Making the Connections: Exploring the Validity and Clinical Utility of Self-reported Personalized Networks. Research Internship Report

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Abstract

While scientific advancements in the past decades have vastly contributed to increase our physical well-being, they failed to target our mental pain. Today, Major Depressive Disorder (MDD) represents a leading cause of burden worldwide. As there is accumulating evidence in favor of the disorder's heterogeneous structure, it is crucial to focus on individual symptom dynamics in research and practice to increase treatment efficacy. Within this project we investigated Perceived Causal Networks (PECAN) as a method to generate personalized networks. Firstly, we used PECAN to examine symptom dynamics both on an individual as well as group-level in a depressive sample, and found considerable variability. Secondly, we investigated whether density and number of feedback loops could be used to indicate depression severity or chronicity, but got inconclusive findings. Lastly, we used PECAN to analyze the specific links between symptoms of MDD and insomnia and found a bidirectional relationship. Interestingly enough, these bidirectional dynamics were mostly present on an indirect-level, and not directly perceived by the majority of participants. While its added value in practice remains to be explored, we could demonstrate the methods' ability to analyze and connect disorder dynamics on multiple levels. While the method could be prone to overestimate heterogeneity, it could consequently be used as a conservative indicator for group-level consistencies.

1 Introduction

There appears to be an alarming disparity between increasing efforts to provide evidence based mental health treatment and the global prevalence of mental disorders (GBD 2019 Mental Disorders Collaborators, 2022). While medical science has shifted towards more individualized treatment, generally referred to as "precision medicine", the field of psychology lags behind (Cuthbert & Insel, 2013). Despite an increase of people seeking treatment, there is no evidence for a decrease in the burden of mental disorders since 1990 (GBD 2019 Mental Disorders Collaborators, 2022).

The root(s) of the problem

With an estimated 279.6 million cases in 2019, Major Depressive Disorder (MDD) is among the most prevalent mental disorders worldwide (GBD 2019 Mental Disorders Collaborators, 2022). However, there is still a lack of understanding regarding its co-occurrence with other disorders (comorbidity) (Fried, 2015), and the observed heterogeneity between patients (Fried & Nesse, 2015). One potential reason for these unresolved issues can be traced back to the predominant categorical conceptualization of mental disorders (Fried, 2015). In the quest to better understand, diagnose and treat mental disorders, the field has been searching for *common causes* and categorizing certain symptom constellations respectively (Borsboom, 2017). This *common cause framework* suggests that symptoms are interchangeable and causally independent manifestations of an underlying cause (Borsboom, 2008). Individuals are thus grouped together using an unweighted sum-score of their symptoms and cut-offs, resulting in hard boundaries between disorders as well as between "healthy" and "unhealthy" individuals (Fried, 2015). This forces treatment providers to treat individuals based on group-level findings, also referred to as the *therapist's dilemma* (Piccirillo, Beck, & Rodebaugh, 2019).

The network approach to psychopathology (Borsboom, 2008), offers an alternative way to conceptualize mental disorders. Here, the latent variable (common cause) is abandoned altogether and mental disorders are viewed as systems of mutually interacting symptoms. Hence, psychopathological phenomena are not explained by one cause per se but rather by their underlying complex symptom dynamics (Borsboom & Cramer, 2013). In theory, the centrality of a symptom refers to its connectedness within the network and determines how important the symptom is for activating further symptoms. Closed causal symptom chains are referred to as feedback loops, and are thought to be associated with disorder maintenance. The density of a network is derived from its connectivity and may be an indicator of how prone a network is to phase transitions (shifts between "healthy" and "unhealthy" states). Furthermore, comorbidity is thought to arise

via "bridge symptoms" connecting symptom clusters of different disorders (Fried et al., 2017). The network theory of mental disorders is extended by the network methodology, allowing us to estimate networks from empirical data (Fried, 2017). This combination of an innovative theoretical foundation and sophisticated statistical tools offers a new perspective to better understand the nature of mental disorders and advance precision medicine in psychopathology.

Personalized networks and their limitations

While nomothetic (group-level) networks estimated from cross-sectional data can provide clues about between-subject symptom relations, they do not allow us to examine within-person dynamics. To identify dynamic relations in idiographic (personalized) networks, most studies have relied on the collection of time-series data through ecological momentary assessment (EMA) (Fisher, Reeves, Lawyer, Medaglia, & Rubel, 2017; Stone & Shiffman, 1994). Hereby, individuals are asked to report on their psychological state on multiple occasions over time. However, there are considerable concerns about the methods' feasibility and validity regarding missing data, identifying appropriate time frames to capture symptom dynamics, participant burden, and failure to incorporate prior clinical knowledge (Bentley, Kleiman, Elliott, Huffman, & Nock, 2019; Fried et al., 2017; Zimmermann et al., 2019; Burger et al., 2020). In fact, directed networks from EMA data appear to differ considerably from case conceptualization, a common process in which therapist and client jointly identify present issues and adapt treatment decisions respectively (Kuyken, Padesky, & Dudley, 2008). This further increases clinicians' hesitancy to adopt the method in practice (Burger et al., 2020).

Perceiving causal dynamics

An alternative way to investigate causal relations between symptoms is "Perceived Causal Relationship" (PCR) scaling (Frewen, Allen, Lanius, & Neufeld, 2012). Here, individuals first identify a set of symptoms from which they suffer S. Then they indicate for each symptom pairing (s_i,s_j) where $s_i, s_j \in S$, the perceived reciprocal relations r_{ij}, r_{ji}, where r_{ij} is the causal relationship from s_i to s_j. Thereby, the individuals themselves build a matrix encoding the symptom relations (adjacency matrix), which is then translated into a network. Not only can PCR scaling be used by clinicians to include prior clinical knowledge into theory formation, but it can also serve as a time-efficient tool to generate idiographic networks in psychotherapy (Deserno et al., 2020; Borsboom & Cramer, 2013). Hence, this method could be crucial to establish a reciprocal knowledge stream in the quest to narrow the gap between research and practice. However, the methods' validity remains understudied (Frumkin, Piccirillo, Beck, Grossman, & Rodebaugh, 2021).

Recently, Klintwall and colleagues (Klintwall, Bellander, & Cervin, 2021) have proposed Perceived Causal Networks (PECAN), a clinically adapted version of PCR including network visualizations. In their study, they investigated heterogeneity, completion times, and immediate test–retest reliability of PECAN results. Furthermore, psychotherapists rated PECAN visualizations regarding their clinical utility. Contrary to prior hesitancy towards incorporating idiographic models in practice (Zimmermann et al., 2019), 96 % rated the networks as useful, and judged them to cover almost 50 % of the information typically assessed by a professional. Thus, PECAN might offer a time-efficient and empirically quantifiable alternative to case conceptualization and serve as a first step in the collaboration between therapist and client.

The current project aimed at further exploring the validity and clinical utility of PECAN. To this end, we examined the following research questions. *(1) Does PECAN account for the heterogeneity of MDD on an individual-level?* We explored whether PECAN results reflected the previously reported level of heterogeneity within MDD. In line with various studies reporting heterogeneity in idiographic models of MDD (Klintwall et al., 2021; Hebbrecht et al., 2020; Fried, 2017), we expected that the individual networks would exhibit a high variability regarding symptom constellation, centrality, and feedback loops. Furthermore, we compared group-level dynamics with existing cross-sectional findings to separate between- from within-person effects (Fried et al., 2017). *(2) Are there PECAN properties linked to depression severity and chronicity?* We were interested whether two intrinsic PECAN characteristics, namely density and feedback loops, could function as indicators for clinical markers. While previous findings have been inconclusive as to whether network density can indicate symptom severity (Pe et al., 2015; Frumkin et al., 2021), the number of feedback loops has been linked to symptom frequencies in PCR networks (Frewen, Schmittmann, Bringmann, & Borsboom, 2013). Taking these findings and the theoretical implications of the network approach into account, we expected that higher density and number of feedback loops would increase the reported severity and duration of participants' depressive symptoms. *(3) What are the PECAN relations between symptoms of MDD and insomnia?* To further demonstrate the methods ability to explore and connect symptom dynamics on various levels, we used PECAN to "zoom" in on the links between symptoms of MDD and insomnia. MDD and insomnia symptoms often co-occur, with insomnia being a primary risk factor for the development of MDD (Baglioni et al., 2011). Furthermore, cognitive-behavioral therapy for insomnia (CBTI) was found to improve symptoms of MDD indirectly via insomnia symptoms (Blanken et al., 2019). Hence, we expected to find causal pathways between both disorders. We wanted to examine how these relationships were perceived by individuals, and explore whether the direction of causation between the disorders varied across the sample.

2 Methods

2.1 Participants

We used the dataset collected by Klintwall and colleagues in the period between 23.08.2020 and 25.11.2020. Participants were recruited via adverts posted in 56 Swedish Facebook groups promoting mental health content and completed two consecutive PECAN ratings. We included participants with an immediate test-retest reliability above 0.5, which was computed by correlating the two individual ratings of symptom severity and casual symptom relations. The final sample of 265 participants consisted of 226 female, 36 male, and three other, with a mean age of 38.89 years ($\pm$12.42). Within this sample 163 participants (61.51 %) scored above cut-off on the Patient Health Questionnaire module for depression (PHQ-9), and hence formed a depression sub-sample.

2.2 Procedure

Participants filled in an online PECAN questionnaire. First, they had to select between seven and 15 behavioral/ emotional problem items (symptoms) they had experienced during the past week (see Table 1). Then they were asked to rate each selected symptom for "severity" on a 0-100 scale. Before rating the perceived causal relations, participants' understanding of causality was tested in three multiple choice questions. Only if answered correctly, they could continue. To rate the perceived causal relations, participants had to report for each symptom, to what degree it was caused by a maximum of three other selected symptoms (or select "none"). If one or more symptoms were selected as causing a given symptom, the participant had to indicate the perceived strength of the causal relationships in percentages. Percentages could also be additionally assigned to "other causes/don't know" (*Unknown/External*). The sum score of assigned percentages should be 100 %, to circumvent participants' assigning 100 % to each relationship. The questionnaire only assessed positive relationships (if there was a causal link from s_i to s_j, s_i was thought to *increase* s_j). Furthermore it did not allow for causality between emotion-related symptoms, as pilot data indicated lower therapist ratings otherwise (e.g., if one of symptoms 18-26 was selected, symptoms from 18-26 could not be selected as a possible cause). As an immediate test-retest, participants were asked to repeat the severity and causal ratings. Lastly, to assess depressive severity participants completed the PHQ-9 covering the DSM-5 criteria for MDD. Participants also indicated their background information including their gender, age, education level, and experience with Cognitive Behavioural Therapy (CBT). Participants who identified as depressed additionally reported their duration of symptomatology by selecting either 1, 3, 6, 12, 24, or 60 months.

