Network analysis of impulse dyscontrol in mild cognitive impairment and subjective cognitive decline

T. Saari[1*], E. E. Smith[23], Z. Ismail[234]

[1]Department of Neurology, University of Eastern Finland, Kuopio, Finland

[2]Hotchkiss Brain Institute, University of Calgary, Calgary, Alberta, Canada

[3]Department of Clinical Neurosciences, University of Calgary, Calgary, Alberta, Canada

[4]Department of Psychiatry, University of Calgary, Calgary, Alberta, Canada

This manuscript has been published in final, edited form in *International Psychogeriatrics.* Please cite as:

Saari, T., Smith, E., & Ismail, Z. (2021). Network analysis of impulse dyscontrol in mild cognitive impairment and subjective cognitive decline. *International Psychogeriatrics,* 1-10. doi:10.1017/S1041610220004123

Word count: 4010

Objectives: To investigate conditional dependence relationships of impulse dyscontrol symptoms in mild cognitive impairment (MCI) and subjective cognitive decline (SCD).

Design: Prospective, observational study.

Participants: 235 patients with mild cognitive impairment (n=159) or subjective cognitive decline (n=76) from the Prospective Study for Persons with Memory Symptoms dataset.

Measurements: Items of the Mild Behavioral Impairment-Checklist impulse dyscontrol subscale.

Results: Stubbornness/rigidity, agitation/aggressiveness, and argumentativeness were frequent and the most central symptoms in the network. Impulsivity, the fourth most central symptom in the network, served as the bridge between these common symptoms and less central and rare symptoms.

* Corresponding author
Contact details:
Yliopistonranta 1B
FIN-70210 Kuopio, Finland
toni.saari@uef.fi

Conclusions: Impulse dyscontrol in at-risk states for dementia is characterized by closely connected symptoms of irritability, agitation and rigidity. Compulsions and difficulties in regulating rewarding behaviors are relatively isolated symptoms.

Keywords: Impulse control disorders; mild cognitive impairment; subjective cognitive decline; mild behavioral impairment; neuropsychiatric symptoms; network analysis

Running title: Impulse dyscontrol networks in MCI and SCD

Abbreviations defined in footnote[†]

[†] bvFTD = Behavioral variant frontotemporal dementia, CERAD = Consortium to Establish a Registry for Alzheimer's disease, GGM = Gaussian graphical models, HiTOP = Hierarchical Taxonomy of Psychopathology, LASSO = least absolute shrinkage and selection operator, MBI = mild behavioral impairment, MBI=C, Mild Behavioural Impairment Checklist, MCI = mild cognitive impairment, MoCA = Montreal Cognitive Assessment, PROMPT = The Prospective Study for Persons with Memory Symptoms, SCD = subjective cognitive decline

Introduction

Impulse dyscontrol refers to a tendency of acting prematurely or without judgment, and is a prominent behavioral symptom in dementia (de Mendonça et al., 2004; Taragano et al., 2009; Rascovsky et al., 2011; Ossenkoppele et al., 2015; Ismail et al., 2016). While impulsivity is recognized as a core component in several psychiatric disorders (Moeller et al., 2001), it is increasingly recognized as a feature in neurodegenerative diseases (Rascovsky et al., 2011; Ossenkoppele et al., 2015). Difficulties in impulse control can also emerge in advance of dementia, at the preclinical or prodromal stages of neurodegenerative disease, as characterized in the dementia risk state mild behavioral impairment (MBI) (Ismail et al., 2016; Gill et al., 2020; Bateman et al., 2020; Ismail et al., 2020).

Operationalizing impulse dyscontrol has proven difficult, as a host of neural substrates and cognitive functions likely underlie its transdiagnostic expressions (Strickland & Johnson, 2020; Moeller et al., 2001; Dalley et al., 2011; Fineberg et al., 2014). Impulsivity is often considered a trait giving rise to several problematic behaviors and symptoms (Moeller et al., 2001; García-Forero et al., 2009). In neurodegenerative diseases, a division to generalized impulsivity, characterized by orbitofrontal dysfunction, and person-based impulsivity, characterized by impulse dyscontrol in social settings has been suggested (Paholpak et al., 2016). In at-risk states for dementia, symptoms of impulse dyscontrol can be prodromal markers of behavioral variant frontotemporal dementia (bvFTD; Rascovsky et al., 2011) or behavioral-dysexecutive variant of Alzheimer's disease (Ossenkoppele et al., 2015). These symptoms vary in their prevalence, conceptual brevity (e.g., hyperorality is a narrower construct than aggressive tendencies), in their biological correlates, interpersonal dimensions, relationships with cognition, clinical significance and the extent to which they overlap with neighboring constructs (Bozeat, 2000; Nyatsanza, 2003; Allegri et al., 2006; García-Forero et al., 2009; Cummings et al., 2015; Rosenberg, Nowrangi, & Lyketsos, 2015; Sano et al., 2018; Ruthirakuhan, Lanctôt, Di Scipio, Ahmed, & Herrmann, 2018; Moheb et al., 2019).

Further challenges arise from traditional neuropsychiatric symptom measures probing a relatively short period of time, e.g. the last month, allowing for both transient states as well as more persistent symptoms. Equating symptoms of this nature with symptoms of predominantly neurological origin may pose a barrier to understanding the nature of neuropsychiatric symptoms. Psychiatric instruments, on the other hand, may be limited by including only symptoms relevant for diagnosing a specific disorder (Fineberg et al., 2014) and, thus, may not represent empirically relevant dimensions (Krueger et al., 2018).

Symptoms of impulse dyscontrol could feasibly have mutually reinforcing relationships. For example, impulsivity could lead to various problematic behaviors (García-Forero et al., 2009), whereas an aggressive outburst could be a response to other people trying to restrict these problematic behaviors (Paschali et al., 2018). However, data on the level of individual impulsivity symptoms have been typically used diagnostically or descriptively, not to explore the possibility of systematic relationships between the symptoms as such (e.g. Morris et al., 1989; Bozeat, 2000; Suhonen et al., 2017). To address this gap, we explore the network structures of these symptoms in individuals with mild cognitive impairment (MCI) or subjective cognitive decline (SCD). To our knowledge, this is the first network analysis of impulse dyscontrol in a pre-dementia sample.

