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The association between depression symptoms and reduced executive functioning is primarily linked by fatigue

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ABSTRACT

Depression is associated with reduced executive functioning. Still, we lack a more detailed understanding of the factors explaining this association. Addressing several limitations in the previous literature, we examine whether poor executive functioning is associated with specific depression symptoms using a network approach. The sample consisted of currently depressed, previously depressed, and never-depressed individuals ($n = 289$; 67% female; M age = 37.4 years). Associations between poor executive functioning and nine depression symptoms were estimated using regularized Gaussian graphical modelling. Results showed associations between poor executive functioning and fatigue/energy loss, interest/pleasure loss, appetite changes, sleep problems, and concentration difficulties. Fatigue/energy loss was the most important symptom bridging depression with poor executive functioning. There were no direct associations between executive functions and core negative affect symptoms. Findings are discussed in the context of motivational impairments, and potential mechanisms such as immunological- and stress-related processes are considered.

1. Introduction

Besides the core symptoms such as depressed mood and interest or pleasure loss, people with depression often report cognitive impairments (Millan et al., 2012). This is reflected in the DSM-5 (American Psychiatric Association, 2013) Major Depressive Disorder criteria as concentration difficulties or indecisiveness. Importantly, cognitive complaints in depression is not only explained by psychomotor slowing but also involves deficits in executive function (e.g., Nuño et al., 2021). Executive functions refers to a cluster of top–down processes needed when concentrating or paying attention, making decisions, and coordinate other low-level cognitive processes to guide behaviour (Banich, 2009; Diamond, 2013). These functions predict diverse self-regulatory behaviours important to mental disorders (Miyake and Friedman, 2012), mediate psychosocial impairment (McIntyre et al., 2013), and have been implicated in the etiology and maintenance of depression (LeMoult and Gotlib, 2019). Impairment in executive functions have been extensively documented by objective neuropsychological tests in depression (Snyder, 2013), and have been increasingly considered a transdiagnostic phenomenon (Abramovitch et al., 2021).

The executive functions have been conceptualized as three interrelated abilities: Inhibition of dominant responses, monitoring and updating information in working memory, and shifting between mental sets or tasks (Friedman and Miyake, 2017; Miyake et al., 2000). These functions are separable (reflecting diversity), but do also correlate, thus capturing some common underlying ability (reflecting unity). Together these functions monitor and maintain goals, synthesize information about the context, and guide cognitive processing (Banich, 2009). Poor executive functioning have biological underpinnings, as demonstrated by structural and functional changes in the prefrontal cortex (Friedman and Miyake, 2017), and substantial genetic influences (Friedman et al., 2008). Although results are mixed, research generally show that depression is associated with some impairment in all executive functions (LeMoult and Gotlib, 2019). Reduced executive functioning is present in

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first episode of depression (Varghese et al., 2022), persists even after remission (Hasselbalch et al., 2011; Rock et al., 2014), and worsen with repeated episodes (Semkovska et al., 2019). Cognitive control training, seeking to alleviate these impairments in executive functioning directly, can lead to improvements in cognitive functioning (Thérond et al., 2021) and reductions in depressions symptoms (Koster et al., 2017). Executive impairments is therefore assumed to be a core feature of depression, should not just be considered an epiphenomenon, and may be a valuable target for interventions to depression (Rock et al., 2014).

Although depression-related impairments in executive functioning have attracted much research, there is still a lack of a more fine-grained understanding of the causes, nature, and mechanisms involved (Grahek et al., 2018). For example, executive functioning in relation to positive affect (i.e., consummatory/hedonic aspects) and motivational processes have received little attention (for notable exceptions, see Craske et al., 2016; Grahek et al., 2019; Pizzagalli, 2014). This is pertinent, as interest and pleasure loss reflect one of the two core symptoms of depression. To gain a more nuanced and precise understanding of the role of executive functions in depression, one way forward may be to break down complex executive impairments into multiple smaller-scale problems, and seek more mechanistic explanations of how these impairments relate to different aspects of depression (Grahek et al., 2018).

This aspiration aligns with the fact that depression is a remarkably heterogenous disorder (Goldberg, 2011), with numerous plausible etiological and maintaining pathways (e.g., Charney and Manji, 2004; Harrington et al., 1996; Hasler, 2010; Wittenborn et al., 2016). Different depression symptoms differ from each other in their risk factors, biological processes, psychosocial functioning, and triggering life events (Fried, 2015). Following this, it would be reasonable to expect that poor executive functioning may also be differentially related to specific depression symptoms. This has not been addressed in the previous literature.