Number	Item	Abbreviation
1	Eats less	eatless
2	No exercise	noex
3	Sleep problems	sleeppro
4	Daytime resting	dayrest
5	Conflicts	confl
6	Hypocondric worries	hypoc
7	Trouble concentrating	troubco
8	Social media use	socmed
9	Stays at home	stayh
10	Procrastinates	procrast
11	Substance use	subst
12	Self-harm	selfh
13	Suicidal thoughts	suicid
14	Eats more	eatmore
15	Compulsions (incl. avoid)	compul
16	Ruminates (incl. avoid)	rumin
17	Worries (incl. avoid)	worry
18*	Flashbacks (incl. avoid)	flashb
19*	Panic (incl. avoid)	panic
20*	Pain (incl. avoid)	pain
21*	Social anxiety (incl. avoid)	socanx
22*	Alone/sad (incl. avoid)	sad
23*	Tired (incl. avoid)	tired
24*	Stressed (incl. avoid)	stress
25*	Bored (incl. avoid)	bored
26*	Angry (incl. avoid)	angry

Table 1: List of PECAN items and their abbreviations. 15-26 included avoidance in their description as a cause (e.g. "I felt, or *wanted to avoid* feeling, sad or alone."). Items 18-26 (*) represent emotional problem items and could not be selected as causing each other.

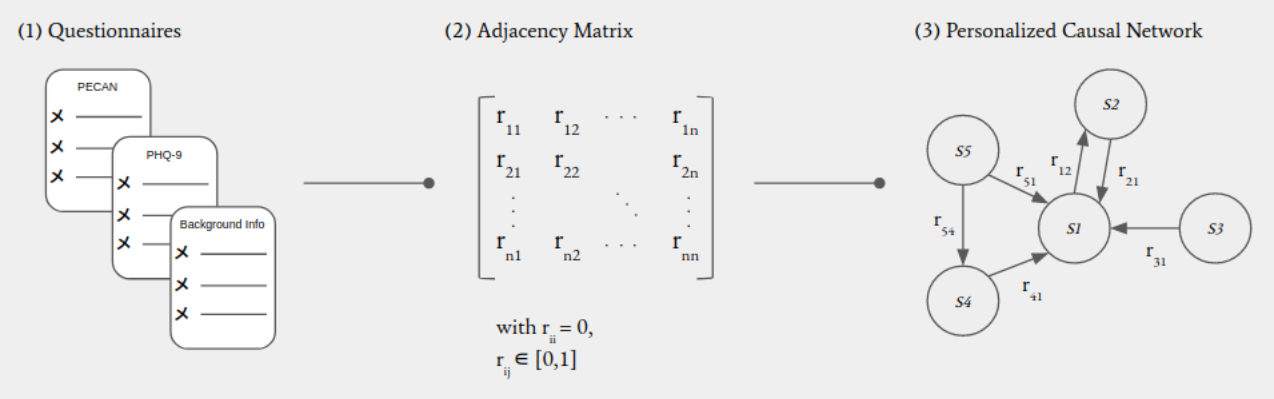


Figure 1: 3-step procedure visualization. First individuals had to complete the online PECAN questionnaire and the PHQ-9 as well as indicate their background information. Their perceived causal ratings were then stored in an adjacency matrix which could then be translated into a personalized causal network.

2.3 Data analyses

All data preprocessing and analyses was performed in R. First, we explored whether our PECAN depression sub-sample accounted for the previously observed heterogeneity in MDD patients. As a measure for the variability between individual symptom profiles, we performed dimensionality reduction using t-SNE and calculated the Hopkins' statistic (Krijthe, van der Maaten, & Krijthe, 2017; Hopkins & Skellam, 1954). This allowed us to examine whether the data was clusterable, and hence identify potential symptom profile clusters in the sample. Within individual networks we used `igraph` (Csardi, 2013) to perform community detection with the infomap algorithm, to identify consistent symptom clusters across individuals. We analyzed feedback loops in the individual networks using `LoopDetectR` (Baum & Wolf, 2020). We calculated degree centrality using `qgraph` (Epskamp, Cramer, Waldorp, Schmittmann, & Borsboom, 2012), where out-degree centrality measured the extent to which a symptom directly influenced other symptoms in the network, and in-degree centrality measured how much influence a symptom received from the remaining symptoms. To combine both measures, we computed the out-/to in-degree centrality ratio for each symptom by dividing out- by in-degree centrality (excluding influence from *Unknown/External*). To allow for division we transformed values of 0 to 0.001. Thus, symptoms that had an out-/to in-degree centrality ratio higher than one had more out-going that incoming effects. In contrast, symptoms that had an out-/to in-degree centrality ratio lower than one received more influence from other symptoms than they imposed on the network themselves.

We also demonstrated how PECAN can be used to explore both group- as well as individual-level symptom dynamics. To see to what extent PECAN results matched group-level network findings, we computed the average undirected network across the depression sub-sample and performed community detection with the spinglass algorithm. We then compared the resulting network to a recently published group-level MDD network (Malgaroli, Calderon, & Bonanno, 2021). To illustrate how the PECAN method can be used to examine individual dynamics, we performed a visual comparison between participants 180989 and 200234.

Within our second research question, we investigated whether the PECAN properties density and number of feedback loops related to depression severity and chronicity. Density corresponded to the number of connections divided by the number of possible connections in the network. We only included feedback loops consisting of three to five edges, as feedback loops containing only two edges were more likely to be instances of content overlap, and feedback loops containing more than five edges were less relevant for therapeutical evaluation. We used the entire sample for severity (PHQ-9 scores) and a sub-sample of participants that identified as depressed for chronicity (self-reported duration of depression). First, we explored how density and the number of feedback loops related to the number of selected symptoms. Then we computed spearman

correlations between density and the number of feedback loops and the outcome variables severity and chronicity. We considered correlations above 0.7 to be strong, those between 0.4 and 0.6 moderate, and those below 0.4 to be weak (Akoglu, 2018). Lastly, we computed two linear models, one for each outcome variable, with the predictors density and number of feedback loops. We used multiple R^2 as a goodness-of-fit measure, explaining how much variance in the outcome variable could be explained by the predictors.

Within our third research question we focused on symptoms of MDD and insomnia in the entire sample. We examined whether symptoms of one disorder were predominantly perceived as causes of symptoms of the other, or whether the relationship was bidirectional. We focused on *Alone/sad*, *Bored* and *Tired* as the core symptoms of MDD, and on *Sleep Problems* and *Daytime resting* as insomnia specific symptoms.

2.4 Visualizations

We used matrices to illustrate symptom relations within (1) a co-occurrence matrix: a high value between s_i and s_j reflects that most participants who reported s_i, also reported s_j; (2) a link presence matrix: a high value between s_i and s_j reflects that when both symptoms are included in a symptom profile they are commonly connected; and (3) a link strength matrix: a high value between s_i and s_j reflects that on average there is a strong connection between both symptoms. The matrices have a square shape meaning that they have the same amount of rows as columns, and hence visualize every possible pair-wise relation between the symptoms (26×26 excluding, or 27×27 including *Unknown/External*, with a 0-diagonal as the questionnaire did not allow for self-reinforcing links, e.g. $s_i \leftrightarrow s_i$). All matrices were directed (non-symmetric), meaning that the relationship $s_i \rightarrow s_j$ was not necessarily the same as the relationship $s_j \rightarrow s_i$. The causal relationships (directed links) can be inferred by going *from* a row symptom *to* a column symptom.

We used network visualizations to exemplify individual networks and summarize our findings, where nodes represent the different symptoms and edges represent the symptom relations. Within the networks, node size is scaled by how often the corresponding symptom was reported in the sample, e.g., a larger node was more commonly selected. Node color represents the out-/to in-degree centrality ratio of the respective symptom, with blue corresponding to a lower and red to a higher out-/to in-degree centrality ratio. Furthermore, the yellow parts in the pie charts around each node denote how much influence the respective nodes received from *Unknown/External*. The edge thickness within the first networks (a), represents the link counts relative to the symptom co-occurrences (corresponds to the link presence matrix). The edge thickness within the second networks (b), represents the average strength of the relationship across all participants who reported the specific link (corresponds to the link strength matrix).

3 Results

3.1 Does PECAN account for the heterogeneity of MDD on an individual-level?

Symptom profiles. We explored the selected symptom profiles across all 163 participants in the depression sub-sample, and found that no two symptom profiles were the same. Most reported symptom profiles contained seven symptoms. This was the minimum number of symptoms required, hence a possible explanation for this outcome could be that participants simply selected symptoms until they reached the required number to continue with the questionnaire. The remaining profiles evenly distributed on a range from eight to 15 symptoms. We found that the individual symptom profiles differed considerably in their composition. Nevertheless, while we found no symptom which was consistently reported across the entire sample, some symptoms were clearly more prevalent (e.g., *Tired, Worries, Trouble concentrating*), whereas others were rarely reported (e.g., *Compulsions*) (see Figure 2). 81 % of the sample selected *Unknown/External* among causes. Dimensionality reduction using t-SNE indicated low clustering across participants, as supported by the Hopkins' statistic of 0.52. Hence, we were not able to identify consistent patient groups. This provides strong evidence for the inter-individual differences between MDD profiles, and shows that the integration of individual findings can add valuable insights and promote deeper understanding in the study of depression.