Methods

Participants

The participants were drawn from the Prospective Study for Persons with Memory Symptoms (PROMPT) registry (Sheikh et al., 2018). The PROMPT registry started in July 2010 to collect data from patients referred to a specialty dementia clinic at the University of Calgary staffed by neurologists and psychiatrists. The participants in the present study visited the clinics between March 2016 and October 2019. Patients were referred to the clinics on the basis of suspected impairment in neuropsychological or behavioral functions. The assessment protocol included taking a detailed medical history, Lawton-Brody Scale for instrumental activities of daily living (Lawton and Brody, 1969), Consortium to Establish a Registry for Alzheimer's disease (CERAD) neuropsychological test battery (Welsh et al., 1994), Montreal Cognitive Assessment (MoCA; Nasreddine et al., 2005), and Mild Behavioural Impairment Checklist (MBI-C; Ismail et al., 2017). All patients referred to the clinic are eligible to participate in the registry, which is done with written informed consent.

The initial sample size was 273, from which we excluded 38 participants with missing data on one or more items of the MBI-C impulse dyscontrol subscale. The final sample size was 235, comprising participants with MCI (n=159) or SCD (n=76) who had no missing data on the MBI-C. MCI was defined as objective evidence of cognitive impairment (test scores more than 1.0 to 1.5 SD below norms on the CERAD battery or MoCA less than 26) with essentially preserved activities of living, consistent with criteria proposed by the National Institute on Aging-Alzheimer's Association workgroups (Albert et al., 2011). Patients reporting cognitive symptoms but without MCI or dementia were defined as having SCD. Exclusion criteria for this retrospective analysis were a diagnosis of dementia, presence of major psychiatric conditions (e.g., schizophrenia, bipolar disorder, major depression). The study was approved by the ethics board of the University of Calgary, and all participants gave informed consent.

Measurement

We used the 12-item impulse dyscontrol subscale of the MBI-C in this study (Table 1). The subscale is consistent with the ISTAART-AA MBI criteria, where impulse dyscontrol refers to a loss of "the ability to delay gratification and control behavior, impulses, oral intake and/or changes in reward" (Ismail et al., 2016, 2017). The MBI-C can be rated by an informant, clinician, or the patient. In this study, nearly all were rated by an informant (Table 2). The MBI-C includes both a binary score (symptom later life emergent and present for at least six months or not) and a severity score (1-3; 1 = mild: noticeable, but not a significant change; 2 = moderate: significant, but not a dramatic change; 3 = severe: very marked or prominent, a dramatic change) per item. Here, we combined this information, so that a score of 0 indicates the symptom has not been present for at least six months, and scores 1-3 correspond to the severity mentioned above. For descriptive purposes, we also present data on the MoCA (Nasreddine et al., 2005). Baseline data of study participants were used in the analyses.

Statistical analyses

We used R version 3.5.3 for all analyses (R Core Team, 2019). The code for all analyses included in the manuscript and supplementary materials are available at osf.io/nt2xh/.

Network analyses

The core idea of network analysis is to depict conditional relationships between variables. Variables are technically called nodes, and the conditional relationships between them are called edges. An edge represents a unique relationship that can be interpreted as a partial correlation, e.g., a direct relationship that remains after the influence of other nodes in the network are adjusted for (Williams et al., 2019). The width of the edge corresponds to the strength of the association.

The network structures were estimated as sparse Gaussian graphical models (GGM) with *qgraph* (Epskamp et al., 2012). We chose Spearman rank correlation as our correlation method as the impulse dyscontrol symptom data were skewed (see e.g., Burger et al., 2020; Epskamp, Borsboom and Eiko I Fried, 2018 for discussion regarding the use of Spearman over polychoric correlations). The networks were regularized with the least absolute shrinkage and selection operator (LASSO; Tibshirani, 1996) that shrinks all edge weights towards zero, while also setting small edge weights to exactly zero. The trade-off between sensitivity and specificity of edge detection is adjusted with parameter γ, the optimal value of which remains debated, but may hinge on the expected strength of relationships in the data (Foygel & Drton, 2010; Fried et al., 2019). Generally, higher values of γ correspond to a sparse network with few false discoveries, whereas a lower value finds more edges,

some of which may be spurious. We estimated GGMs with both the default *qgraph* γ = .5, as well as a slightly more liberal .4. The justification for the latter is that the MBI-C impulse dyscontrol domain formulation is relatively novel and containing heterogenous symptoms whose intercorrelations have not been investigated previously, thus, by relying on just the default sparse estimate we might exclude weak but theoretically nontrivial edges.

We used a novel yet simple method of integrating the rate of positive answers (whether symptom was present or not for at least six months) into the network as a visual aid. With this method, the rate of positive answers is matched to different hues on a color gradient, where extreme values of symptom positivity represent extreme values on the gradient. These colors, then, were used in graphical arguments for nodes. We used relative as opposed to absolute values due to restriction of range (Table 1). The potential benefit of this method is to observe descriptive data and network relationships in the same visual space (without having to look at Table 1 in this instance).

We also computed predictability with the *mgm* package (Haslbeck and Waldorp, 2016) of each node by the neighboring nodes, which can be interpreted akin to R^2 (Haslbeck and Waldorp, 2018). To do this, the networks were re-estimated as mixed graphical models. Predictability is visualized by the non-white ring around each node; no circle corresponds to the neighboring nodes being poor predictors of the target node, whereas a full circle would indicate the node being entirely predicted by the neighboring nodes.

Next, we calculated strength as a centrality estimate for both the sparse and liberal networks. Strength is a sum of the connected edges to a node, giving a quantitative estimate of how many and how strong connections each node has. The strength estimates are standardized (z-scores), allowing comparisons between the two networks. We also used bootstrapping procedures in the *bootnet* (Epskamp, Borsboom and Eiko I. Fried, 2018) package to assess the robustness of the regularized networks.

Finally, acknowledging the recent literature on non-regularized symptom networks (Williams et al., 2019; Williams and Rast, 2019), we re-estimated the network without regularization in *mgm* (Haslbeck and Waldorp, 2016). This equals to setting γ to 0 (Foygel and Drton, 2010). The rationale for using non-regularized methods stems from the notion that regularized networks, such as ours relying on LASSO, excel in high-dimensional settings (e.g., the number of variables > *n*), whereas the opposite is true in most applied settings in psychological and biobehavioral sciences (e.g., *n* > the number of variables), our study not being an exception. However, the limitations of LASSO are more prominent in exceedingly large sample sizes (Williams et al., 2019), alleviating concerns of using the

method in our study. Thus, the non-regularized network is presented in the supplementary materials.

