (Müller & Apps, 2019). Alternatively, fatigue may arise once the individual perceives that the costs of being attentive outweigh the rewards (Boksem & Tops, 2008).

This study is among the first to model unique associations between centrality of specific depressive symptoms and cognitive risk factors for depression. These findings suggest that heterogeneity of depressive symptoms may reflect different pathways towards depression. The results may also account for prior inconsistencies in the literature pertaining the association between cognitive functioning and depressive symptomatology. At the same time, these findings should be interpreted with caution. Several participants were excluded due to low ESM response rates. This may have resulted in decreased statistical power to detect significant associations. Given the exploratory nature of this proof-of-principle study, we did not control for multiple comparisons. Items were selected based on DSM-5 and clinical experience, but were not formally validated. Moreover, our analyses rely on a rather minimal set of depressive symptoms which do not fully capture the wide variety of depressive symptoms.

Given content overlap and strong associations between the items “rumination” and “negative thoughts”, we estimated separate network models for each of these items. Sensitivity analysis rendered highly similar results, adding to the reliability of the pattern of findings observed in the current study. Nonetheless, results need to be replicated in a larger sample before firm conclusions can be made.

Regarding centrality indices, it should also be acknowledged that there has been debate regarding the nature, reliability and clinical relevance of centrality measures derived from VAR models (Bringmann et al., 2019; Piccirillo et al., 2019). However, a recent study examining eating disorder symptoms has shown that symptoms that were identified as central using group-level VAR models predicted eating disorder severity at one and six months (Levinson et al., 2021).

Our study provides partly temporal control of the effects, as symptom centrality were estimated based on the two weeks preceding lab assessment of attention. However, we had no data which could inform whether reduced attentional functioning may explain symptom centrality the next two weeks. It would be interesting for future research to investigate whether associations between level of cognitive functioning and depressive symptom centrality differ pending on clinical status. The sample was a convenience sample consisting of subjects with both ongoing and remitted depression with and without comorbid disorders. For example, a majority of participants had an ongoing anxiety disorder. The potential role of comorbidity on the associations between symptom dynamics and attentional functioning was not examined in the present study.

Pleasurable and arousing stimuli in the context of approach behavior is associated with increased orienting efficiency (Bradley, 2009). Interventions which targets reward-processes and anhedonia symptoms in depression (Craske et al., 2016) may therefore improve orienting. Another common treatment for depression that could be relevant to increase orienting efficiency is behavioral activation, which targets reward-related processes through increasing approach behavior (Nagy et al., 2020). Wells' attention training technique (ATT; Wells, 1990), which has shown promise in recurrent depression (Papageorgiou & Wells, 2000) may also improve orienting. During ATT, subjects are guided to listen to sounds originating from different locations (e.g., inside and outside the consulting room), or audiotaped sounds at different loudness and from different spatial locations. ATT seems to target orienting and may therefore improve orienting efficiency. Finally, cognitive training seems to improve cognitive functioning in depression and improve symptoms (Koster et al., 2017). Although speculative, it could be that interventions which successfully improves attention may alleviate anhedonia and fatigue specifically.

Conclusion

We set-out to model the associations between depression symptom centrality in daily life and observed impairments of attentional processing in a mixed sample of patients with ongoing and remitted major depression. We estimated person-specific VAR network models and examined the associations between level of symptom centrality, and measures of alerting, orienting, and executive control based on the ANT. Results showed associations between centrality of low positive affect and fatigue, and reduced orienting efficiency. These findings point towards the importance of taking into account individual symptom dynamics when considering cognitive functioning in the context of depression.

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