Another serious limitation with previous research is that it has been primarily based on comparisons of clinical versus non-clinical groups, or by examining executive functions in relation to a sum-score on depression inventories (e.g., Snyder, 2013). Relying on case-control studies implies that depression is qualitatively distinguishable from periods of normal low mood. However, subthreshold depression is often a precursor for later major depressive disorder, and most studies show that depression is an endpoint along a continuum of depressive symptomatology (Ruscio and Ruscio, 2000). Given that there is no naturally occurring clear-cut threshold between depression cases and controls, this type of research may mask etiological important relationships between executive impairment and depression (Fried, 2015). Moreover, examining the association between executive impairments and a sum-score from a continuous depression measure makes it impossible to detect potentially important symptom-specific relationships (Fried, 2017). Following this line of reasoning we propose that relying on depression sum-scores makes it impossible to illuminate whether poor executive functioning is related to the core symptoms of depression, or other aspects of depression.

This study explore the associations between poor executive functioning and depression using network analysis (Borsboom and Cramer, 2013), which can identify unique shared associations in highly multivariate data (Epskamp and Fried, 2018). Using this approach enables us to conduct a comprehensive analysis of the role of executive functioning in depression at the symptom-level and address some of the short-comings in the present literature.

Many studies have examined the association between executive impairments and depression, however, most studies have been hampered by small samples, and/or only examining one type of executive function (Snyder, 2013). A few studies have used symptom-specific approaches or network analysis. For example, Hoorelbeke et al., (2016) used network analysis to explore the associations between a cognitive control task (the Paced Auditory Serial Addition task), self-reported executive impairments, and a composite measure of depression symptoms. Hoorelbeke et al. (2019) examined associations between "cognitive complaints" (i.e., the subjective experience of executive- and working memory impairments) and "depressive complaints" using network analysis of time-series data. A study by Beevers et al. (2019) examined associations between specific depression symptoms and two types of negative cognitive biases. Changes in attentional bias has been found to be associated with reduced anxiety symptoms as measured by the Hamilton Rating Scale for Depression in a previously depressed sample (Kraft et al., 2019). More recently, Coussement and Heeren (2022) examined the associations between symptoms of generalized anxiety, symptoms of depression, and attention control, and found that sleep problems and fatigue emerged as hubs bridging depression, generalized anxiety and impairments in attention control. However, to the best of our knowledge, no studies have examined the links between broad measures of executive functioning and individual depression symptoms.

Addressing the aforementioned limitations in the literature, we model depression as a network of depression symptoms ("nodes") and the association between them ("edges"), and include nodes representing poor executive functioning based on laboratory measures, in line with recent recommendations (Bernstein et al., 2017; Jones et al., 2017). Following a diversity account of executive functioning, we include three nodes reflecting inhibition, shifting, and updating (of working memory). We also address other shortcomings in the extant literature by using a large sample ($n = 289$), including individuals demonstrating low, medium, and high levels of depression symptomatology. The main aim of the paper is to examine whether poor executive functioning is related to specific depression symptoms.

2. Methods

2.1. Sample

This study is a secondary analysis of data collected in a project examining executive impairments in depression (Research Council of Norway project no. 175387/V50). Depressed, previously depressed, and non-depressed individuals ($N = 306$) were recruited from outpatient psychiatric clinics, newspaper advertisements and by posters in Oslo, Norway. Inclusion criteria were age 18–65 years and fluency in Norwegian. Diagnostic status was assessed by clinical psychologists or trained psychology students using the Norwegian version of the Structured Clinical Interviews for DSM-IV criteria I (SCID; First and Gibbon, 2004). The Norwegian version of SCID has shown acceptable interrater reliability (e.g., Nordahl et al., 2005; Preljevic et al., 2012). Participants who fulfilled criteria for psychotic disorder, manic episodes, or developmental disorders (e.g., attention deficit hyperactivity disorder or Asperger's syndrome) were excluded. Participants were interviewed on neurological status and head injuries, and excluded if they reported any neurological illnesses, moderate to severe brain injury, or any head injury within the past 6 months. Depression symptoms were assessed using *Beck's Depression Inventory II* (Aasen, 2001; Beck et al., 1996). 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 and the Norwegian Social Science Data Services.

2.1.1. Sample characteristics

Seventeen participants who had missing values on one or more executive measure or depression symptoms were excluded from the analysis. The final sample ($n = 289$) included 193 (67%) female and 96 (33%) men. Mean age was 37.4 years ($SD = 13.1$). About half of them (56%) had an educational level comparable to bachelor's level or above. BDI sum scores ranged from 0 to 48 with a mean of 8.6 ($SD = 11.1$). Internal consistency for the BDI was good (McDonald's omega = 0.96). Fifty-five participants (19%) had current major depressive disorder (MDD), 51 (18%) had previous MDD, and 182 (63%) had no previous or current MDD. Thirty (10%) used antidepressants. Correlations between variables

are presented in Table S2 (in Supplementary Materials), and descriptive statistics per diagnostic group are presented in Table S3 (in Supplementary Materials).