Table 2. Impulse dyscontrol symptom data

	Frequency, %	Mean (0-3)	SD
1. Agitated or aggressive	43 %	0.64	0.91
2. Argumentative	28 %	0.44	0.83
3. Impulsive	25 %	0.37	0.75
4. Sexually Disinhibited	2 %	0.03	0.18
5. Frustrated or Impatient	46 %	0.69	0.91
6. Recklessness	12 %	0.16	0.5
7. Stubborn or Rigid	33 %	0.47	0.78
8. Change in Eating Behaviors	12 %	0.22	0.67
9. Food No Longer Enjoyable	16 %	0.24	0.64
10. Hoarding	4 %	0.04	0.26
11. Repetitive Behaviors or Compulsions	12 %	0.16	0.51
12. Substance Use, Gambling, Shoplifting	4 %	0.09	0.45

Results

Sample characteristics

Table 2 shows the clinical and demographic characteristics of the study patients. The patients were predominantly Caucasian and male, and had their impulse dyscontrol symptom data mostly rated by an informant (5 were self-rated, 1 rated by a clinician). The cognitive status of 68% of the participants was MCI, whereas the remaining 32% had SCD. Severity of individual impulse dyscontrol symptoms was generally low (range 0.09 – 0.69).

Table 2. Clinical and demographic characteristics of the study participants

	M (SD) or n (%)	Missing, n (%)
Age, M (SD)	64.49 (10.63)	0
Male, n (%)	133 (57%)	1 (< 1%)
Caucasian, n (%)	214 (94%)	7 (3%)
MoCA total score, M (SD)	22.19 (4.45)	20 (9%)
Informant rating, n (%)	215 (97%)	20 (9%)
Cognitive status		0
MCI, n (%)	159 (68%)	
SCD, n (%)	76 (32%)	
Education levels		19 (8%)
Less than high school, n (%)	38 (18%)	
High school, n (%)	51 (24%)	
Community college, trade or professional school, n (%)	48 (22%)	
University degree, bachelor's or higher, n (%)	76 (35%)	

Other, n (%)	3 (1%)

MCI = mild cognitive impairment, SCD = subjective cognitive decline, MoCA = Montreal Cognitive Assessment.

2.2. Network analyses

Figure 1 displays the networks with the sparse (γ = .5), as well as the slightly more liberal tuning parameter (γ = .4).

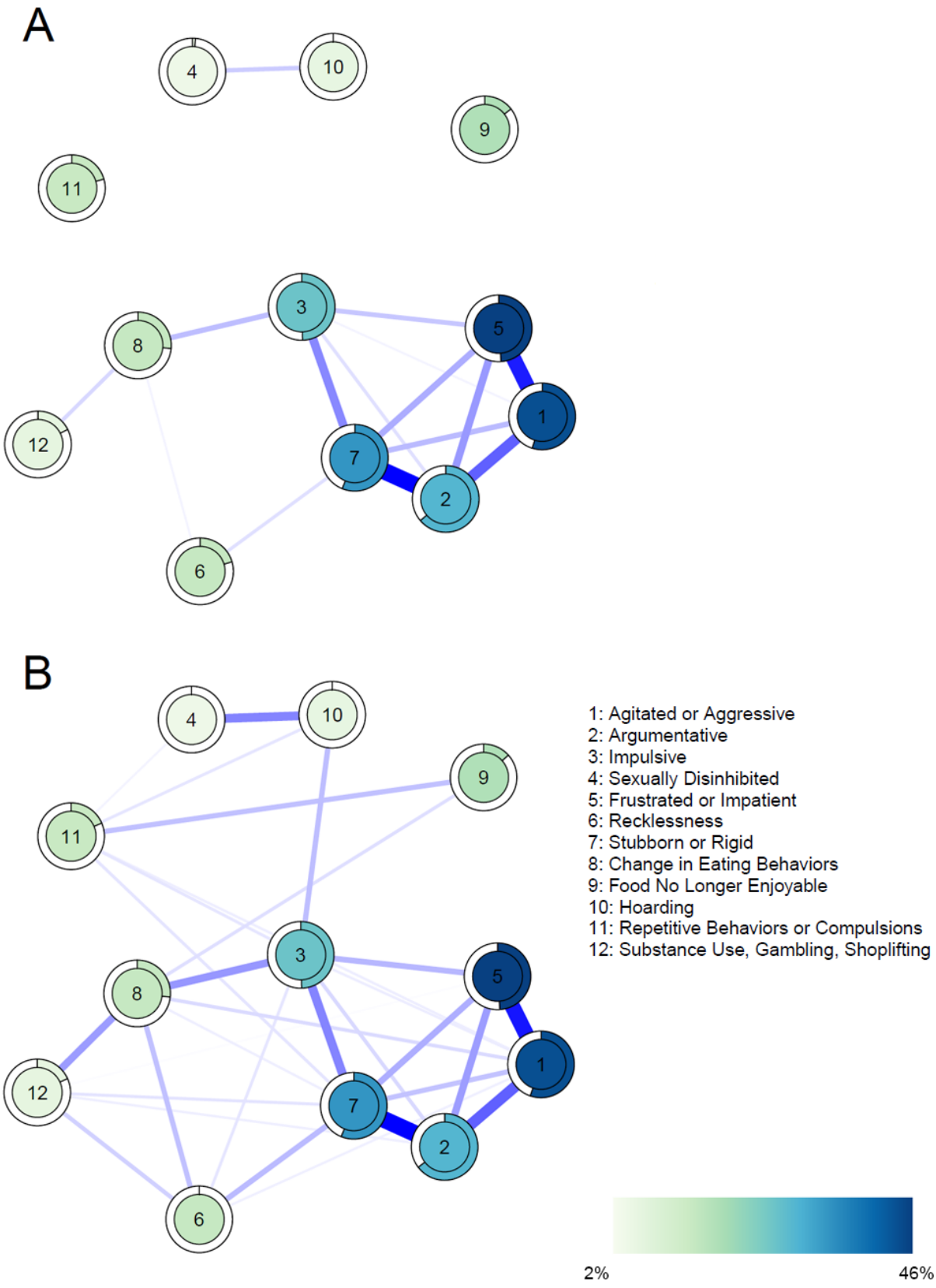

Figure 1. Impulse dyscontrol symptom networks, with sparse (A; γ = .5) and a slightly more liberal (B; γ = .4) configuration. Numbered nodes correspond to each symptom probed in the MBI-C impulse dyscontrol domain, and blue lines between them denote edges, or conditional relationships between nodes. Here all edges are positive. The circle around each node is the predictability estimate, or the

degree to which neighboring nodes can predict a node (akin to R2). Colors of the nodes and circles are based on their frequency (Table 1), where the symptom with the lowest frequency is depicted as light green, and the highest frequency as dark blue, with the remaining nodes falling in between these two.

