Depressive symptomatology in older adults treated with behavioral activation: A network perspective

Noortje P. Janssen, Melissa Guineau, Peter Lucassen, Gert-Jan Hendriks, Nessa Ikani

PII: S0165-0327(24)00389-6
DOI: https://doi.org/10.1016/j.jad.2024.02.073
Reference: JAD 17240

To appear in:

Received date: 27 December 2023
Revised date: 16 February 2024
Accepted date: 19 February 2024

Please cite this article as: N.P. Janssen, M. Guineau, P. Lucassen, et al., Depressive symptomatology in older adults treated with behavioral activation: A network perspective, (2023), https://doi.org/10.1016/j.jad.2024.02.073

This is a PDF file of an article that has undergone enhancements after acceptance, such as the addition of a cover page and metadata, and formatting for readability, but it is not yet the definitive version of record. This version will undergo additional copyediting, typesetting and review before it is published in its final form, but we are providing this version to give early visibility of the article. Please note that, during the production process, errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

© 2024 Published by Elsevier B.V.
Depressive symptomatology in older adults treated with behavioral activation: A network perspective

Noortje P Janssen*, Behavioural Science Institute, Radboud University, Thomas van Aquinostraat 4, 6525 GD, Nijmegen, The Netherlands; Department of Primary and Community Care, Research Institute of Health Sciences, Radboud University Medical Centre Nijmegen, Nijmegen, The Netherlands; Institute for Integrated Mental Health Care Pro Persona, Nijmeegsebaan 61, 6525 DX, Nijmegen, The Netherlands.
Noortje.P.Janssen@radboudumc.nl

Melissa Guineau*, Behavioural Science Institute, Radboud University, Thomas van Aquinostraat 4, 6525 GD, Nijmegen; The Netherlands; Institute for Integrated Mental Health Care Pro Persona, Nijmeegsebaan 61, 6525 DX, Nijmegen, The Netherlands
M.Guineau@propersona.nl

Peter Lucassen, Department of Primary and Community Care, Research Institute of Health Sciences, Radboud University Medical Centre Nijmegen, Nijmegen, The Netherlands
Peter.Lucassen@radboudumc.nl

Gert-Jan Hendriks, Behavioural Science Institute, Radboud University, Thomas van Aquinostraat 4, 6525 GD, Nijmegen; The Netherlands; Institute for Integrated Mental Health Care Pro Persona, Nijmeegsebaan 61, 6525 DX, Nijmegen, The Netherlands
Gertjan.Hendriks@ru.nl

Nessa Ikani, Department of Developmental Psychology, Tilburg University, Warandelaan 2, 5037 AB, Tilburg, The Netherlands; Institute for Integrated Mental Health Care Pro Persona, Nijmeegsebaan 61, 6525 DX, Nijmegen, The Netherlands
N.ikani@tilburguniversity.edu

*shared first authorship

Corresponding author:
Noortje Janssen Noortje.P.Janssen@radboudumc.nl

Number of Tables: 1
Number of figures: 2
Abstract

Background: Late-life depression is a serious mental health problem. Behavioral Activation (BA) is an effective, accessible psychotherapeutic treatment for older adults. However, little is known about which symptoms decrease and how associations between depressive symptoms change during BA treatment.

Methods: Using data from a cluster-randomized trial for older adults with late-life depression, we estimated a partial correlation network and a relative importance network of depressive symptoms before and after 8 weeks of BA treatment in primary care (n = 96). Networks were examined with measures of network structure, connectivity, centrality as well as stability.

Results: The most central symptoms at baseline and post-treatment were anhedonia, fatigue, and feeling depressed. In contrast, sleeping problems had the lowest centrality. The post-treatment network was significantly more interconnected than at baseline. Moreover, all symptoms were significantly more central post-treatment.

Conclusion: Our findings highlight the utility of the network approach to better understand symptom networks of depressed older adults before and after BA treatment. Results show that network connectivity and centrality of all symptoms increased after treatment. Future studies should investigate longitudinal idiographic networks to explore symptom dynamics within individuals over time.