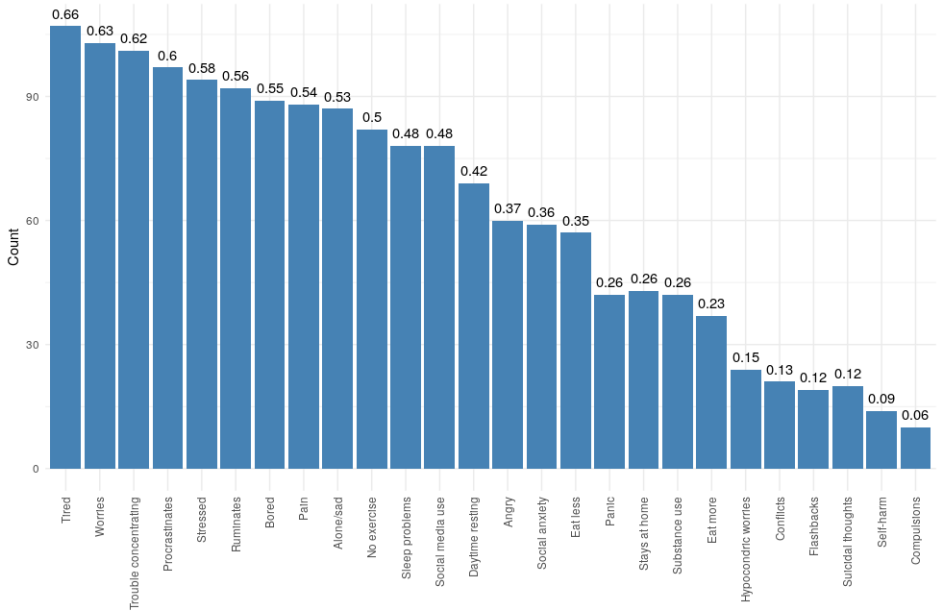


Figure 2: Count of each symptom and proportion of the sample that selected it. The symptoms are ordered from most (left) to least (right) prevalent.

Symptom relations. After looking at the symptom combinations across participants, we investigated symptom relations within individuals. Community detection, which we used to identify symptom clusters within individual networks, showed that the majority of networks ($N = 137$) only contained one community ($\mu = 1.25$). To examine the separate pairwise symptom relations across individuals, PECAN allows to focus on symptom co-occurrence as well as the presence and strength of specific links between them (see Figure 3, 4 & 5). Take for example *Tired* and *Daytime resting*: 78 % of the times *Daytime resting* was reported, *Tired* was also selected. Not only were these symptoms frequently reported together, but they were also often connected: 80 % of the times *Daytime resting* and *Tired* co-occurred, participants reported a causal influence from *Tired* to *Daytime resting* to which they on average allocated 59.35 %. In contrast, only 9 % reported the link *Daytime resting* → *Tired*. Hence, the link between *Daytime resting* and *Tired* was predominantly characterized by *Tired* causally influencing *Daytime resting*. The most consistently reported relationship was the unidirectional link *Compulsions* → *Suicidal thoughts*, which was however only reported by three participants. The ability of PECAN to grasp the directionality of relations within networks constitutes a major advantage in comparison to cross-sectional network studies that only allow for the interpretation of associations between symptoms. Important to note however, is that the present PECAN questionnaire did not allow participants to indicate links between emotion-related symptoms.

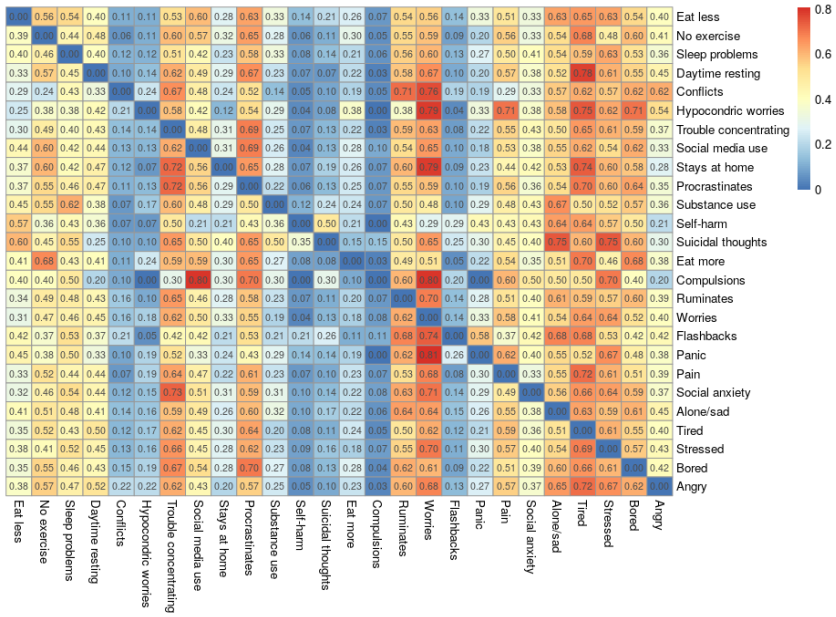


Figure 3: This non-symmetric matrix shows how often a row and a column symptom were reported together relative to their occurrence, e.g., 80 % of the times *Compulsions* was reported, it co-occured with *Worries*. However, only 8 % of the times *Worries* was reported, it co-occurred with *Compulsions*.

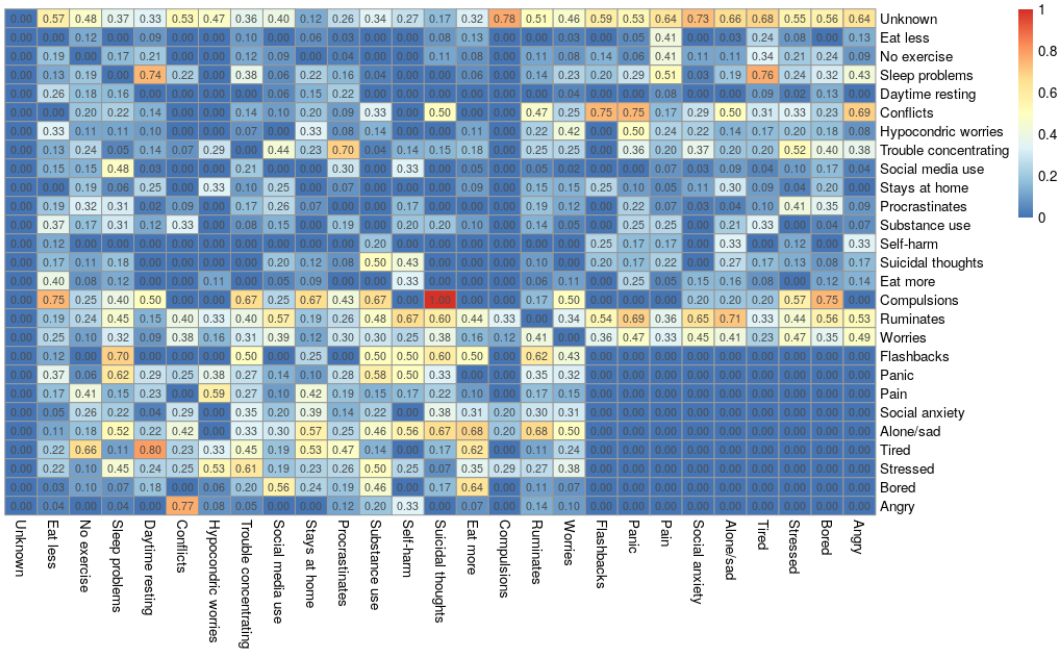


Figure 4: This non-symmetric matrix shows the relative value denoting how often there was an edge from a row symptom to a column symptom when they were both present. Hence, e.g., 50 % of the times when *Compulsions* and *Worries* were reported, there was the link *Compulsions* → *Worries*. The lower right of the matrix is empty as no connections between emotion-related symptoms were allowed.

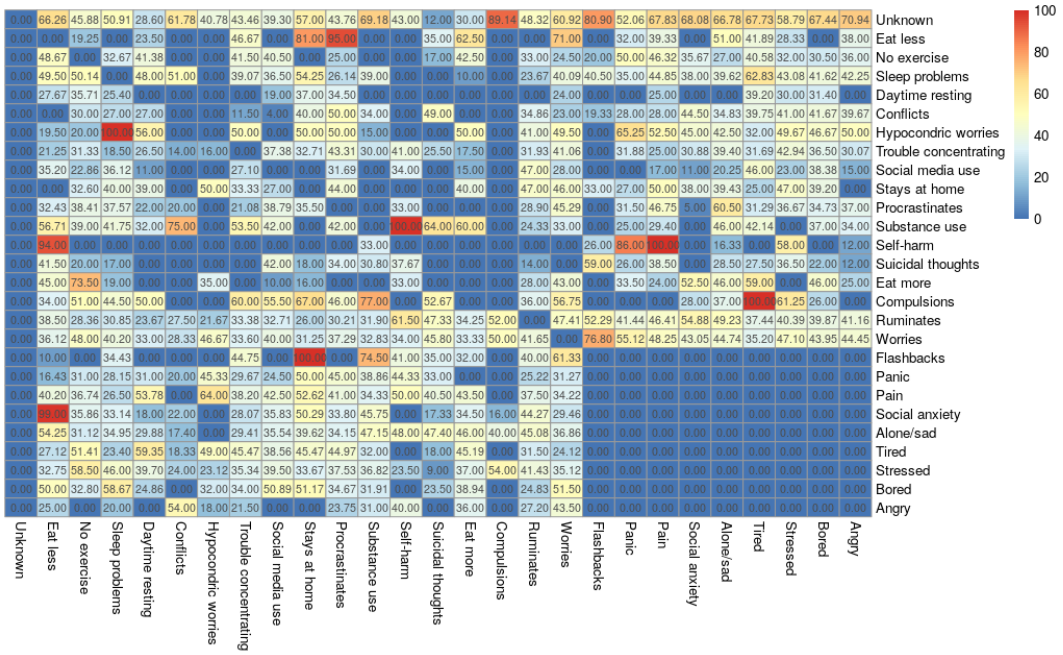


Figure 5: This non-symmetric matrix shows the average edge weights. Hence, e.g., across all *Compulsions* → *Worries* edges, there was an average edge weight of 56.75 %. The lower right of the matrix is empty as no connections between emotion-related symptoms were allowed.