In the first network, we observed that the node *'Food no longer enjoyable'* and *'Repetitive behaviors and compulsions'* did not have any edges connecting to other nodes (Figure 1A). These nodes are connected in the second network, however, as well as in the mixed-graphical models underlying predictability estimates. We can also find that *'Agitated or aggressive', 'Frustrated or impatient', 'Argumentative', 'Stubborn or rigid'* and *'Impulsive'* all are connected to one another. On the other hand, more unusual behaviors of changes in eating behaviors, hoarding, sexual disinhibition, trouble regulating substance use or gambling and recklessness are relatively sparsely connected. Despite not having the strongest connections, the *'Impulsive'* symptom seems to bridge the otherwise unconnected constellations of frequent and rare symptoms.

The strength estimates indicate that *'Stubborn or rigid'* and *'Argumentative'* seem to be the two most central nodes (Figure 2). *'Argumentative'* also had the highest predictability (.64 and .65 in the networks). *'Sexually disinhibited'* and *'Hoarding'* were not predicted by their neighboring nodes. Altogether, the findings in Figure 1 and 2 could be interpreted as several of the argumentative-aggressive symptoms being widely connected to one another, whereas the other impulse dyscontrol symptoms, although classically recognized in the literature, occur less frequently and in relative isolation to other symptoms.

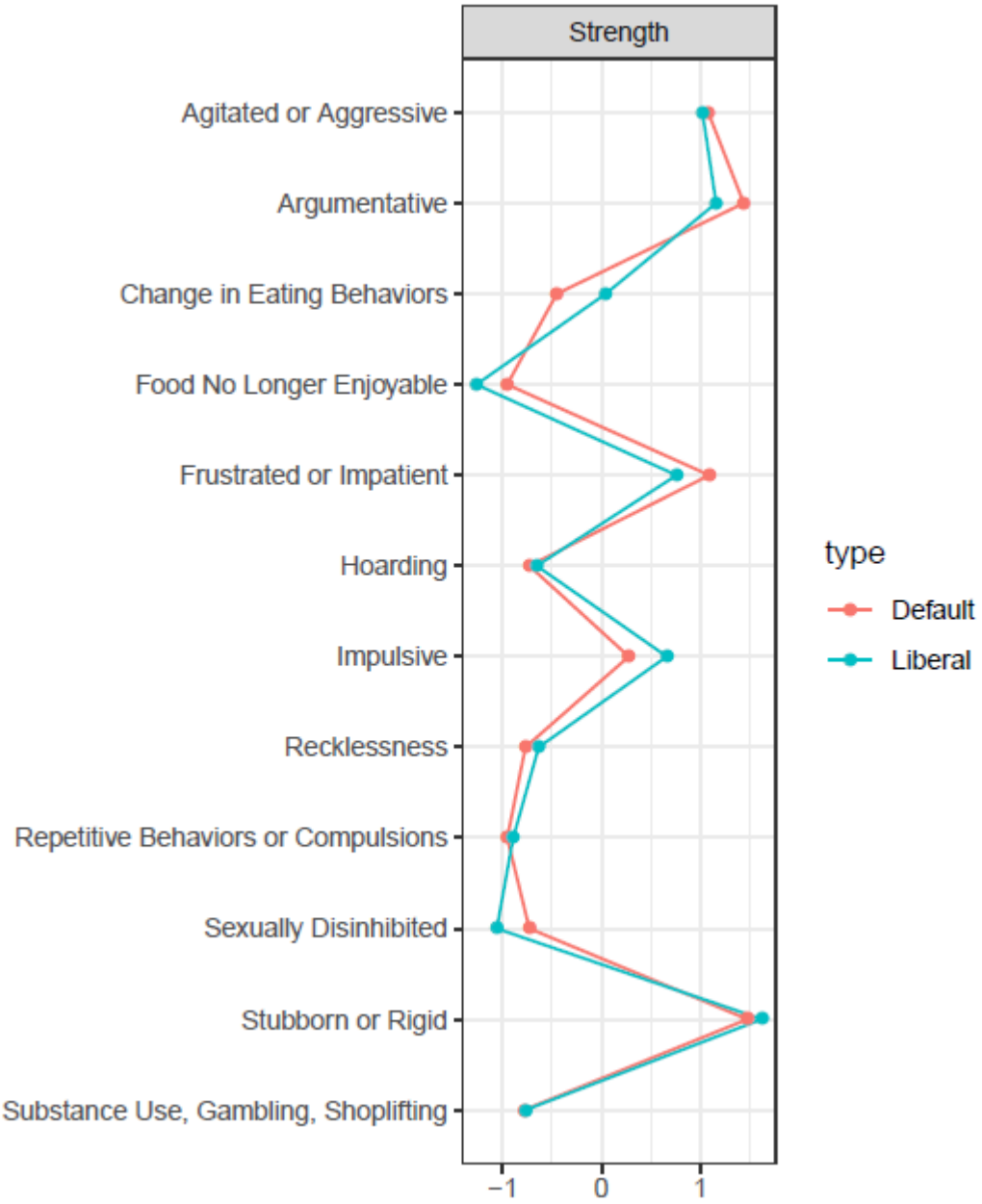

Figure 2. Standardizes strength estimates of individual nodes in the networks in Figure 1. Strength indicates the summary of edges each node has: the nodes with the highest values have the most and/or strongest edges in the networks, demonstrating their centrality in the network. Low values indicate few and/or weak edges to other nodes.