Keywords: behavioral activation, depression, older adults, network analysis

Running title: Symptom networks of late-life depression after BA

Introduction

Late-life depression is a serious mental health problem that is most often treated with antidepressants (Hetlevik et al., 2019; Verhaak et al., 2012). Antidepressants have less favorable effects in older adults compared to younger adults and are associated with risks, such as adverse interactions with medications (Alexopoulos, 2019; Coupland et al., 2011; Holvast et al., 2017a; Holvast et al., 2017b). Importantly, older adults report preferring psychological therapy as opposed to pharmacotherapy, but there is a lack of accessible treatment options (Hetlevik et al., 2019; Wuthrich & Frei, 2015). Behavioral Activation therapy (BA) might be able to fill this treatment gap because of its (cost-)effectiveness,
simplicity, and feasibility in older adults (Ekers et al., 2014; Janssen et al., 2023; Orgeta et al., 2017).

BA is a short psychological treatment that aims to increase the time spent on rewarding activities while decreasing the time spent on non-rewarding activities. Lewinsohn (1974) postulated that the interaction between behavioral avoidance and depressed feelings that take place after an important life event can create a downward spiral, exacerbating depressive feelings. He theorized that the key mechanism to disrupting this spiral was to increase positively reinforcing behavior which would in turn lead to enhanced feelings of reward. Studies investigating potential mechanisms have not yet been able to unravel which processes contribute to change in depression symptoms during BA (Janssen et al., 2020). The most researched mechanism is the aforementioned relationship between activation and experience of reward from one’s environment, but the evidence supporting this mechanism is weak (Dimidjian et al., 2006; Ryba et al., 2014). The investigation of mechanisms of change of BA is important as it enables us to discern therapeutic components and mechanistic pathways that influence outcomes, thereby enabling the refinement of treatment techniques and ultimately enhancing overall treatment efficacy.

Previous studies on the effectiveness and working mechanisms of BA assessed changes in depression severity using sum-scores, without focusing on individual depressive symptoms (i.e. Janssen et al., 2020; Orgeta et al., 2017; Uphoff et al., 2020). While this approach is useful to assess treatment outcomes, it inherently assumes that statistical covariance equates to a latent entity. This approach conceals the effects of BA on specific symptoms and possibly conceals reciprocal relationships among symptoms. As such, there is a need to examine changes in (reciprocal) associations between depressive symptoms following BA.

The network approach is a promising way to investigate associations between depressive symptoms targeted by BA. This approach allows for the examination of how symptoms (i.e., nodes) are associated with other symptoms (represented by edges; Borsboom & Cramer, 2013; Cramer et al., 2010). Within this approach, it is also possible to identify central symptoms that describe the importance and influence of nodes to spread activation throughout the network (Borsboom et al., 2021). Moreover, it is also possible to identify the interconnectedness of a network (i.e., network connectivity; Fried & Cramer, 2017). According to the connectivity hypothesis, a strongly connected network predicts greater vulnerability to psychopathology (Cramer et al., 2016).
Research on symptom networks in older adults is scarce. The few studies that investigated depression symptom networks in older adults solely focused on network characteristics (e.g., edges and centralities) in cross-sectional samples (e.g., Belvederi Murri et al., 2020; Belvederi Murri et al., 2022; Eli et al., 2022) and did not explore differences in centrality and connectivity that have occurred during treatment. With respect to connectivity, research in adults has shown inconclusive results (Wichers et al., 2021). Some studies found that depressed adult patients had increased network connectivity when compared to remitted patients or healthy controls (Pe et al., 2015; van Borkulo et al., 2015). On the other hand, other studies found increased connectivity after treatment (e.g., Bos et al., 2018; McElroy et al., 2019) which indicates improvement of one symptom leads to improvements in other symptoms, a so-called ‘positive spiral’ (McElroy et al., 2019). There are, however, no studies that have investigated how network centrality and connectivity change after BA.