Feedback loops. We also found that 82.82 % of individual networks included feedback loops ranging from two to 12 edges, 75 % of which consisted of two to six edges. The identified feedback loops showed considerable variation regarding length and included symptoms. However, we found some symptoms to be more often involved in feedback loops than others (see Figure 6). A symptoms' prevalence in feedback loops can give insight into its importance in maintaining (negative) effects on the network, and thereby inform us about promising intervention targets. The most commonly reported symptom within feedback loops was *Ruminates*. In contrast, out of the sample that reported *Bored*, the symptom was involved in feedback loops in only 30 %. Hence *Bored*, while prevalent, did not play a vital role in maintaining network dynamics on a group-level. However, the importance of a symptom in maintaining network dynamics is not only characterized by how many participants report it within feedback loops in general, but also by the number of feedback loops it is involved in within each participant. Consequently, a symptom which is reported by fewer participants within feedback loops but is involved in a large proportion of them, might be considered more important than a symptom which is reported by more participants within feedback loops but is only part of a small proportion of them. For example, while the symptom *Eat less* was only reported by 19 % of the individuals that selected it, as part of feedback loops, it appeared on average in 69 % of the feedback loops within those individuals. Hence, while less participants included *Eat less* in feedback loops, it was a very active symptom in maintaining symptom dynamics in the ones who did. This, once again, underlines the importance of considering individual-level findings in practice and also use it as a complementary layer of information in research. Among the most common feedback loops were *Ruminates* $\leftrightarrow$ *Alone/sad* (present in 18 % of the sample) and *Trouble concentrating* $\leftrightarrow$ *Stressed* (present in 15 % of the sample). In case of the latter, however, it could be argued that both symptoms are not distinct from each other and rather an example of content overlap, which would render this loop to be less meaningful.

Centrality. Another metric to measure a symptoms' influence on activating and maintaining network dynamics is centrality. Hence, identifying the most central symptoms is crucial to determine where to intervene. We found that on a group-level, *Unknown/External* had the highest out-degree centrality, implying that participants had a difficulty to fully explain the causal influences within their network by their selected symptoms. Furthermore, *Compulsions* and *Ruminates* had the highest out-/to in-degree centrality ratio, and hence, on average more out-going than incoming effects (see Figure 7). In contrast, *Daytime resting, Eat more, Hypocondric worries* and *Self-harm* had the lowest out-/to in-degree centrality ratio.

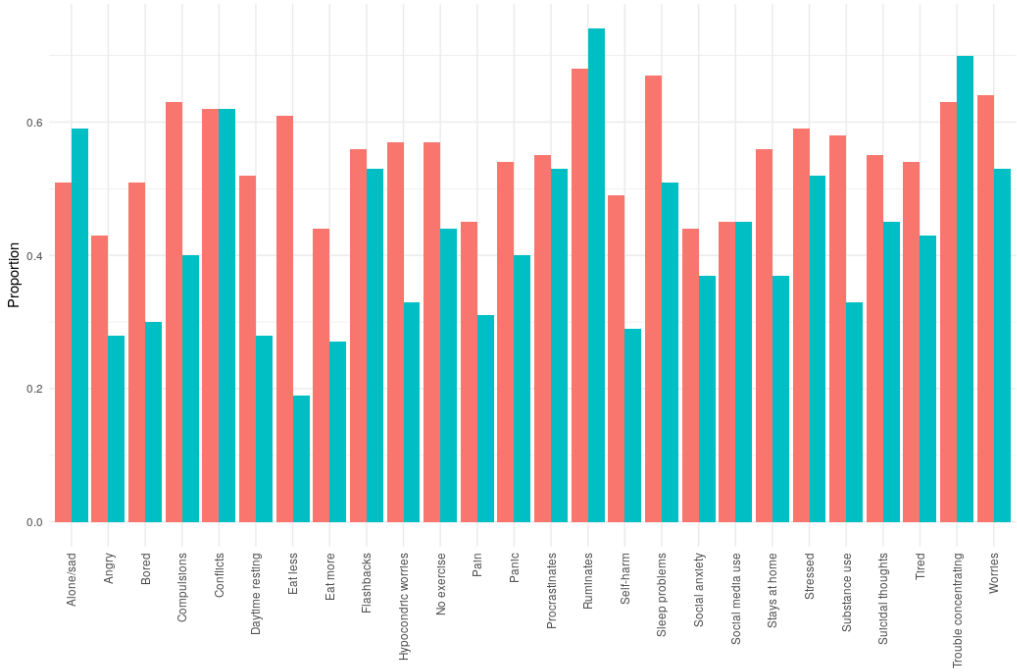


Figure 6: The coral bars show the average proportion of feedback loops within an individual that included the symptom. The blue bars denote the proportions of participants in which the symptom was part of feedback loops out of all participants who selected the symptom.

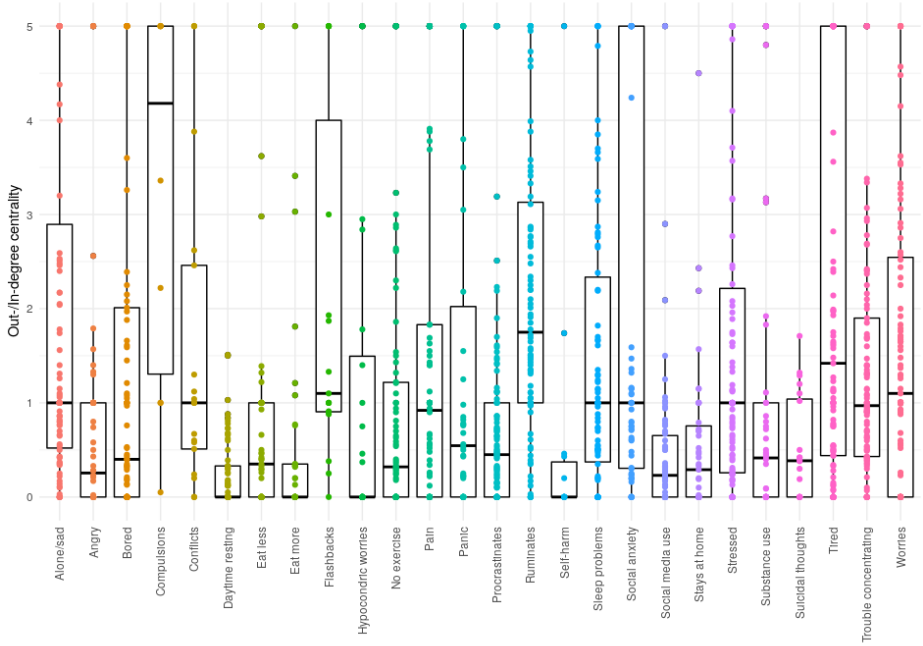
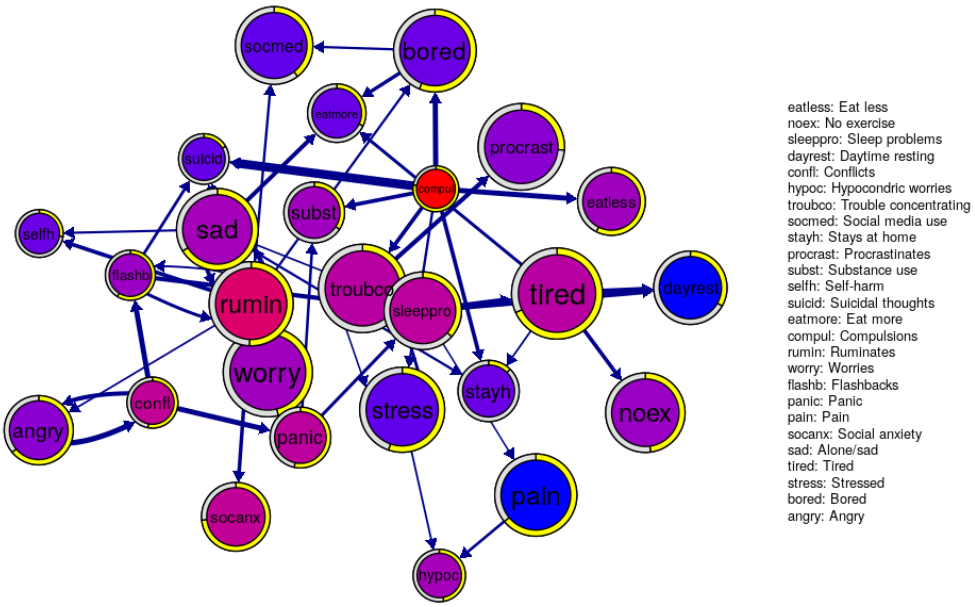


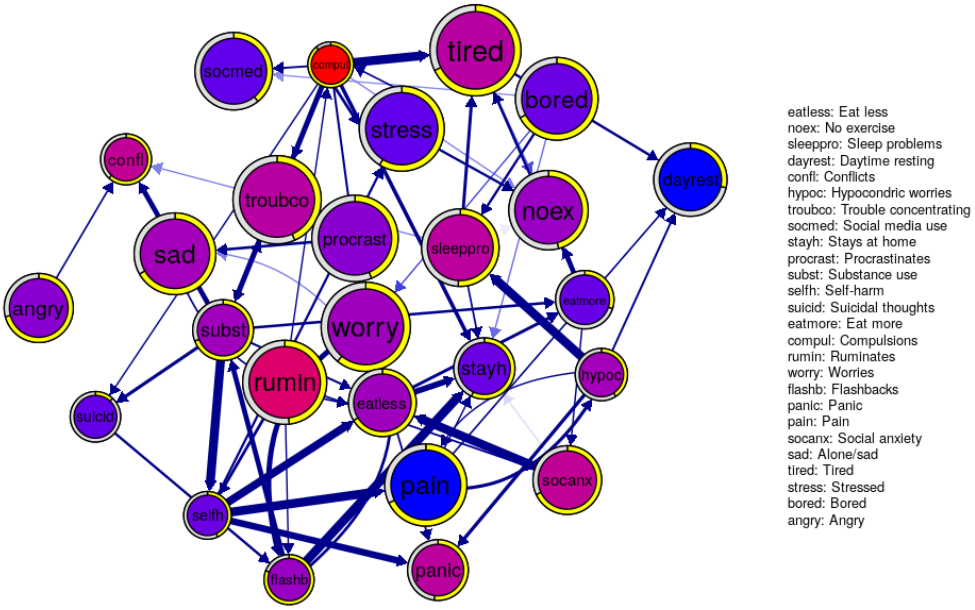
Figure 7: Out-/to in-degree centrality ratio for each symptom ($x > 1$: out- $>$ in-degree; $x = 1$: out- $=$ in-degree; $x < 1$: in- $>$ out-degree). We capped the values at 4 for a meaningful visualization.