2.2. Neuropsychological assessment of executive functioning

Neuropsychological assessment of executive functions was administrated in a fixed order within one session. Participants could take breaks when needed. We briefly present the tasks here. For further details, see the Supplementary Materials. The Stop Signal Task, the Intra-Extra Dimensional task, and the Spatial Working Memory task were administrated using the *Cambridge Neuropsychological Test Automated Battery* (2009).

2.2.1. Inhibition

The Stop-Signal Task (SST) directs the participant to override a prepotent go-response when presented with an infrequent stop signal (a beep). Inhibitory efficiency is operationalized as a stop-signal reaction time (SSRT). The SSRT is estimated through automatic adjustment of the delay between the go stimulus and the stop signal. A longer SSRT represents reduced inhibition ability (Logan et al., 1997). Analyses excluded four participants with scores +3 *SD*.

In the Stroop task inhibition variant (The Color-Word Interference Test; Delis et al., 2001), the participant is instructed to name the printed color of color-word names, thus requiring to inhibit the pre-potent reading response of the word. Higher interference cost scores (the contrast between completion times on simple color naming and on inhibition conditions) reflects reduced inhibitory control. Analyses excluded five participants with scores +3 *SD*.

2.2.2. Shifting

The Stroop switching task is identical to the Stroop inhibition task variant, except that participants occasionally have to switch to the non-inhibitory response set (reading the color-word). Higher switch cost scores (the contrast between completion times on inhibition condition and switching conditions) reflects reduced shifting ability. Analyses excluded four participants with scores +3 *SD*.

The Intra-Extra Dimensional task (ID/ED) requires participants to pay attention to different examples within a stimulus dimension and shift attention from one set of stimuli to a new, formerly unimportant set of stimuli across nine stages. Shifting ability is operationalized as total errors adjusted for whether the entire task is completed. A high total error adjusted score represents reduced shifting ability (Kaplan et al., 2006). Analyses excluded two participants with scores +3 *SD*.

2.2.3. Updating

The Spatial Working Memory task (SWM; Owen et al., 1990) requires subjects to search through several visually presented boxes to locate tokens. After a token is located, the token will not appear in the same box during that same trial. The number of boxes is gradually increased until a total of eight boxes have to be searched. Accuracy of working memory is operationalized as the between-trial errors score (registered when the subject searches for a token in a box where a token has previously been found). Higher between-trial error scores indicate failures in updating working memory. Analyses excluded two participants with scores +3 *SD*.

In the present version of Paced Auditory Serial Addition Test (PASAT; Gronwall, 1977; Landrø et al., 2004) participants listen as 60 one-digits is read at a 2-s rate. Participants are asked to add each digit number presented to the digit preceding it and tell the sum to the test administrator. The number of total correct responses reversed reflects decreased updating ability. Analyses excluded one participant with a score +/3 *SD*.

2.3. Statistical analyses

We calculated nine depression symptom scores corresponding to the DSM-5 depression criteria using the means of relevant BDI items (for details, see Table S1 in Supplementary Materials). This approach was chosen because there is a large conceptual overlap between several BDI items - network analysis assumes that each symptom represents distinct constructs - and to ensure adequate statistical power (Epskamp and Fried, 2018). To rule out the possibility that resulting network structure is fully dependent on the chosen DSM-5 model, we also examined an alternative model including all 21 BDI items.

Three composite measures of executive functioning were calculated based on the average of relevant indicators. The indicators were standardized before calculating the composite measures. “Inhibition” reflects the average of Stroop interference cost and SSRT, “shifting” reflects the average of the ID/ED score and Stroop switching cost, and “updating” reflects the average of the SWM score and the PASAT score.

Network analysis was performed using the R package *qgraph* using default settings (Epskamp et al., 2012) to estimate a network (a graphical Gaussian model) where nodes represent depression symptoms and inhibition, shifting, and updating. Edges between nodes represents conditional independence relationships (regularized partial correlations) between nodes when controlling for the effects of all other nodes. See Epskamp and Fried (2018) for a detailed description of the statistical procedure. Importantly, this procedure eliminates spurious associations (edges) attributable to the influence of other nodes in the network and shrinks trivially small associations to zero, thereby removing potentially “false positive” edges from the network and producing a sparse graph comprising only the strongest edges. Following guidelines for clinical network analysis (Epskamp and Fried, 2018), node variables were non-paranormally transformed using the R package *huge* (Zhao et al., 2015). We computed expected influence centrality to quantify the importance of each node in the resulting network (Robinaugh et al., 2016). Nodes that serve as bridges between depression symptoms and poor executive functioning were identified by computing the bridge expected influence index using the R package *networktools* (Jones, 2021; Jones et al., 2021). Bootstrapping routines implemented in R package *bootnet* (Epskamp, 2020) were used to gain information on the precision of the parameter estimates. See Supplementary Materials for more details.