Bootstrapping procedures indicate that there were some differences in precision of the parameter estimates between the two network configurations. Notably, the strength correlation stability coefficient was .44 for the sparse network (Figure 1A), and .52 for the more liberal network (Figure 1B). Scores above .5 are recommended, but scores below .25 are considered concerning (Epskamp, Borsboom and Eiko I. Fried, 2018). Regarding specific edges, the edges *'Argumentative'-'Stubborn or*

rigid' and *'Agitated or aggressive'-Frustrated or impatient'* were stronger than most other edges in the networks.

The non-regularized network estimates more edges (33 edges out of maximum 66 compared to 15 and 31 of the sparse and liberal networks, respectively), which should be interpreted cautiously (Supplemental Figure S9). Similar patterns to regularized networks, however, emerge.

Discussion

The aim of this study was to explore the network structure of impulse dyscontrol in participants with MCI or SCD. We found that the most frequent symptoms, related to hostile or otherwise interpersonally troubling impulsivity, formed a closely connected cluster of symptoms, whereas the less frequent but more specific symptoms were relatively unconnected. Being argumentative or stubborn/rigid were the most central symptoms in the network. Additionally, impulsivity was also important as it bridged some of the less frequent symptoms with the argumentative cluster in addition to being the fourth most central symptom.

The relative isolation of compulsive-repetitive symptoms as well as finding food no longer enjoyable may be related to several factors. For example, it has been suggested that repetitive symptoms in bvFTD may be isolated responses to internal or external stimuli rather than an attempt to relieve anxiety associated with compulsions (Moheb et al., 2019); thus, their relative isolation in the networks is not surprising. Cognitive mechanisms, such as breakdown of response inhibition, have been considered an endophenotype bridging compulsive and impulsive symptoms (Dalley et al., 2011; Fineberg et al., 2014). However, while compulsive features can manifest in disorders characterized by impulsivity and vice versa, the neural circuits underlying these behaviors are partially separable (Fineberg et al., 2014). On the other hand, finding food no longer enjoyable can be related to other constructs as well, such as apathy (Ismail et al., 2008; Hu et al., 2019).

Despite these and other conceptual challenges, neuropsychiatric symptom research often relies on summary scores of NPS measures as markers of psychopathology. While offering a convenient quantitative summary for the construct, summary scores can be a barrier for understanding psychopathology on a systematic level (Strickland & Johnson, 2020; Borsboom & Cramer, 2013; Fried & Nesse, 2015; Marin, Firinciogullari, & Biedrzycki, 1993). For example, assessing both common and rare symptoms (e.g., Cummings et al., 1994; Griffiths et al., 2019) as well as generalized and socially dependent impulsivity (Paholpak et al., 2016) can be justified based on their clinical significance, but the relationships between these symptom constellations remain obscure in summary scores.

Conversely, by examining the network structure of impulse dyscontrol, we can begin to formulate a more nuanced understanding of its systematic features.

Other modelling approaches, such as factor analysis, have been used to elucidate the structure of psychopathology in neurodegenerative disorders. However, despite statistical similarities, the clinical orientation differs between factor analytic models and networks (van Bork, 2019). NPS factors have been typically interpreted as subsyndromes with a common origin (e.g., Canevelli et al., 2013), which, in the case of persons at risk for dementia, is often equivalent to neuropathological changes. However, the network interpretation of impulse dyscontrol might be more appropriate for this construct, specifically. A recent review including neural and psychometric evidence of impulsivity concluded that the construct captures highly diverging behaviors and thus, it is not surprising that robust neural associations are rare (Strickland & Johnson, 2020). Our finding that the symptoms differ in their centrality suggests that there might be varying etiological factors involved, potentially related to different types of dementia or different effects of underlying neurodegenerative changes.

It seems plausible that the central symptoms in the network, such as aggressiveness and argumentativeness, may capture reinforcing aspects with a shared etiology. More rare symptoms, such as sexual disinhibition, need to be screened for their clinical significance, but they did not emerge as central symptoms in participants with SCD or MCI in this memory clinic sample. While our analyses need further corroboration, it may be expected that replicable biological correlates of impulse dyscontrol in at-risk or prodromal states may be challenging to find (Strickland & Johnson, 2020). Rather, constraining biomarker discovery to specific symptoms (Fried & Nesse, 2015), or to clusters of symptoms with the most clinical relevance might establish more robust correlations. This notion is also supported by a recent systematic review on biomarker associations of agitation and aggression in AD (Ruthirakuhan, Lanctôt, Di Scipio, Ahmed, & Herrmann, 2018), where marked heterogeneity was noted in operationalizing these constructs associated with impulsivity.

Based on our findings, the clinical picture of impulse dyscontrol in SCD and MCI is predominantly characterized by antisocial conduct with less emphasis on compulsive and generalized impulsive features. While related to e.g. frustration or agitation, impulsivity as such was less endorsed than these symptoms, signaling the differences. The finding that the associations to impulsiveness were not as strong as other edges in the network may be related to differential cognitive loadings of impulse dyscontrol symptoms. Impulsivity as such has been associated with cognitive mechanisms, such as response inhibition (Fineberg et al., 2014), which, by definition, had to be relatively intact for SCD participants. Thus, as the expected prevalence of impulse dyscontrol symptoms may differ

based on the combination of cognitive loading of individual symptoms and the level of cognitive decline of the person, impulse dyscontrol symptoms may have differential clinical utility in SCD and MCI. Less frequent symptoms, such as sexual disinhibition, were not central nodes in the network. These findings outline the challenges in operationalizing impulse dyscontrol as a unitary construct (Moeller et al., 2001; Fineberg et al., 2014), and support the idea of dividing impulsivity to more granular subcomponents (Dalley et al., 2011; Robbins et al., 2012; Paholpak et al., 2016).

Classification efforts in psychopathology research may offer some guidance in interpreting the broader aspects of our results. For example, the recent empirically-based Hierarchical Taxonomy of Psychopathology (HiTOP; Krueger et al., 2018) model suggests that the broad higher-order spectra of antagonistic externalizing and disinhibited externalizing play a part in antisocial behavior, whereas only disinhibited externalizing is implicated in substance use disorders. These spectra are concordant with the symptom clusters found in a study of bvFTD and early-onset Alzheimer's disease (Paholpak et al., 2016). While not discounting the importance of rare but disturbing symptoms, the major relationships found in this study could arguably be characterized as persistent externalizing disturbances, more antagonistic than disinhibitive in nature.