Summary networks. To visualize our findings across the sample, we created summary networks. While network 1 (Figure 8a) visualizes the prevalence of symptom links, network 2 (Figure 8b) indicates their strength. We can see that, on average, *Ruminates* and *Compulsions* had the strongest out to in-degree centrality ratio, meaning they influenced the network more than they were influenced by the remaining symptoms. However, this influence is scaled by their prevalence in the sample. While *Ruminates* was a frequently reported symptom (larger node), *Compulsions* was only reported by 6 % of the sample (see Figure 2). The networks also explain the influence of *Unknown/External* on each symptom through pie charts. For example, while *Compulsions* was very strongly influenced by *Unknown/External*, *Suicidal thoughts* only received little influence, and could thus be almost fully explained by the remaining symptoms causing it. Both networks together can be used to get a better understanding of the group-level PECAN dynamics. For instance, while the edge from *Compulsions* to *Tired* seems very relevant in network 2, there is no edge between these symptoms in network 1. This indicates that while this link was very strong, it was rarely reported.

Group-level comparison. To see whether those group-level PECAN dynamics match existing group-level network findings, we compared an undirected average PECAN structure (P_{net}) with a summary network of robust MDD edges (M_{net}) (Malgaroli et al., 2021). M_{net} included robust edges of 12 networks reported across five cross-sectional studies. It included *Anhedonia, Concentration difficulties, Depressed mood, Fatigue, Psychomotor (agitation/retardation), Sleep, Suicidality, Weight*, and *Worthlessness*, and was divided into two communities. *Fatigue* and *Depressed mood* were the most central symptoms forming the two separate communities and showing little robust connection to each other. The link *Depressed mood–Anhedonia* was the most frequent, and the link *Anhedonia–Fatigue* was the most frequent inter-community edge. To enable direct comparison, P_{net} included only *Alone/sad, Bored, Eat less and Eat more, Sleep problems, Suicidal thoughts, Tired*, and *Trouble concentrating*. This sub-sample included three communities: (1) *Sleep problems, Tired*, (2) *Trouble concentrating, Bored*, and (3) *Eat less, Suicidal thoughts, Eat more, Alone/sad*. *Tired* and *Trouble concentrating* were the most central symptoms, and the strongest links were *Tired–Sleep problems*, and *Tired–Trouble concentrating*. While P_{net} and M_{net} showed considerable variability in their structure, the symptom *Tired* (or *Fatigue*) played an important role in both networks. In general, however, the comparison between different MDD network studies is challenging due to methodological inconsistencies, different study designs, and variability in sample size, population, and included symptoms. Hence, more effort is needed to reduce between-study heterogeneity and enable meaningful comparison of network findings.



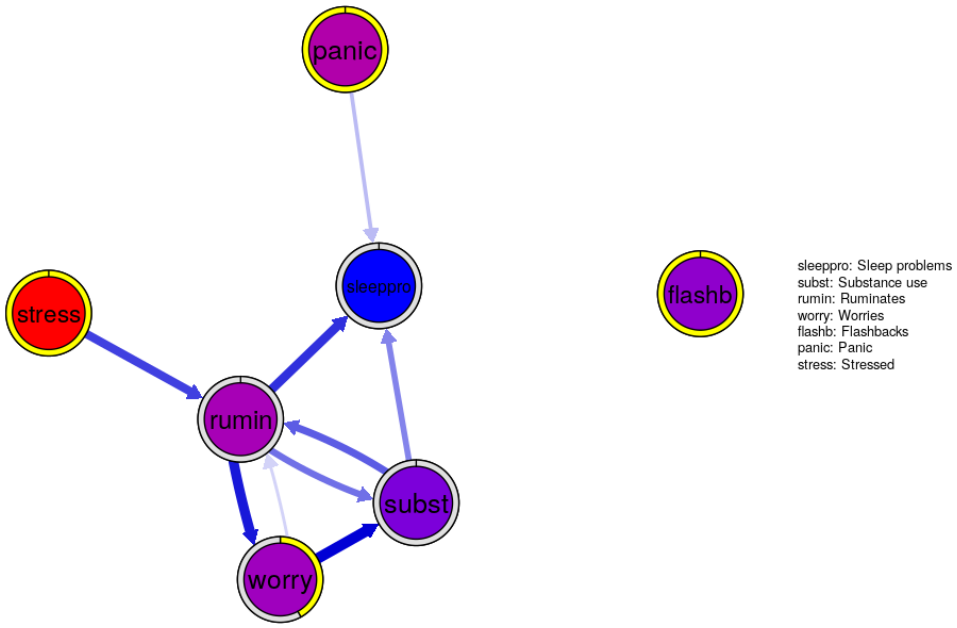
(a) Network 1. Edge thickness represents the count of links between two symptoms relative to their co-occurrence. We only included links that were reported over 50 % of the times both symptoms were present.



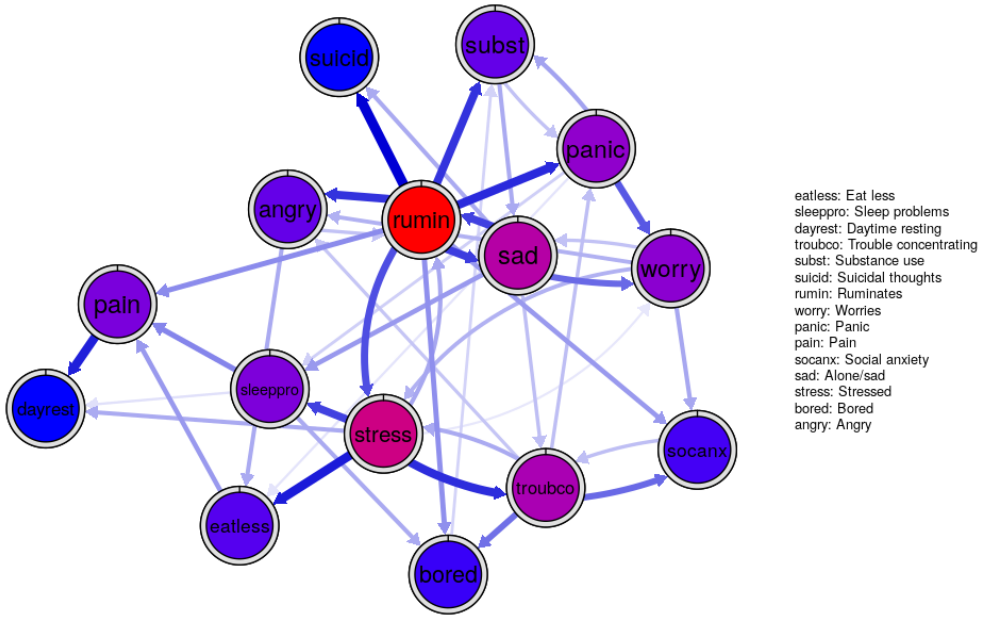
(b) Network 2. Edge thickness represents the average strength of the causal relationships. We only included links that had an average edge weight above 50 %.

Figure 8: Summary networks. Node size is scaled by how often the symptoms were reported, e.g., *Compulsions* is a small node as it was only selected by 6 % of the sample. Node color represents the out/in-degree centrality ratio and ranges from blue (low value) to red (high value). The yellow part in the pie charts around the nodes denote how much each node is influenced by *Unknown/External*.

Individual-level comparison. Besides being able to compute average PECAN networks to infer group-level findings, the methods' strong suite lies in its capacity to enable the time-efficient generation as well as systematic interpretation of individual networks. To illustrate the latter, and highlight the variability among individual networks regarding all the aspects we have investigated so far, we chose to perform a short visual comparison between two participants. To this end, we chose participant 180989 and participant 200234 due to their differing symptom profiles (see Figure 9a & 9b). While participant 180989 selected seven symptoms, participant 200234 selected 15 symptoms. Their individual networks show that participant 180989 exhibited a rather sparse, while participant 200234 exhibited a more densely connected network. Both participants shared six symptoms (*Panic, Ruminates, Sleep problems, Stressed, Substance use, Worries*). Participant 180989 appeared to amount substantial causal influence towards *Unknown/External*. In contrast, participant 200234 allocated no causal influence towards *Unknown/External*. Hence, the network of participant 200234 can be seen as more informative regarding the causal structure of symptom dynamics, as the selected symptoms can be fully explained by each other. While participant 180989 included two communities (*Flashbacks* fully isolated), participant 200234 only included one community. In participant 180989 the strongest links were *Worries* $\rightarrow$ *Substance use* (64 %), *Ruminates* $\rightarrow$ *Worries* (58 %), and *Ruminates* $\rightarrow$ *Sleep problems* (52 %). While all of these symptoms were reported by participant 200234, these links were not present. In participant 200234 the strongest links were *Stressed* $\rightarrow$ *Eat less* (67 %), *Pain* $\rightarrow$ *Daytime resting* (66 %), *Ruminates* $\rightarrow$ *Panic* (63 %), and *Stressed* $\rightarrow$ *Trouble concentrating* (62 %). Both participants showed the links *Panic* $\rightarrow$ *Sleep problems*, *Stressed* $\rightarrow$ *Ruminates* and *Ruminates* $\rightarrow$ *Substance use*. In participant 180989, we found three feedback loops with a maximum length of three edges. Interestingly, *Stressed* directly influenced *Ruminates* which was part of all three identified feedback loops. Hence, the symptom *Stressed* can be seen to induce the self-maintaining processes in form of feedback loops. In contrast, we found a total of 173 feedback loops with a maximum length of 10 edges in participant 200234. The strongest feedback loop in participant 180989 was *Ruminates* $\rightarrow$ *Worries* $\rightarrow$ *Substance use* $\rightarrow$ *Ruminates*, while it was *Ruminates* $\leftrightarrow$ *Alone/sad* in participant 200234. As in participant 180989 *Stressed* had the highest out-/to in-degree centrality ratio, and appeared to play an important role in activating self-maintaining effects on the network, it could be seen as a promising intervention target. In contrast, intervention in participant 200234 could primarily focus on *Ruminates*, as it exerts the most influence on the remaining network. Concluding, there was evident variability in both networks regarding symptom constellation and interrelations resulting in vastly different individual networks and subsequent treatment decisions.