3. Results

3.1. Associations between poor executive functioning and depression symptoms

Table 1 shows the associations between poor executive functioning, depression symptoms, as well as age and education. Poor executive functioning was correlated with BDI, age, and education.

Fig. 1 shows the results from the network analysis. Green edges represent positive regularized partial correlations, whereas red ones represent regularized negative partial correlations. There are five depression symptom nodes connecting to poor executive functioning-nodes. The edges are as follows: ‘updating’ is connected to ‘fatigue or energy loss’, ‘interest or pleasure loss’, and ‘concentration difficulties’; ‘shifting’ is connected to ‘fatigue or energy loss’, ‘appetite changes’, and ‘sleep changes’; ‘inhibition’ is connected to ‘sleep change’ and ‘concentration difficulties'.

Bootstrapped confidence intervals of edge weights suggest that edges are fairly stable (Figure S1 in Supplementary Materials). Many edge-weights were not significantly different from others (Figure S2 in Supplementary Materials). Among the edges connecting executive functions with depression symptoms, no edge pairs had significantly different edge-weights. This precludes comparing differences in the edge-weights.

Controlling for the possible effects of age, education and sex on the edges between poor executive functioning and depression symptoms, we estimated the same network including age, education, and sex (male = 0; female = 1) as nodes. Results showed that ‘updating’ was connected to ‘fatigue or energy loss‘, ‘interest or pleasure loss’, and ‘concentration difficulties or indecisiveness’, and that ‘shifting’ was connected to ‘fatigue or energy loss‘, ‘sleep problems’, and ‘appetite changes’ (see Figure S6 in Supplementary Materials).

Table 1
Means, standard deviations, and correlations (not corrected for multiple testing) of study variables.

Variable	*M*	*SD*	1	2	3	4	5	6	7	8	9	10	11	12	13	14
1. Depressed mood	0.3	0.6														
2. Interest or pleasure loss	0.4	0.6	.71**													
3. Appetite changes	0.4	0.7	.58**	.49**												
4. Sleep problems	0.7	0.8	.54**	.52**	.47**											
5. Agitation	0.3	0.5	.52**	.50**	.46**	.36**										
6. Fatigue or energy loss	0.6	0.8	.69**	.72**	.55**	.63**	.48**									
7. Worthlessness	0.4	0.6	.77**	.75**	.55**	.62**	.49**	.75**								
8. Concentration difficulties or indecisiveness	0.4	0.7	.63**	.69**	.58**	.54**	.48**	.77**	.73**							
9. Suicidal thoughts	0.2	0.4	.63**	.54**	.35**	.40**	.36**	.52**	.57**	.51**						
10. BDI	8.6	11.1	.84**	.83**	.68**	.69**	.60**	.87**	.90**	.86**	.63**					
11. Age	37.4	13.2	.03	.18**	.01	.08	.00	.15**	.07	.08	−.02	.11				
12. Education (reversed)	−16.1	2.8	.24**	.25**	.15*	.14*	.22**	.19**	.28**	.19**	.15*	.26**	−.06			
13. Updating	−0.01	0.82	.19**	.24**	.19**	.21**	.13*	.31**	.22**	.28**	.11	.28**	.43**	.12*		
14. Shifting	−0.05	0.63	.11	.07	.14*	.16**	.05	.17**	.10	.11	.04	.15*	.12*	.06	.19**	
15. Inhibition	−0.05	0.66	.17**	.12*	.14*	.05	.08	.16**	.17**	.21**	.13*	.19**	.28**	.09	.36**	−.10

Note. * indicates $p < .05$. ** indicates $p < .01$.