The aim of the current study was twofold. First, we investigated whether BA, delivered by mental health nurses in primary care for older adults with clinically relevant depressive symptoms, led to reductions in individual depressive symptoms from pre- to post-treatment. The results were compared to treatment as usual (TAU) to investigate whether potential observed differences were specific for BA. Second, we explored potential differences in symptom networks of depressive symptoms at pre- versus post-treatment for participants randomized to BA. In our preregistration, we followed the connectivity hypothesis and hypothesized a significantly lower post-treatment network connectivity compared to the pre-treatment network (Cramer et al., 2016; van Borkulo et al., 2015). However, studies on differences between pre- and post-treatment networks point to a significantly higher overall post-treatment network connectivity (Bos et al., 2018; McElroy et al., 2019). Due to these inconsistencies, we explicitly deviated from our preregistered hypothesis and did not hypothesize any specific direction regarding connectivity, nor did we hypothesize any direction regarding the network structure or specific changes for individual nodes or edges. Hence, we describe our results in an exploratory manner.
Methods

Design and participants

This study used data from the BeATDeP65 (Behavioural Activation Treatment for Depressed older adults in primary care) trial, conducted at general practices in the Netherlands. The BeATDeP65 trial is a cluster-randomized controlled multicenter trial with two parallel treatment groups, investigating the (cost-)effectiveness of behavioral activation (BA) in comparison with TAU for late-life depression in Dutch primary care (Janssen et al., 2017). Primary care centers (PCCs) were randomly allocated to either BA or TAU by an independent statistician using computer generated random numbers.

The sample consisted of 161 patients diagnosed with depression or clinically relevant depressive symptoms (i.e., PHQ-9 score ≥ 10). All patients received treatment (BA or TAU) at various PCCs in the Netherlands. All patients had been referred by their general practitioner (GP) and all data were collected between July 2016 and November 2021. The inclusion criteria for the original study were: (1) 65+ years of age and (2) having moderate to severe clinically relevant depressive symptoms (i.e., PHQ-9 score ≥ 10). Exclusion criteria were: (1) current severe mental illness in need of specialized treatment, high risk of suicide, drug and/or alcohol abuse as assessed with the Mini International Neuropsychiatric Interview (MINI5.0.0) ((Van Vliet & De Beurs, 2007), (2) psychotherapy in the previous 12 weeks or current treatment by a mental health specialist, and (3) moderate to severe cognitive impairment, as measured with the Montreal Cognitive Assessment (MoCA<18; (Nasreddine et al., 2005)). Patients using antidepressants were eligible if a stable dose had been maintained for at least 12 weeks. The preregistration for this study is available on the Open Science Framework (https://osf.io/mrt6q). Any deviations from the preregistration are marked as such within this manuscript.

Procedure

Older adults who visited their GP with depressive symptoms were informed about the study with an information letter. After obtaining consent, a research assistant planned a home visit. During this visit, participants received the baseline questionnaires which had to be completed within the following week. Questionnaires included questions about depressive symptoms, cognitive impairment, possible treatment predictors and mediators (e.g., rumination and loneliness), and a cost-effectiveness measure, see (Janssen et al., 2017) for a detailed description of the procedures and measures. Approximately one week after the baseline meeting, the eight-week treatment started. Nine weeks after the baseline meeting, the post-
treatment home visit and questionnaires were planned. Participants also received several questionnaires during treatment and the follow-up period (Janssen et al., 2017). For the current study, data of the baseline measure (week 0) and post-treatment measure (week 9) were used.

**Ethics statement**
The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. All procedures used in the original study were approved by the local medical ethical committee of the Radboud University Medical Center (CMO Arnhem-Nijmegen; 843001606).

**Treatment**

*Behavioral activation*

BA was delivered by mental health nurses (MHNs) at various PCCs in the Netherlands who received a two-day training by licensed specialists. In addition, MHNs received biweekly online group-supervision. The BA intervention was based on the ‘Behavioural Activation Clinicians’ guide of Martell et al. (2013) including one 45-minute face-to-face session followed by seven 30-minute face-to-face sessions. In the first session, a functional analysis was made, focusing on the interaction between feelings and activities. In the following sessions, participants were encouraged to register their activities and mood, and plan pleasurable or fulfilling activities.

*Treatment as usual*

Health professionals in the TAU arm were encouraged to choose interventions that were consistent with the guidelines of the Dutch College of GPs, such as antidepressant medication and counselling sessions with a mental health nurse (Van Gelderen et al., 2012). They had the liberty to determine the frequency and duration of their interventions based on individual needs.