(a) Individual network of participant 180989.



(b) Individual network of participant 200234.

Figure 9: Individual networks. Edge thickness represents the strength of the causal relationships (we included all reported links). Node color represents the out/in-degree centrality ratio and ranges from blue (low value) to red (high value). The yellow part in the pie charts around the nodes denote how much each node is influenced by *Unknown/External*.

3.2 Are there PECAN properties linked to depression severity & chronicity?

Finding PECAN properties that reliably predict relevant clinical markers is key to establish the methods' utility in practice. Hence, we investigated whether two intrinsic properties of PECAN, namely density and the presence of feedback loops (including 3-5 edges) could be used as indicators for the severity and chronicity of participants' depression.

Apart from density in the chronicity sub-sample, no variable was normally distributed. Hence, we computed spearman correlations. We first looked at the relation between density and feedback loops and the number of selected symptoms. We expected that density and the number of feedback loops would increase the more symptoms were selected. However, we only found a weak positive correlation for both density ($r = 0.27, p = 1.2e-05$) and number of feedback loops ($r = 0.29, p = 2.4e-06$). This indicates that participants who selected more symptoms, not necessarily reported more links or feedback loops. Thus, the links and therefore loops that were reported, might be seen as meaningful rather than a byproduct of a large network. For severity, we again found weak positive correlations for both density ($r = 0.27, p = 7.2e-06$) and the number of feedback loops ($r = 0.2, p = 0.00084$). For chronicity, we also found a weak positive correlation for both density ($r = 0.24, p = 0.0063$) and the number of feedback loops ($r = 0.17, p = 0.052$). Thus, both depression severity and chronicity slightly increased density and the number of feedback loops.

For severity as the outcome variable, our linear model had a significant effect for both density ($p = 5.286e-06$) and the number of feedback loops ($p = 0.001195$). However, both predictor variables explained rather little of the variance observed in the outcome variable, with density explaining only 7.59 %, and number of feedback loops explaining only 3.92 %. For chronicity as the outcome variable, our linear model also had a significant effect for both density ($p = 0.004058$) and the number of feedback loops ($p = 0.03603$). Here, again, both predictor variables failed to explain much of the observed variance in the outcome variable, with density explaining 6.47 %, and number of feedback loops explaining 3.5 %. Thus, both models had a rather bad fit which questions whether density and the number of feedback loops can be seen as reliable indicators for depression severity and chronicity in our sample.

3.3 What are the PECAN relations between symptoms of MDD and insomnia?

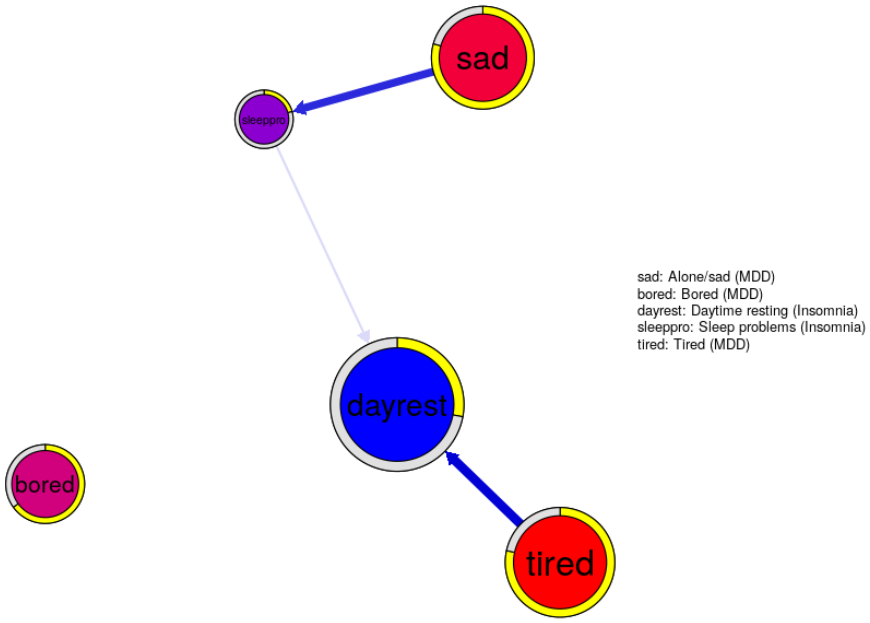
Within our last research question, we used the PECAN method to focus on specific symptom dynamics, and concentrated on the relations between symptoms of MDD and insomnia in the entire sample. We did not find a predominant direct pathway between the two disorders. Across participants who exhibited symptoms from both disorders, 29.94 % of individual networks only showed direct links from MDD to insomnia symptoms

(see Figure 10a & 10b), and no direct connections vice versa. In contrast, 26.11 % showed the opposite direct causal pathway (see Figure 11a & 11b). 27.39 % of the sample included a bi-directional relationship (see Figure 12a & 12b), and 16.56 % showed no direct causal links between the disorders. In the *MDD* $\rightarrow$ *insomnia* group, the most commonly reported and strongest link was *Tired* $\rightarrow$ *Daytime resting*. While *Daytime resting* was also the most prevalent symptom in this group, *Sleep problems* was rarely reported. In the *insomnia* $\rightarrow$ *MDD* group, the most common symptoms were *Tired* and *Sleep problems* and the most reported inter-disorder connection was *Sleep problems* $\rightarrow$ *Tired*. Interestingly, within this group *Daytime resting* was rarely reported. Lastly, within the *MDD* $\leftrightarrow$ *insomnia* group, the strongest and most prevalent connection was also *Sleep problems* $\rightarrow$ *Tired*. While the link *Tired* $\rightarrow$ *Daytime resting* was a commonly reported but weak, the link *Bored* $\rightarrow$ *Sleep problems* was rarely reported but strong.

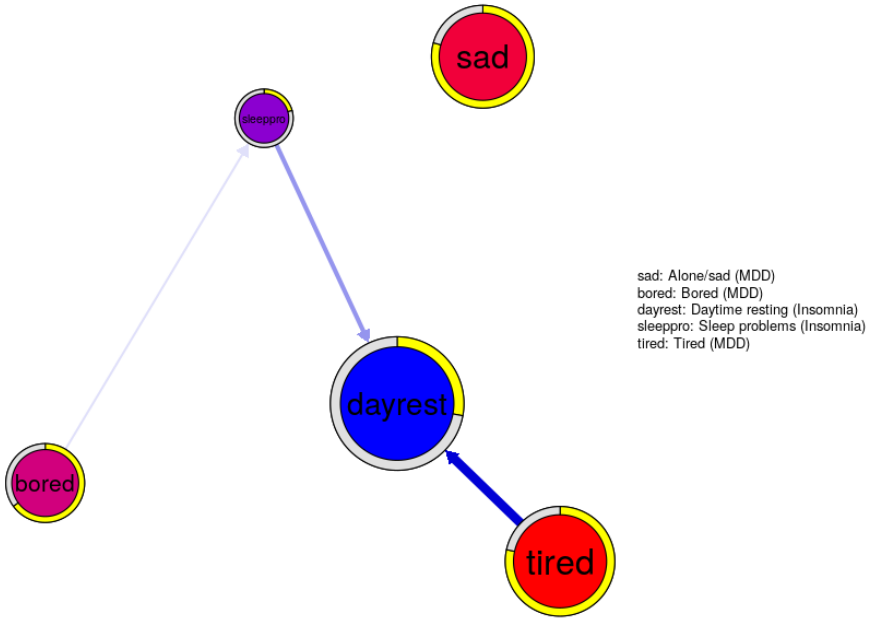
As we identified these sub-groups only based on direct causal links (i.e., $s_{MDD} \rightarrow s_{insomnia}$), we further explored participants' feedback loops to examine possible indirect relationships between symptoms of both disorders (i.e., $s_{MDD} \rightarrow s_{other} \rightarrow s_{insomnia}$). We found that 40.43 % of the *MDD* $\rightarrow$ *insomnia* group, and 48.48 % of the *insomnia* $\rightarrow$ *MDD* group, included feedback loops involving symptoms of both disorders. Furthermore, we found that 30.77 % of the group which did not exhibit any direct relationship between the disorders still showed feedback loops including symptoms of both disorders. Hence, even though most participants did not show bidirectional dynamics on a direct-level, they did show an indirect mutually causing relationship between both disorders via feedback loops.

To facilitate interpretation of group-level findings, we generated summary networks of the relevant subset of MDD and insomnia symptoms (see Figure 13a & 13b). The most common and strongest links between MDD and insomnia symptoms were *Sleep problems* $\rightarrow$ *Tired*, occurring 81 % of the times both symptoms were present with an average edge weight of 58.16 %, and *Tired* $\rightarrow$ *Daytime resting*, occurring 76 % of times both symptoms were present with an average edge weight of 55.59 %. Across participants, *Alone/sad* and *Tired* had the highest out-/to in-degree centrality ratio and hence represented the most influential nodes. However, contrary to *Tired*, *Alone/sad* did not appear influential in inter-disorder relations between MDD and insomnia. *Daytime resting* had the lowest out-/to in-degree centrality ratio (see Figure 14).