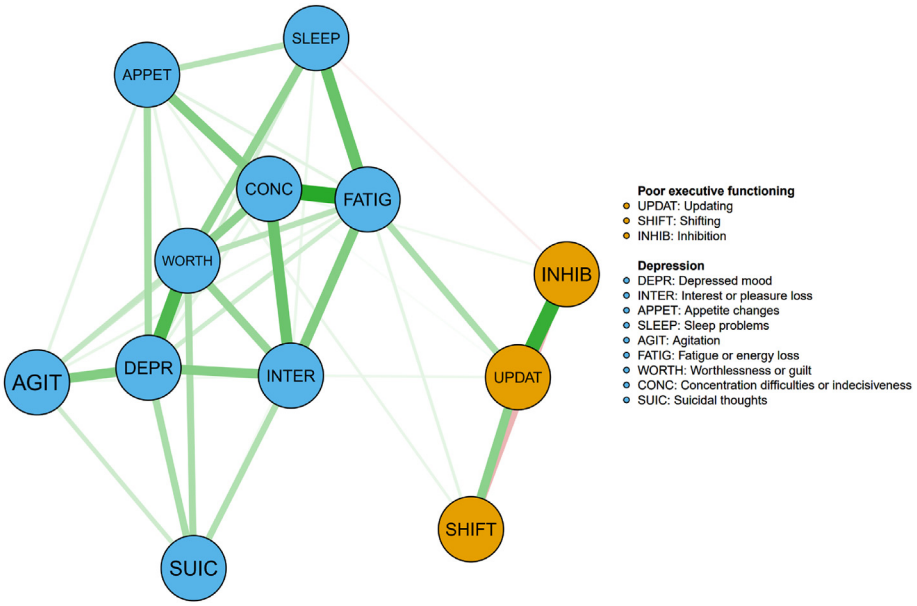

Fig. 1. *Regularized Partial Correlation Network of Poor Executive Functioning and Depression Symptoms*. Note. Edge thickness reflects the magnitude of the association (green = positive, red = negative). The thickest edge is 'concentration difficulties or indecisiveness' – 'fatigue or energy loss' (edge weight = 0.34). The thickest edge between executive functioning and depression symptoms is 'updating – 'fatigue or energy loss' (edge weight = 0.13). (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

3.1.1. *Expected influence of nodes*

The most influential nodes (Fig. 2) were 'fatigue/energy loss', 'depressed mood', 'worthlessness/guilt', 'concentration difficulties or indecisiveness', and 'interest or pleasure loss'. Expected influence estimates were highly stable (CS-coefficient = .75), and bootstrapped difference test between the nodes' expected influences revealed that most were significantly different from other nodes (see Figure S3 and S4 in Supplementary Materials).

3.1.2. *Bridge expected influence of nodes*

Bridge expected influence indices between poor executive functioning and depression symptoms (Fig. 2) show that 'fatigue/energy loss' is the most influential symptom, and 'updating' and 'shifting' are the most influential executive functions. Bridge expected influence estimates were fairly stable (Figure S3 in Supplementary Materials), with a CS-coefficient of 0.28, which is above the recommended minimum CS-coefficient of 0.25 (Epskamp et al., 2018). Bootstrapped difference test between the nodes' bridge expected influences showed that, among depression symptoms, only 'fatigue or energy loss' were significantly more influential than other nodes (Figure S5 in Supplementary Materials).

3.2. *Alternative model including all BDI items*

In the alternative model (Figure S7 in Supplementary Materials), edges between poor executive functioning and depression symptoms included the following symptoms: 'appetite changes', 'sleep problems', 'loss of energy', 'tiredenss/fatigue', 'self-dislike', 'self-criticalness', 'concentration difficulties', 'loss of interest', and 'indecisiveness'. The most influential node in bridging poor executive functioning and depression symptoms was 'loss of energy' (Figure S8 in Supplementary Materials). Overall, compared to the DSM-5 model, results were similar. Stability analyses are presented in Figure S9-12 in the Supplementary Materials.

4. Discussion

Overall, the main finding in this study is that reduced executive functioning is associated with fatigue/energy loss, interest/pleasure loss, sleep problems, appetite changes and concentration difficulties. Fatigue/energy loss was identified as the most influential symptom bridging poor executive functioning and depression symptoms. Strikingly, there were no direct associations between poor executive functioning and core negative affective symptoms such as depressed mood and worthlessness.