Having laid the groundwork for the systematic study of impulse dyscontrol symptoms in a dementia context, the next step could be to enrich these models with neuropsychological and neuroimaging variables. Network models, like all models, need to question whether the variables included are sufficient and non-redundant in explaining the phenomenon of interest. For example, motor disinhibition is considered a part of both impulsivity and compulsivity (Robbins et al., 2012). Neuropsychological variables could bridge some of the gaps in the networks, whereas inclusion of neuroimaging variables could point towards the neural associates of specific symptoms and the degree to which these are mediated by the included neuropsychological variables.

Strengths

Using MBI-C as the measure of impulse dyscontrol was a strength of this study. The MBI-C requires the symptoms to persist for at least 6 months, excluding many transient and reactionary states. The long reference range contrasts with traditional measures which allow for brief presentation of symptoms, for instance over the last month. Using measures with short reference ranges could have contributed to the marked prevalence and severity of psychopathology even in normal cognitive aging as well as MCI (Choi et al., 2000; Lyketsos et al., 2002).

Limitations

Our study could have established more precise estimates with a larger sample size. However, we had relatively few edges to estimate (theoretical maximum of 66), and sample sizes of roughly 200 have been used in similar situations (e.g., Funkhouser et al., 2020). It is also worth noting that this is one of the largest clinical samples of MBI-C data. Nevertheless, small edges may be unstable at our reported sample size, and should be interpreted cautiously (Schönbrodt & Perugini, 2013).

The overall symptom severity was relatively mild in our data and the symptom data may be biased owing to informant-reporting and cognitive heterogeneity of the sample. However, these properties reflect the challenges in real-world memory clinic referrals. Furthermore, the networks here are primarily statistical constructs, not theoretical. There are multiple relevant methods for modelling statistical associations between symptoms with roughly equivalent fit, and the theoretical relevance cannot be deduced from statistical parameters (Fried, 2020). However, as impulsivity tends to elude simple conceptualizations, network approaches were as appropriate as any for examining the symptom-to-symptom associations of this under-researched facet of psychopathology in SCD and MCI.

Strength correlation stability of the sparse network was slightly below the recommended cut-off, perhaps limiting the interpretation of the strength estimates in Figure 2. However, the second network fared better, and yielded similar results as the first one. Indeed, the interpretation of this coefficient stems from simulation studies and should not be considered a 'definite guideline' (Epskamp, Borsboom & Fried, 2018). Finally, we did not include concomitant medication in our network models, although drugs affecting central nervous system could affect the symptoms analyzed in this study.

Future directions

Following the formidable number of exploratory network studies conducted in psychiatric domains, the generalizability and replicability of psychological networks has become a natural frontier for future studies (e.g., Funkhouser et al., 2020; Fried et al., 2018). The generalizability of network structures across clinical and non-clinical domains has the potential to offer tentative mechanistic insights into psychopathology. This could also be a future avenue for impulse control difficulties that are present in many major psychiatric and neurological conditions, but also in non-clinical populations to a lesser extent. Extending impulse dyscontrol research to both individuals with a neurodegenerative disease as well as non-clinical populations could also help answer whether and how symptom networks differ in these groups. Enriching networks with cognitive and neuroimaging variables could help bridge the gaps between these literatures that on occasion seem to be studying overlapping phenomena with diverging terminology and methods.

Another future direction would be to analyze networks of impulse dyscontrol in MCI and SCD separately. A recent study showed that the Neuropsychiatric Inventory-Questionnaire domains associated with impulse dyscontrol – namely, agitation/aggressiveness, aberrant motor behavior and appetite disturbances (Ismail et al., 2016) – were more prevalent in MCI than in SCD (Sannemann et al., 2020). These discrepancies may be due to more substantial cognitive deficits in MCI and might even differ across MCI subgroups.

Conclusion

Impulse dyscontrol in at-risk states for dementia is characterized by closely connected symptoms of irritability, agitation, and rigidity with less emphasis on compulsive and generalized impulsive features. Our results contribute to the ongoing discussion regarding the nature of impulse dyscontrol and its relationships to neighboring constructs.

Conflicts of interest: None

Description of authors' roles: T. Saari was involved with the statistical design of the study, carrying out the analyses, and wrote the paper. Z. Ismail designed the study, wrote the paper, did clinical assessments for data collection, consented patients, and supervised all aspects of the study. E. E. Smith was involved in designing the study, writing the paper, did clinical assessments for data collection, consented patients, and supervised aspects of the study, along with supervising the PROMPT registry database.

Acknowledgements: The PROMPT registry is funded by the Katthy Taylor Chair in Vascular Dementia of the University of Calgary, with support from the Brain and Mental Health Research Clinics of the University of Calgary.

TS was supported by grants from Finnish Cultural Foundation and the Finnish Brain Foundation.

References

Albert, M. S. *et al.* (2011) The diagnosis of mild cognitive impairment due to Alzheimer's disease: Recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. *Alzheimer's & Dementia* 7, 270–279. DOI: 10.1016/j.jalz.2011.03.008.

Allegri, R. F. *et al.* (2006) Neuropsychiatric symptoms as a predictor of caregiver burden in Alzheimer's disease. *Neuropsychiatric Disease and Treatment* 2, 105–110.

Bateman, D. R. *et al.* (2020) Agitation and impulsivity in mid and late life as possible risk markers for incident dementia. *Alzheimer's & Dementia: Translational Research & Clinical Interventions* 6, 1–22.

Borsboom, D. and Cramer A. O. J. (2013) Network Analysis: An Integrative Approach to the Structure of Psychopathology. *Annual Review of Clinical Psychology* 9, 91–121. DOI: 10.1146/annurev-clinpsy-050212-185608.

Bozeat, S. (2000) Which neuropsychiatric and behavioural features distinguish frontal and temporal variants of frontotemporal dementia from Alzheimer's disease? *Journal of Neurology, Neurosurgery & Psychiatry* 69, 178–186. DOI: 10.1136/jnnp.69.2.178.

Burger, J., *et al.* (2020) Bereavement or breakup: Differences in networks of depression. *Journal of Affective Disorders* 267, 1–8. DOI: 10.1016/j.jad.2020.01.157.

Canevelli, M., *et al.* (2013). Behavioral and psychological subsyndromes in Alzheimer's disease using the Neuropsychiatric Inventory: Behavioral subsyndromes in Alzheimer's disease. *International Journal of Geriatric Psychiatry* 28, 795–803. DOI: 10.1002/gps.3904

Choi S. H., *et al.* (2000) The Korean version of the Neuropsychiatric Inventory: a scoring tool for neuropsychiatric disturbance in dementia patients. *Journal of Korean Medical Science* 15, 609–615.