In general, we could not identify clear disorder clusters but found an inter-disorder cluster constituted out of *Daytime resting, Sleep problems* and *Tired*. Our findings show that the causal relationship between MDD and insomnia is commonly perceived by individuals reporting symptoms of both disorders, but that the majority perceives it to be unidirectional. Future studies should focus on closer examining the nature of the indirect pathways connecting symptoms of MDD and insomnia.

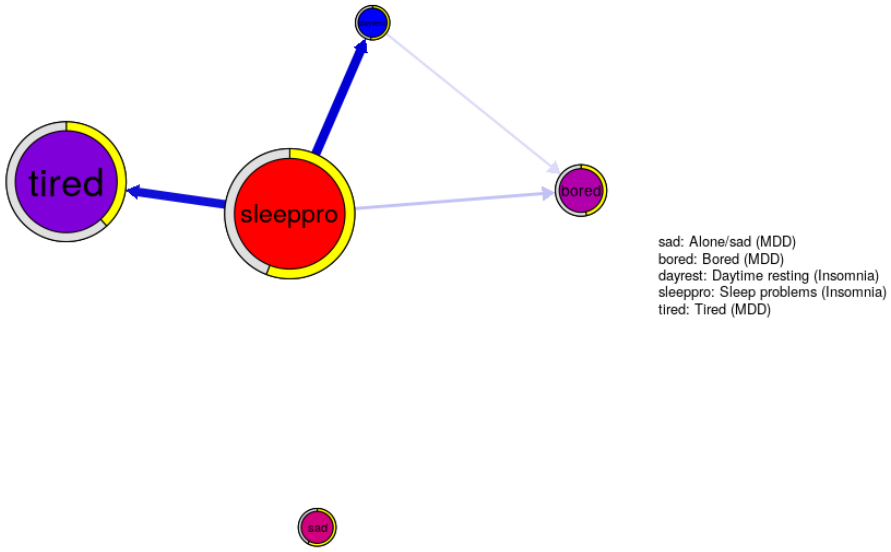


(a) *MDD* → *Insomnia* group network 1. Edge thickness represents the count of links between symptoms relative to their co-occurrence. We only included links that were reported over 50 % of the times both symptoms were present.

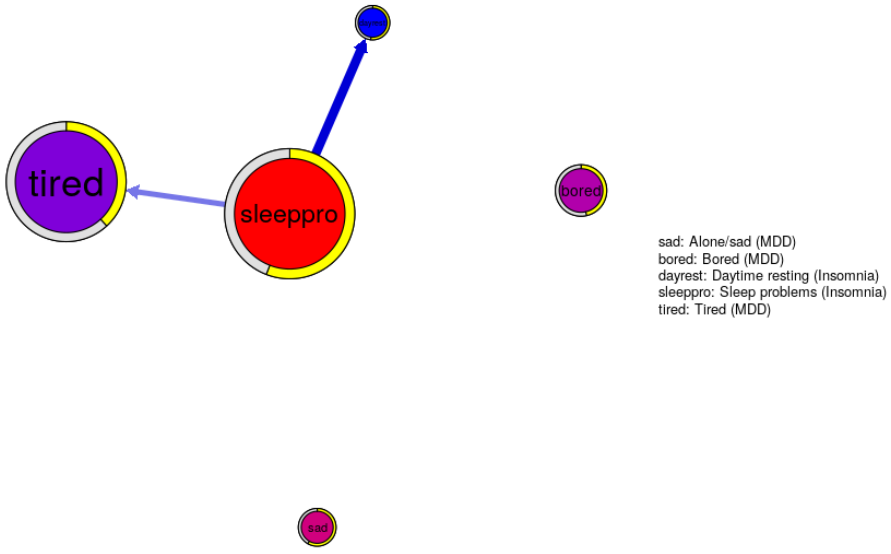


(b) *MDD* → *Insomnia* group network 2. Edge thickness represents the average strength of the causal relationships. We only included links that had an average edge weight above 50 %.

Figure 10: Networks of *MDD* → *Insomnia* group. Node size is scaled by how often the symptoms were reported. Node color represents the out/in-degree centrality ratio and ranges from blue (low value) to red (high value). The yellow part in the pie charts around the nodes denote how much each node is influenced by *Unknown/External*.

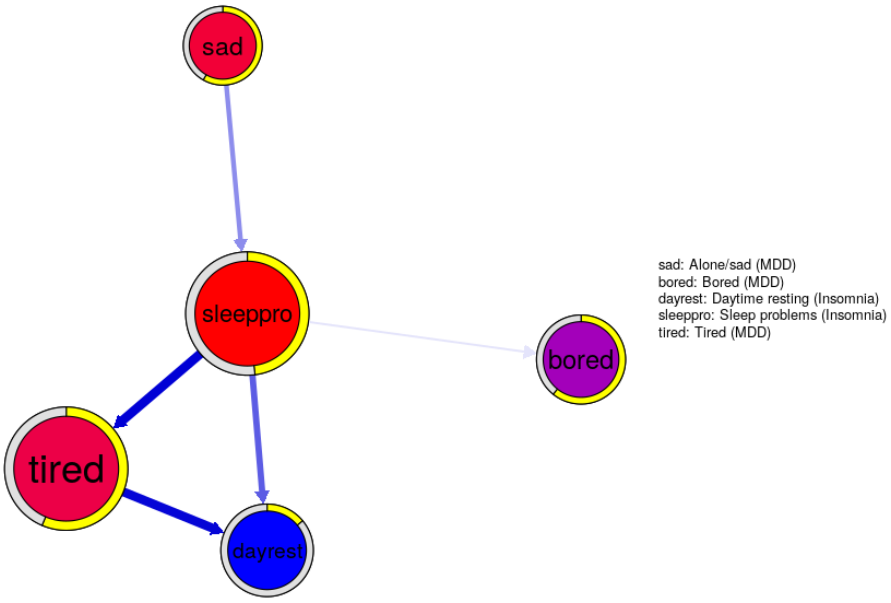


(a) *Insomnia* → *MDD* group network 1. Edge thickness represents the count of links between symptoms relative to their co-occurrence. We only included links that were reported over 50 % of the times both symptoms were present.

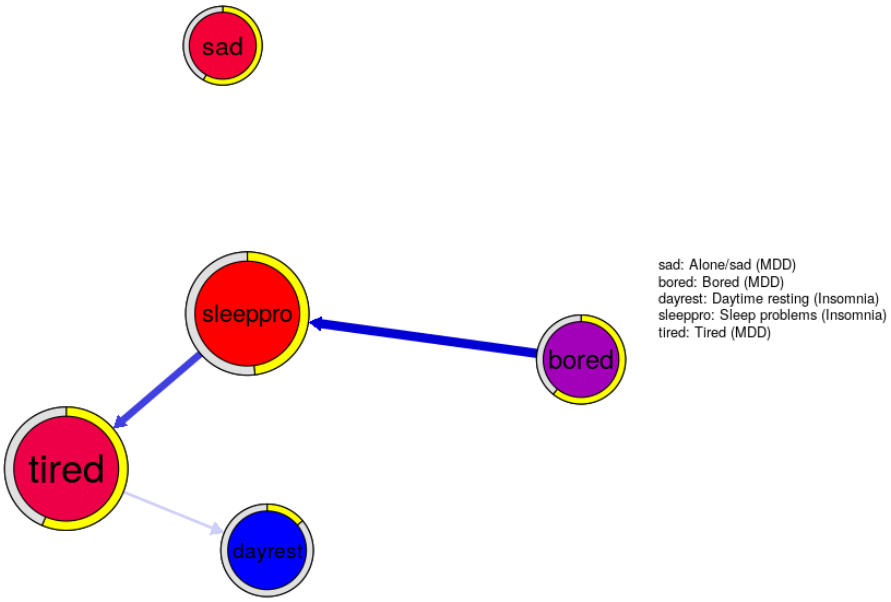


(b) *Insomnia* → *MDD* group network 2. Edge thickness represents the average strength of the causal relationships. We only included links that had an average edge weight above 50 %.

Figure 11: Networks of *Insomnia* → *MDD* group. Node size is scaled by how often the symptoms were reported. Node color represents the out/in-degree centrality ratio and ranges from blue (low value) to red (high value). The yellow part in the pie charts around the nodes denote how much each node is influenced by *Unknown/External*.

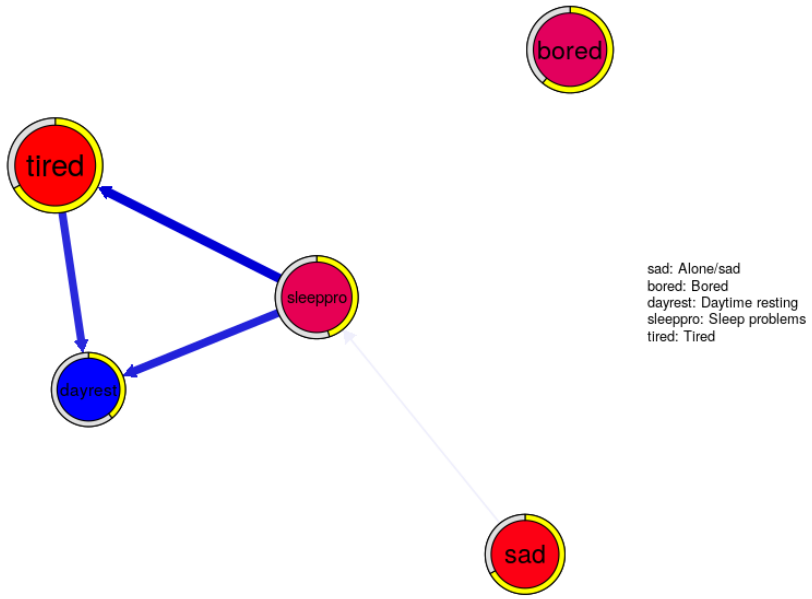


(a) *MDD* ↔ *Insomnia* group network 1. Edge thickness represents the count of links between symptoms relative to their co-occurrence. We only included links that were reported over 50 % of the times both symptoms were present.