**Measures**

Patient Health Questionnaire-9 (PHQ-9)(Cameron et al., 2011). The PHQ-9 is a self-report instrument assessing depressive symptoms during the last week and includes 9 items ranging
from 0 (not at all) to 3 (nearly every day). The PHQ-9 was administered at baseline, week 2, 4, and 7, post-treatment, and every three months during the 12-month follow-up.

Quick Inventory of Depressive Symptomatology (QIDS-SR)(Rush et al., 2003). The QIDS-SR is a self-report instrument and assesses the severity of depressive symptoms during the last two weeks. The 16 items were answered on a four-point scale (range 0-3) that described different responses (e.g., with 0 indicating ‘I do not feel sad’ and 3 indicating ‘I feel intensely sad virtually all the time’). The QIDS-SR was administered at baseline, post-treatment, and every three months during the 12-month follow-up.

Data analysis
To investigate whether a standardized BA program for older adults led to a significant reduction in individual depressive symptoms from pre- to post-treatment when compared to TAU, a repeated-measures (RM) analysis of variance (ANOVA) with Bonferroni pairwise comparisons was used. Treatment condition (BA or TAU) was included as the between-subjects factor and Time (pre-to post-treatment) was included as the within-subjects factor. The interaction between time (pre-to-post treatment) and condition (BA or TAU) was also included. The significance level was set at $p < .05$. IBM SPSS version 29.0 was used for these analyses.

Network analysis.
The analyses were conducted in the R programming environment (Version 4.2.1; (Team, 2020)). The R code is available on the Open Science Framework (https://osf.io/2wyhf). The de-identified dataset is available upon request. To explore differences in patterns of interactions among depressive symptoms at pre- versus post-treatment for participants randomized to BA, a network analysis was conducted. We computed two networks: a partial correlation network to visualize the associations between the symptoms and a relative importance network to assess directionality.

Node selection. In the presented networks, nodes represent depression symptoms. To reduce the possible impact of measurement error and improve node reliability, multiple indicators per node were used, as suggested by de Ron et al. (2022). To this end, the average score per symptom (i.e., item) was calculated based on each individual’s score on the PHQ-9 (Cameron et al., 2011) and the QIDS-SR (Rush et al., 2003). This average symptom score (i.e., item) was used as a separate node in the network (de Ron et al., 2022). The thickness of
an edge signifies the magnitude of the association. Green edges represent positive associations and red edges represent negative associations.

**Partial correlation network.** Pre-treatment and post-treatment partial correlation networks were plotted using the R package bootnet (Epskamp et al., 2018). A partial correlation network estimates correlations between all possible pairs of nodes, while controlling for the influence of all other nodes in the network. Node placement was determined by the node layout from the pre-treatment network to ease comparison.

In the preregistration, the computation of regularized partial correlation networks using graphical LASSO estimation with EBIC model selection was described (Epskamp & Fried, 2018). However, regularizing partial correlation networks via the graphical LASSO could be problematic, given that this procedure might remove too many genuine edges that are mistaken for false-positive edges (Lafit et al., 2019; Williams & Rast, 2020). Given that this is the first study investigating change in symptomatology of older adults following a psychotherapeutic intervention, we prioritized sensitivity and emphasized the hypothesis generating aspects of network analyses. Therefore, we opted to (1) analyze a non-regularized partial correlation network and (2) use a low hyperparameter value (gamma = 0.0) to maximize the stability of the network and prioritize sensitivity. Upon the analysis of results, the non-regularized partial correlation network demonstrated to be more stable compared to the graphical LASSO network (i.e., CS-coefficient of .365 and .521 compared to .208 and .438, see for more information the results section). As such, we decided to deviate from the preregistration and report the results of the partial correlation network.

**Centrality indices.** The most central symptoms in the pre-treatment and post-treatment network were identified using the centrality index expected influence (EI). EI is calculated by summing all edge weights for a given node while taking into account the sign of the edge (Robinaugh et al., 2016). Specifically, EI assesses a node’s influence with its immediate neighbors (i.e., nodes with which it shares an edge). Because associations among depressive symptoms could be either positive or negative (e.g., Berlim et al., 2021; Bos et al., 2018; McElroy et al., 2019), EI provides a more accurate estimate of node centrality compared to strength centrality, which only takes the absolute values of edges into account (Robinaugh et al., 2016). The R package qgraph (Epskamp et al., 2017) was used to compute this index.