Our results highlight a link between fatigue and poor executive

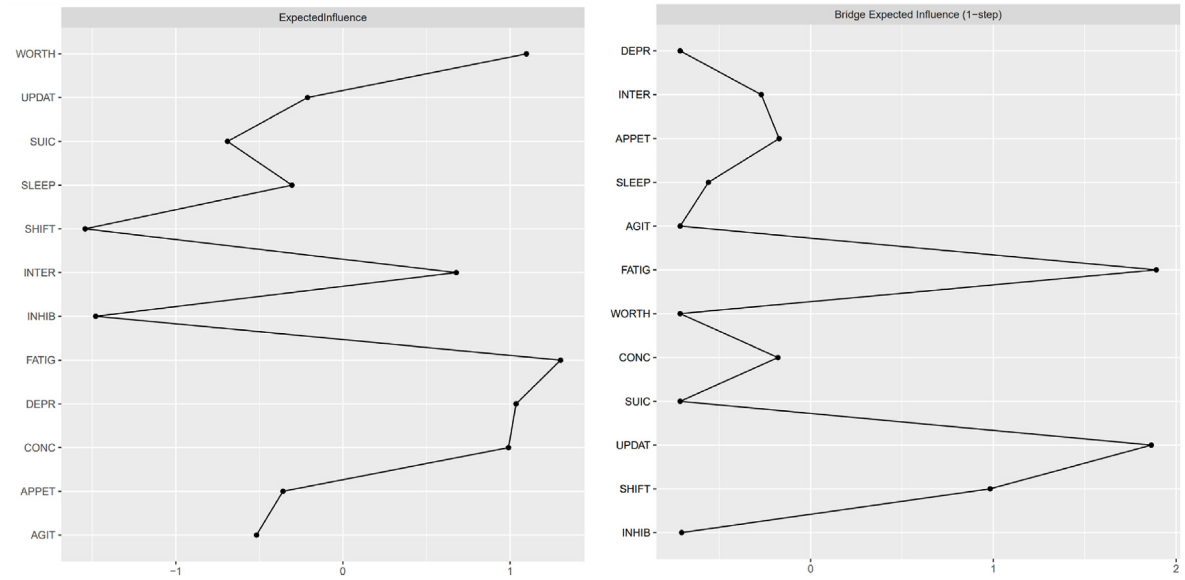

Fig. 2. Expected Influence and Bridge Expected Influence of Nodes. *Note.* Centrality indices (z-scores) for expected influence (left) and bridge expected influence (right). WORTH = Worthlessness or guilt; SUIC = Suicidal thoughts; SLEEP = Sleep problems; INTER = Interest or pleasure loss; FATIG = Fatigue or energy loss; DEPR = Depressed mood; CONC = Concentration difficulties or indecisiveness; APPET = Appetite changes; AGIT = Agitation; SHIFT = Shifting; UPDAT = Updating; INHIB = Inhibition.

functioning. Some have proposed that exertion of cognitive control consumes a considerable amount of glucose (Gailliot, 2008). Following this, a general depression-related dampening of executive functions could be viewed as consequence of an energy conservation mechanism. This is in line with research showing that depression is associated with reduced metabolic and neural activity in brain regions supporting executive functions (for example the prefrontal cortex; Drevets, 2000). This could also explain the observed association between poor executive functioning and concentration difficulties.

However, a recent review of the literature shows that the association between reduced glucose levels and reduced executive functioning may best be explained by reduced motivation to exert cognitive effort, rather than a direct effect of glucose depletion (Shenhav et al., 2017). For instance, fluctuations in glucose levels may instead lead to a reallocation of goals, seeking to maximize rewards while minimizing the costs associated with cognitive effort. As fatigue increases, the value of exerting effort on a task declines, and leads to reduced effort and reduced performance in cognitive tasks (reduced task accuracy and slower reaction times; Müller and Apps, 2019). Note here that this explanation parallels the previously mentioned motivational accounts of poor executive functioning (Grahek et al., 2019).

Our findings showed a link between poor executive functioning and sleep problems, which is in line with previous reports (Lowe et al., 2017). However, it is possible that sleep problems could also explain the associations between poor executive functioning and fatigue/energy loss. For example, that executive functioning may be reduced when sleep problems are severe enough and leads to fatigue. Although possible, the present results are not in line with this, as including sleep problems as node in the network effectively controls for this possibility. Nevertheless, this node reflected a BDI item measuring both increased and decreased sleep, leaving us still questioning this possible confound. Including more refined measures of sleep would provide better statistical control for this.

It is important to appreciate that poor executive functioning and fatigue is observed in many other psychiatric and somatic disorders often comorbid with depression. Reduced executive functioning has in fact been associated with most mental disorders (Snyder et al., 2015), suggesting that broad executive impairments are nonspecific to depression. Fatigue is often present in mental disorders that are co-morbid to depression (Mozuraityte et al., 2022), in neurological disorders (Chaudhuri and Behan, 2004) and cancer (Wagner and Cella, 2004), and during and after infections (for example in dengue fever; Seet et al., 2007), as well as in the diagnostic criteria for generalized anxiety disorder (Del Barrio, 2016). The link between executive functioning and fatigue is therefore likely to be nonspecific to depression.

Previous research has underscored the importance of poor executive functioning in the processing of negative material and the maintenance of negative affect (LeMoult and Gotlib, 2019). Poor executive functioning affect people's ability to regulate negative affect through less effective implementation of adaptive emotion regulation strategies and more frequent use of maladaptive strategies (Joormann and Vanderlind, 2014). For example, reduced ability to inhibit irrelevant negative information from entering working memory and reduced ability to update working memory may alter information processing, resulting in prolonged processing of negative material (Joormann and Vanderlind, 2014). In this way, poor executive functioning hampers the ability to reinterpret negative situations in a more adaptive way and may impair the ability to disengage from rumination (Koster et al., 2011). Surprisingly, however, results showed no direct links between poor executive functioning and core negative affective symptoms. This is in contrast to the previous literature emphasizing the importance of reduced executive functioning for negative mood (Joormann and Vanderlind, 2014). Note, however, that we cannot exclude that the missing link between executive functioning and core negative affective symptoms is a false negative.