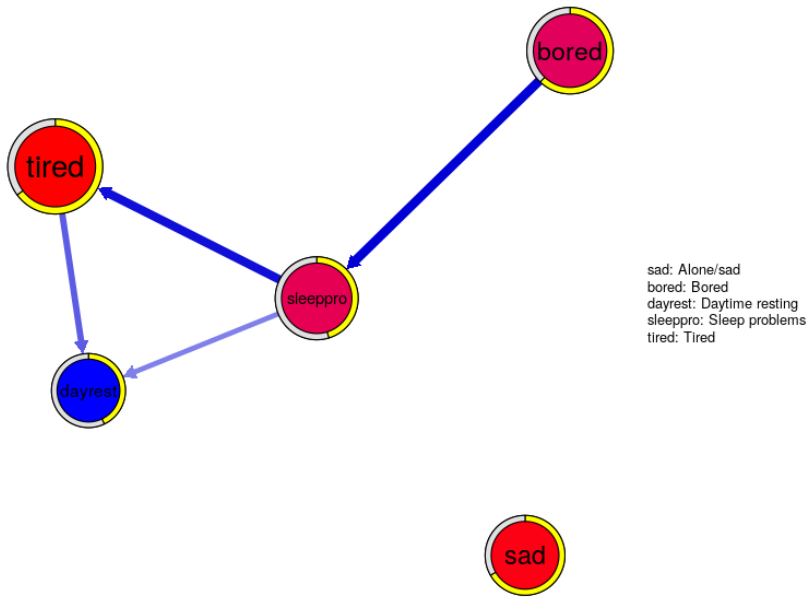


(b) *MDD* ↔ *Insomnia* group network 2. Edge thickness represents the average strength of the causal relationships. We only included links that had an average edge weight above 50 %.

Figure 12: Networks of *MDD* ↔ *Insomnia* group. Node size is scaled by how often the symptoms were reported. Node color represents the out/in-degree centrality ratio and ranges from blue (low value) to red (high value). The yellow part in the pie charts around the nodes denote how much each node is influenced by *Unknown/External*.



(a) Group-level *MDD–Insomnia* network 1. Edge thickness represents the count of links between symptoms relative to their co-occurrence. We only included links that were reported over 50 % of the times both symptoms were present.



(b) Group-level *MDD–Insomnia* network 2. Edge thickness represents the average strength of the causal relationships. We only included links that had an average edge weight above 50 %.

Figure 13: Group-level networks of MDD and insomnia symptom subset. Node size is scaled by how often the symptoms were reported. Node color represents the out/in-degree centrality ratio and ranges from blue (low value) to red (high value). The yellow part in the pie charts around the nodes denote how much each node is influenced by *Unknown/External*.

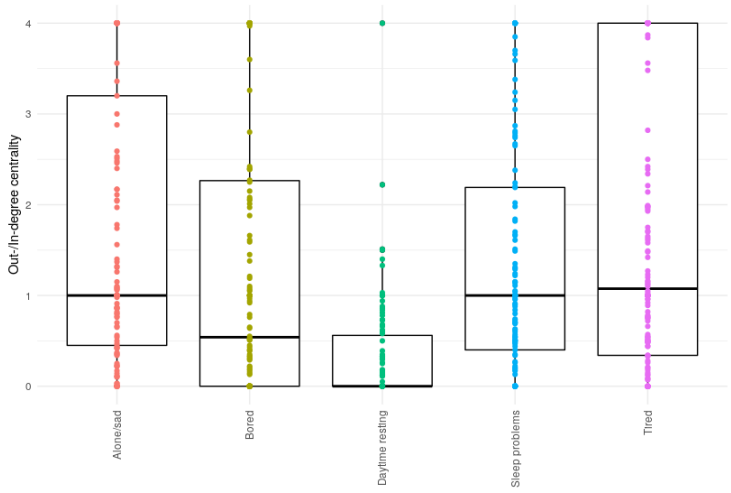


Figure 14: Out-/In-degree centrality ratio for the specific MDD and insomnia symptoms ($x > 1$: out- $>$ in-degree; $x = 1$: out- $=$ in-degree; $x < 1$: in- $>$ out-degree). We capped the values at 4 for a meaningful visualization.

4 Discussion

Within the current project we have presented an extensive demonstration of how the PECAN method can be used to analyze symptom dynamics on the individual as well as group-level. Within a sub-sample of participants with above cut-off PHQ-9 scores, we found a large heterogeneity considering symptom constellations. Interestingly, according to the Diagnostic and Statistical Manual of Mental Disorders (Fifth Edition) (DSM-5), a depression diagnosis requires the presence of either *Depressed mood* or *Anhedonia*. However, the symptoms *Alone/sad* and *Bored*, which can be seen as analogous in the present study, were only present in just above 50 % of the sample. While it could be that affected individuals have difficulty perceiving and therefore reporting some symptoms more so than others, the found heterogeneity most definitely challenges the current status quo in depression diagnostics.

Large variability was also reflected in the individual symptom relations. However, we also found some consistencies across the sample. For instance, we found that *Daytime resting* was often (partially) caused by *Tired* with an average influence of 59.35 %, and that this relation was mostly unidirectional. The ability of PECAN to uncover directionality within symptom relationships, allowed us to not only investigate directionality within symptom pairs but also to analyze the composition of entire feedback loops. Here, again, we found large variation between participants considering loop length and respective symptom constellation, e.g., the most common feedback loop *Ruminates* $\leftrightarrow$ *Alone/sad* was present in only 18 % of the sample.

Ruminates was most frequently reported within feedback loops, and seemed to be a very active symptom in the network. On average, if *Ruminates* was reported within feedback loops, it was involved in over 70 % of them. Furthermore, *Ruminates* was also among the symptoms with the highest out-/to in-degree centrality ratio, meaning that it usually had more out-going than incoming effects. Therefore, on a group-level, *Ruminates* represented a more influential node and played an active role in activating and maintaining network dynamics. Hence, our data suggests that intervening on *Ruminates*, could potentially have benefiting effects on the entire network. However, in light of the identified heterogeneity, future studies should explore whether this is indeed a sensible intervention target on an individual-level, and use PECAN to choose intervention strategies to investigate whether the method can be used to infer promising treatment decisions.

Throughout our analysis, we found that *Unknown/External* played an important role within individual networks. In fact, the majority of participants included *Unknown/External* as a central cause in their network. Hence, most symptoms were (partially) caused by unknown or external influences, and thus could not be fully explained by the remaining symptoms in the network. Therefore, the more influence is exerted by *Unknown/External* in a network, the less information we can deduce by looking at the network alone. It is not clear whether the observed importance of *Unknown/External* was simply due to the limited symptom list, or whether participants lacked the ability to grasp the causal factors to some extent. In case of the former, future studies should not only expand the symptom list, but also include outside factors such as extraordinary life events. Furthermore, a qualitative analysis of free-text answers could be performed to better understand how the PECAN questionnaire can be optimized in this regard. Considering the latter, future studies should aim at identifying different response styles. These might be characterized by different levels of insight or certain personality traits correlating with perceived benefit and explanability of the individual networks. Consequently, potentially identifying sub-populations for which the PECAN method might be more beneficial is key to establish the method in personalized therapy.

As part of exploring the clinical utility of PECAN, we analyzed whether network density and number of feedback loops predicted the severity and chronicity of individuals' depressive symptoms. We found weak correlations between each indicator and outcome variable. While both linear models had a significant effect, both density and number of feedback loops could only account for less than 8 % of the observed variance in each outcome variable. Possible reasons for these inconclusive findings could be some of our methodological drawbacks. For instance, our depression duration measure was based on self-report, and might therefore not have been very reliable. Furthermore, the current PECAN questionnaire did not allow for relations between emotion-related symptoms, which might have affected the magnitude of both density and feedback loops.

Finally, we used PECAN to analyze the dynamics linking MDD and insomnia. We found distinct groups on a direct level, having either only connections from one to the other disorder, bidirectional connections, or no connection at all. Interestingly, we found that even the groups exhibiting no direct bidirectional links, showed bidirectional dynamics on an indirect level. The proportions ranged from 30 to 50 %, and can be considered to be a conservative estimate as we did not take bidirectional links outside of feedback loops into account. Our findings indicate that symptoms of MDD and insomnia mutually interact with each other, but that the majority of participants do not directly perceive this bidirectional relationship. Future studies should focus on these symptom dynamics on an indirect level to see whether there are common intermediary symptoms connecting both disorders. Furthermore, future studies should look at more distinct symptoms as it is questionable to treat *Tired* as a symptom exclusive to MDD.

The current project exemplified that the PECAN method allows to analyze symptom dynamics on various levels. Not only can it be used to examine dynamics on an individual and group-level, and hence separate within- from between-subject findings, but it is also able to abstract direct- and indirect-level symptom relations. Taken together, these different angles enable a more complete analysis of network findings, and allow us to draw a more comprehensive picture of the underlying phenomena. In doing so, we found that PECAN retrieved a large variability in a depressive sub-sample that ranged from symptom combinations to symptom relations. Furthermore, we also found heterogeneity in the specific relation between symptoms of MDD and insomnia, which were however characterized by underlying bidirectional dynamics. As the PECAN method relies on self-report, however, it might be more prone to overestimate heterogeneity due to e.g., lack of insight or simply careless responding. While this possibility should be taken into account, it would conversely entail that PECAN can be used as a conservative estimate for consistencies in the sample. Hence, the commonalities that we found, while rare, could be more readily seen to be representative of "true" group-level patterns. In addition, retrieving symptom dynamics via self-report opens up new avenues for the study of personalized networks, such as studying hypothetical scenarios or including information about symptoms' (present or past) severity. Besides the methods extensive range of application, the major strong suite of PECAN lies in its simplicity. PECAN allows for the simple and intuitive generation of individual networks with little to no prior methodological know-how. Hence, the method could more easily be adopted in practice, without any additional long-term participant burden, as is the case and often criticized in EMA. Altogether, PECAN's versatility and simplicity distinguish it from other methods to build and analyze symptom networks. More importantly, it enables it's use in both research and practice, thereby facilitating to bridge the gap between the two realms, and ultimately helping us to finally reduce the burden of mental disorders.

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