Cummings J, *et al.* (2015) Agitation in cognitive disorders: International Psychogeriatric Association provisional consensus clinical and research definition. *International Psychogeriatrics* 27(1): 7–17. DOI: 10.1017/S1041610214001963.

Cummings, J. L., *et al.* (1994) The Neuropsychiatric Inventory: Comprehensive assessment of psychopathology in dementia. *Neurology* 44, 2308–2308. DOI: 10.1212/WNL.44.12.2308.

Dalley, J. W., Everitt, B. J. and Robbins T. W. (2011) Impulsivity, Compulsivity, and Top-Down Cognitive Control. *Neuron* 69, 680–694. DOI: 10.1016/j.neuron.2011.01.020.

de Mendonça, A., *et al.* (2004) Frontotemporal mild cognitive impairment. *Journal of Alzheimer's Disease* 6, 1–9. DOI: 10.3233/JAD-2004-6101.

Epskamp, S., *et al.* (2012) **qgraph** : Network Visualizations of Relationships in Psychometric Data. *Journal of Statistical Software* 48, DOI: 10.18637/jss.v048.i04.

Epskamp S., Borsboom, D. and Fried, E. I. (2018) Estimating psychological networks and their accuracy: A tutorial paper. *Behavior Research Methods* 50, 195–212. DOI: 10.3758/s13428-017-0862-1.

Epskamp, S., Borsboom, D. and Fried, E. I. (2018) Estimating Psychological Networks and their Accuracy: Supplementary Materials.: 8.

Fineberg N. A., *et al.* (2014) New developments in human neurocognition: clinical, genetic, and brain imaging correlates of impulsivity and compulsivity. *CNS Spectrums* 19, 69–89. DOI: 10.1017/S1092852913000801.

Foygel, R. and Drton, M. (2010) Extended Bayesian Information Criteria for Gaussian Graphical Models. *arXiv:1011.6640 [math, stat]*. Available at: http://arxiv.org/abs/1011.6640 (accessed 2 April 2020).

Fried, E. I. (2020). Lack of theory building and testing impedes progress in the factor and network literature. In press at *Psychological Inquiry*. DOI: 10.31234/osf.io/zg84s

Fried, E. I. and Nesse, R. M. (2015) Depression sum-scores don't add up: why analyzing specific depression symptoms is essential. *BMC Medicine* 13, DOI: 10.1186/s12916-015-0325-4.

Fried E. I., *et al.* (2018) Replicability and Generalizability of Posttraumatic Stress Disorder (PTSD) Networks: A Cross-Cultural Multisite Study of PTSD Symptoms in Four Trauma Patient Samples. *Clinical Psychological Science* 6, 335–351. DOI: 10.1177/2167702617745092.

Fried, E. I., *et al.* (2019) Using network analysis to examine links between individual depressive symptoms, inflammatory markers, and covariates. *Psychological Medicine*: 1–9. DOI: 10.1017/S0033291719002770.

Funkhouser, C. J., *et al.* (2020) The replicability and generalizability of internalizing symptom networks across five samples. *Journal of Abnormal Psychology* 129, 191–203. DOI: 10.1037/abn0000496.

García-Forero, C., *et al.* (2009) Disentangling impulsiveness, aggressiveness and impulsive aggression: An empirical approach using self-report measures. *Psychiatry Research* 168, 40–49. DOI: 10.1016/j.psychres.2008.04.002.

Gill, S., *et al.* (2020) Using Machine Learning to Predict Dementia from Neuropsychiatric Symptom and Neuroimaging Data1. *Journal of Alzheimer's Disease*: 1–12. DOI: 10.3233/JAD-191169.

Griffiths, A. W., *et al.* (2019) Validation of the Cohen-Mansfield Agitation Inventory Observational (CMAI-O) tool. *International Psychogeriatrics*: 1–11. DOI: 10.1017/S1041610219000279.

Haslbeck, J. M. B. and Waldorp, L. J. (2016) mgm: Structure Estimation for Time-Varying Mixed Graphical Models in high-dimensional Data. *aRxiv preprint:1510.06871v2*. Available at: http://arxiv.org/abs/1510.06871v2.

Haslbeck, J. M. B. and Waldorp, L. J. (2018) How well do network models predict observations? On the importance of predictability in network models. *Behavior Research Methods* 50, 853–861. DOI: 10.3758/s13428-017-0910-x.

Hu, S., *et al.* (2019) P1-317: Validation of the Mild Behavioral Impairment Checklist (MBI-C) in a clinic-based sample. *Alzheimer's & Dementia* 15, P365–P365. DOI: 10.1016/j.jalz.2019.06.872.

Ismail, Z., *et al.* (2008) A functional neuroimaging study of appetite loss in Alzheimer's disease. *Journal of the Neurological Sciences* 271, 97–103. DOI: 10.1016/j.jns.2008.03.023.

Ismail Z., *et al.* (2016) Neuropsychiatric symptoms as early manifestations of emergent dementia: Provisional diagnostic criteria for mild behavioral impairment. *Alzheimer's & Dementia* 12, 195–202. DOI: 10.1016/j.jalz.2015.05.017.

Ismail Z., *et al.* (2017) The Mild Behavioral Impairment Checklist (MBI-C): A Rating Scale for Neuropsychiatric Symptoms in Pre-Dementia Populations. *Journal of Alzheimer's Disease* 56, 929–938. DOI: 10.3233/JAD-160979.

Ismail, Z., *et al.* (2020) *Mild Behavioral Impairment and Subjective Cognitive Decline predict Mild Cognitive Impairment*. medRxiv, preprint, 25 May. Neurology. DOI: 10.1101/2020.05.24.20112284.

Krueger R. F., *et al.* (2018) Progress in achieving quantitative classification of psychopathology. *World Psychiatry* 17, 282–293. DOI: 10.1002/wps.20566.

Lawton, M. P. and Brody, E. M. (1969) Assessment of Older People: Self-Maintaining and Instrumental Activities of Daily Living. *Gerontologist* 9: 179–186.