Another explanation for this divergence between our results and theory could be that previous studies did not account for the possible conditional dependence (e.g., fatigue) of both negative affect and reduced executive functioning which is likely to be present in depression samples. An alternative explanation is that the association between executive functioning and negative affect may be less pronounced in samples with relatively mild symptoms (as is the case for this study) versus samples with more severe symptoms. Although the present study covers the whole continuum of depression severity, from minimal to severe, mean symptom level was low and only 20% had ongoing major depressive disorder. Relevant to this are studies showing that individuals with higher depression severity demonstrate more pronounced executive impairments (McDermott and Ebmeier, 2009). A study including a sample demonstrating more severe symptoms could therefore lead to different findings.

Our results show that interest/pleasure loss and appetite changes was associated with poor executive functioning. However, this finding must be interpreted with caution as stability estimates showed that interest/pleasure and appetite changes loss was not significantly more influential compared to other nodes. Given that the estimates are accurate, this finding is in line with a recent discussion of anhedonia in executive functioning (Grahek et al., 2019). Motivation anhedonia is characterized as reduced motivation or drive to pursue rewards, and manifests in reduced appetitive behaviors and reduced interest in engaging in previously rewarding behaviors (Treadway and Zald, 2011). The presence of anhedonia has been found to impair the weighing of costs and benefits of exerting effort, and is associated with changes in reward-related processes, such as reduced approach motivation, reward anticipation and reward learning (Dillon et al., 2014). The behavioral results of anhedonia are decreased willingness to modify behavior to obtain rewards, impaired ability to learn from obtaining rewards, and dissociation between experienced pleasure and willingness to invest effort into achieving pleasure (Grahek et al., 2018). In this framework, poor executive functioning emerges as a consequence of lowered expected value of control and do not necessarily reflect a reduced ability to exert control. Aberrant dopamine signaling in mesolimbic areas has been linked with motivation and reward processing in depression (Nestler and Carlezon, 2006), which in turn mediate cognitive control (Yee and Braver, 2018). Although this is a plausible mechanism explaining our finding, our study cannot conclude whether this explains the observed relationship between interest/pleasure loss, appetite changes, and reduced executive functioning.

Fatigue, anhedonia, and other sickness-related behaviors have been emphasized as important maintaining factors in contemporary cognitive theories of depression (Beck and Bredemeier, 2016). Sickness behaviors refers to the coordinated change occurring in physically ill animals and humans during the course of infection (Dantzer et al., 2008). These include for example lassitude, lethargy, confusion, reduced social exploration, loss of appetite and sleepiness, and is often accompanied by fever. Following these clues leads to a literature implicating immunological mechanisms, as these have been associated with depression and fatigue (Lee and Giuliani, 2019), sickness behaviors (Dantzer et al., 2008), and reduced executive functioning (Marsland et al., 2006). Alternatively, executive impairment in depression has been hypothesized to be the result of a general “wear and tear”-mechanism denoting allostatic load (McEwen, 2003). Increased allostatic load is linked to reduced executive functioning (D'Amico et al., 2020), depression (McEwen, 2003), social stress (Saxbe et al., 2020), and immunological reactivity (Juster et al., 2010). Incorporating more refined measures of immunological markers, stress, and executive functioning in future studies would shed light on these matters.

Links between executive functioning, fatigue and anhedonia may be explained by another common cause, for example shared genetic influences. Both depression and executive functioning have substantial genetic components, and associations between poor executive functioning and depression symptoms have largely been shown to reflect correlated genetic influences (Friedman et al., 2018; Gustavson et al., 2019). A recent genome-wide interaction study shows that the genetic link between depression and reduced cognitive function may be explained by single nucleotide polymorphisms associated with neuronal development, neuroprotection, and maintenance of optimal cognition (Thalamuthu et al., 2022). Studies examining genetic influences on the association between executive functioning and specific depression symptoms are lacking.

Our model of executive functioning was based on measurement of three abilities: inhibition, shifting, and updating. This is consistent with a diversity-account of executive functions. The three executive functions we examined where chosen because they are commonly discussed in the depression literature. This model represents an intermediate level of complexity, and is not a comprehensive model of executive functioning. For example, we could apply the bi-factor model developed by Friedman et al. (2008), where a common executive functioning latent variable predicts all tasks (reflecting unity), and diversity is captured by a specific updating and a specific shifting factor. Recent studies, using this bi-factor model, have shown that depressive symptoms are primarily associated with the common executive functioning in both adults (Friedman et al., 2018) and youths (Snyder et al., 2019). Examining our data using a bi-factor model could provide further knowledge on the association between executive functioning and depression symptoms. However, such an approach requires at least three indicators per latent variable, and was therefore impossible to pursue due to limitations in the data.