Lyketsos C. G., *et al.* (2002) Prevalence of Neuropsychiatric Symptoms in Dementia and Mild Cognitive Impairment: Results From the Cardiovascular Health Study. *JAMA* 288, 1475. DOI: 10.1001/jama.288.12.1475.

Marin, R. S., Firinciogullari, S. and Biedrzycki, R. C. (1993) The sources of convergence between measures of apathy and depression. *Journal of Affective Disorders* 28, 117–124.

Moeller, F. G., *et al.* (2001) Psychiatric Aspects of Impulsivity. *American Journal of Psychiatry* 158, 1783–1793. DOI: 10.1176/appi.ajp.158.11.1783.

Moheb, N., et al. (2019) Repetitive Behaviors in Frontotemporal Dementia: Compulsions or Impulsions? *The Journal of Neuropsychiatry and Clinical Neurosciences* 31, 132–136. DOI: 10.1176/appi.neuropsych.18060148.

Morris, C. H., Hope, R. A. and Fairburn, C. G. (1989) Eating Habits in Dementia: A Descriptive Study. *British Journal of Psychiatry* 154, 801–806. DOI: 10.1192/bjp.154.6.801.

Nasreddine, Z. S., *et al.* (2005) The Montreal Cognitive Assessment, MoCA: A Brief Screening Tool For Mild Cognitive Impairment. *Journal of the American Geriatrics Society* 53, 695–699. DOI: 10.1111/j.1532-5415.2005.53221.x.

Nyatsanza, S. (2003) A study of stereotypic behaviours in Alzheimer's disease and frontal and temporal variant frontotemporal dementia. *Journal of Neurology, Neurosurgery & Psychiatry* 74, 1398–1402. DOI: 10.1136/jnnp.74.10.1398.

Ossenkoppele, R., *et al.* (2015) The behavioural/dysexecutive variant of Alzheimer's disease: clinical, neuroimaging and pathological features. *Brain* 138, 2732–2749. DOI: 10.1093/brain/awv191.

Paholpak, P., *et al.* (2016) Person-Based Versus Generalized Impulsivity Disinhibition in Frontotemporal Dementia and Alzheimer Disease. *Journal of Geriatric Psychiatry and Neurology* 29, 344–351. DOI: 10.1177/0891988716666377.

Paschali, M., *et al.* (2018) A systematic evaluation of impulsive–aggressive behavior in psychogeriatric inpatients using the staff observation aggression scale-revision (SOAS-R). *International Psychogeriatrics* 30, 61–68. DOI: 10.1017/S1041610217001600.

R Core Team (2019) *R: A Language and Environment for Statistical Computing*. Vienna, Austria: R Foundation for Statistical Computing. Available at: https://www.R-project.org/.

Rascovsky, K., *et al.* (2011) Sensitivity of revised diagnostic criteria for the behavioural variant of frontotemporal dementia. *Brain* 134, 2456–2477. DOI: 10.1093/brain/awr179.

Robbins, T. W., *et al.* (2012) Neurocognitive endophenotypes of impulsivity and compulsivity: towards dimensional psychiatry. *Trends in Cognitive Sciences* 16, 81–91. DOI: 10.1016/j.tics.2011.11.009.

Rosenberg, P. B., Nowrangi, M. A. and Lyketsos, C. G. (2015) Neuropsychiatric symptoms in Alzheimer's disease: What might be associated brain circuits? *Molecular Aspects of Medicine* 43–44, 25–37. DOI: 10.1016/j.mam.2015.05.005.

Ruthirakuhan, M., *et al.* (2018) Biomarkers of agitation and aggression in Alzheimer's disease: A systematic review. *Alzheimer's & Dementia* 14, 1344–1376. DOI: 10.1016/j.jalz.2018.04.013.

Sannemann, L. *et al*. (2020). Neuropsychiatric symptoms in at-risk groups for AD dementia and their association with worry and AD biomarkers—Results from the DELCODE study. *Alzheimer's Research & Therapy* 12, 131. DOI: 10.1186/s13195-020-00701-7

Sano, M., *et al.* (2018) Identifying Better Outcome Measures to Improve Treatment of Agitation in Dementia: A Report from the EU/US/CTAD Task Force. *The Journal of Prevention of Alzheimer's Disease* 5, 98–102.

Schönbrodt, F. D., and Perugini, M. (2013). At what sample size do correlations stabilize? *Journal of Research in Personality*, 47, 609–612. DOI: 10.1016/j.jrp.2013.05.009

Sheikh, F., *et al.* (2018) Prevalence of mild behavioral impairment in mild cognitive impairment and subjective cognitive decline, and its association with caregiver burden. *International Psychogeriatrics* 30(2): 233–244. DOI: 10.1017/S104161021700151X.

Strickland, J. C., and Johnson, M. W. (2020). Rejecting impulsivity as a psychological construct: A theoretical, empirical, and sociocultural argument. *Psychological Review*. DOI: 10.1037/rev0000263

Suhonen, N-M., *et al.* (2017) The Modified Frontal Behavioral Inventory (FBI-mod) for Patients with Frontotemporal Lobar Degeneration, Alzheimer's Disease, and Mild Cognitive Impairment. *Journal of Alzheimer's Disease* 56(4): 1241–1251. DOI: 10.3233/JAD-160983.

Taragano, F. E., *et al.* (2009) Mild Behavioral Impairment and Risk of Dementia: A Prospective Cohort Study of 358 Patients. *The Journal of Clinical Psychiatry* 70(4): 584–592. DOI: 10.4088/JCP.08m04181.

Tibshirani, R. (1996) Regression Shrinkage and Selection via the Lasso. *Journal of the Royal Statistical Society. Series B (Methodological)* 58(1): 267–288.

van Bork, R. (2019). *Interpreting psychometric models*. University of Amsterdam.

Welsh, K. A., *et al.* (1994) The Consortium to Establish a Registry for Alzheimer's Disease (CERAD). Part V. A normative study of the neuropsychological battery. *Neurology* 44(4): 609–614. DOI: 10.1212/WNL.44.4.609.

Williams, D. R. and Rast, P. (2019) Back to the basics: Rethinking partial correlation network methodology. *British Journal of Mathematical and Statistical Psychology*: bmsp.12173. DOI: 10.1111/bmsp.12173.

Williams, D. R., *et al.* (2019) On Nonregularized Estimation of Psychological Networks. *Multivariate Behavioral Research* 54(5): 719–750. DOI: 10.1080/00273171.2019.1575716.