Our findings cannot delineate the precise contribution of depression severity or status to executive functioning. Even though severe depression is often associated with worse performance and having recurrent depression is associated with greater impairments, it is still not clear whether the relationship is linear (McDermott and Ebmeier, 2009). A meta-analysis has shown that the strength of the association between executive functioning and depression varies substantially (Semkovska et al., 2019), and may vary depending on the domain of executive functioning (Rock et al., 2014). Moreovera longitudinal study by Mac Giollabhui et al. (2018) examining attentional functioning suggested that the relationship between depression symptoms and attention is complex and reciprocal, and may not be confined to a depressive episode. The cross-sectional design of the present study precludes such modelling and can therefore not illuminate whether the relationship between executive functioning and specific depression symptoms may change over time. The limited sample size precludes the reliable examination of whether depression status has an effect on the association between executive functioning and specific depression symptoms (e.g., network comparison test, moderated network modelling).

Our approach also has other limitations. The estimated network is based on cross-sectional data, precluding causal inference. Nevertheless, the present partial correlation network is indicative of potential causal effects and can be viewed as a hypothesis-generating structure (Epskamp and Fried, 2018). Compared to other studies of executive functioning and depression the sample size in the present study is relatively large. However, compared to network studies the sample size is quite small. A larger sample size generally helps to identify differences between edge weights and node centrality estimates more accurately (Epskamp et al., 2018). For example, as the estimated edge-weights were susceptible to sampling variations we could not interpret differences in the magnitude of associations between edges that were present. The small sample size is likely the reason for the reduced accuracy of network estimates in this study. Larger samples and more indicators for executive functioning can enable more complex modelling, for example by combining structural equation modelling and network analysis (Epskamp et al., 2017) and a more refined measurement model according to Miyake & Friedman's model (2012). Even though our study included a sample demonstrating the full range of depressive symptoms, participants were not evenly spaced across the severity spectrum. A larger sample would increase sensitivity (reducing the risk for false negatives), and provide the possibility to examine potential moderators, such as clinical status and sex, in more detail. Each participant's depression status was evaluated by one rater and reliability (i.e., inter-rater) was therefore not assessed. Our primary analysis was based on a selection of BDI items, which we on face value deemed conceptually overlapping with the current DSM-criteria for major depressive disorder. However, this approach excludes depression symptoms not included in the DSM, as well as other relevant indicators which has clinical importance (Fried et al., 2016). A more comprehensive approach would be to examine depression symptoms using broader measures, and by using measures which are more suited to capture for example anhedonia and fatigue. Relatedly, because anhedonia is a multi-faceted phenomenon (Rizvi et al., 2016; Treadway and Zald, 2011), potential unique associations between anhedonia and executive function may be lost when we averaged motivational and hedonic components. Similar limitations are also relevant to our alternative model, as several BDI items collapse two symptoms. For example

regarding appetite changes (both increased and decreased appetite) and sleep problems (both sleeping too much or too little). These different manifestations of appetite changes and sleep problems may have different causes. Using symptom indicators which are more precise can lead to a more multidimensional solution and thus a more complex conceptualization of depression and poor executive functioning.

In conclusion, although awaiting replication, the present study suggests that reduced executive functioning and depression symptoms is primarily linked through fatigue. This study may have several clinical implications. Patients who report fatigue are likely experiencing more problems with executive functioning. Educating patients about this can help them to better understand their symptoms and treatment options. Treatments that specifically targets fatigue could potentially improve executive functioning, for example exercise (Ishihara et al., 2021; Puetz et al., 2006). On the other hand, treatments focusing on increasing cognitive functioning (e.g., cognitive remediation therapy; McBride et al., 2017; Thérond et al., 2021) could prove effective in reducing fatigue. This, however, needs to be confirmed in future studies.

Author contributions

BK developed the study concept, performed data analysis, interpreted results, drafted and revised the work. RJ, NL, and TCS organized the study. RB and RJ collected the data. AH and VSU performed data analysis. RB, RJ, AH, VSU, TCS, and NIL interpreted the results and provided critical revisions. All the authors approved the final manuscript for submission.

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Ethical standards

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional guides on the care and use of laboratory animals.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

Nils Inge Landro reports financial support was provided by Research Council of Norway. Nils Inge Landro reports a relationship with Lundbeck Ltd that includes: consulting or advisory and travel reimbursement.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.psycom.2023.100120.

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