**Stability analysis.** The stability of the pre-treatment and post-treatment networks was examined using the R package bootnet (Epskamp & Fried, 2015). First, 95% confidence intervals were calculated for the edges by using a non-parametric 1,000-sample bootstrap.
Next, a 1,000-sample case-dropping bootstrap was used to calculate the stability of the centrality indices via correlation stability (CS) coefficients. This CS coefficient reflects the maximum proportion of cases that could be dropped from the analyses, while still retaining a correlation of .7 or higher with the original centrality indices within an 95% confidence interval.

**Network comparison test.** Network differences between the pre- and post-treatment partial correlation networks were evaluated based on the overall global network structure, network connectivity (i.e., global EI, the sum of all edge weights, signifying the total amount of positive connectivity between nodes) and centralities. The R package `NetworkComparisonTest` (NCT; (Van Borkulo et al., 2022)) was used to test for significant differences.

**Relative importance network.** To assess the directionality of the associations, a pre-treatment and post-treatment relative importance network was computed using the R package `relaimpo` (Grömping, 2007). In a relative importance network, each edge signifies the relative importance of a node as a predictor of another node, adjusted for all other nodes in the network (Johnson & LeBreton, 2004). The edges in a relative importance network are directed as well as weighted. Each edge is assigned a relative importance metric (lmg), that quantifies this relation on a scale of 0 to 1 (Grömping, 2007; Johnson & LeBreton, 2004).

**Centrality indices.** The most central symptoms in the pre-treatment and post-treatment network were identified using the centrality index out-strength. Out-strength is calculated by summing the directed edge weights originating from a given node and ending at all other nodes. This quantifies the extent to which a node has predictive influence on other nodes in the network. We also assessed the stability of the relative importance network, similar to the graphical LASSO network.

**Missing data.** Missing data for the pre-treatment measure of the QIDS-SR and the post-treatment measure of the QIDS-SR and the PHQ-9 were imputed by using the R package `missForest` (Stekhoven & Stekhoven, 2022). This imputation method is based on the randomForest procedure (Breiman, 2001) and fits a random statistical forest of regression trees for each variable. These results are then used to predict missing values. Although there is no fixed standard for the number of trees, we decided to specify the number of trees for this dataset at 1000, in order to improve our results (Breiman, 2001).

**Results**

**Sample descriptives**
The sample (N = 161) consisted of 97 participants who identified as female (60.2 %) and 64 participants who identified as male (39.8%). The mean participant age was approximately 75 years (SD = 6.57; range 65-92). Educational level was low for 66 participants (42.3%), medium for 56 (34.8%) participants, high for 34 (21.1%) participants and unknown for 5 (3.1%) participants. Within this sample, 96 participants were in the BA group and 65 participants were in the TAU group. All participants (N=161) were included in the RM ANOVA.

The analytical sample for the network analysis included solely participants in the BA group (n = 96), consisting of 61 participants who identified as female (63.5 %) and 35 who identified as male (36.5%). Their mean participant age was 76 years (SD = 6.85; range: 65–92). Educational level was low for 39 participants (40.6%), medium for 28 (29.2%) participants, high for 25 (26.0%) participants and unknown for 4 (4.2%) participants.

**Differences between pre-and post-treatment individual depressive symptoms**

The RM ANOVA revealed a significant main effect of Time on all depressive symptoms (all p-values < .001). Moreover, there were significant Time X Treatment condition (BA or TAU) interactions for the symptoms feeling depressed, changes in weight/appetite, decreased concentration and psychomotor agitation or retardation (all p-values <.022), signifying a larger decrease in the BA group compared to the TAU group. Importantly, an independent sample t-test showed no significant differences between these symptoms at pre-treatment (all p-values > .070). See Table 1 for a complete overview of test statistics of the RM ANOVA.

<insert Table A1>

**Pre- and Post-BA partial correlation networks.**

Figure 1 shows the partial correlation network before BA and figure 2 shows the partial correlation network after BA. The bootstrapped confidence intervals (CI’s) for the edges indicated that edges in both the pre-treatment and the post-treatment network were fairly stable (see figure S1 and S2 published as supplementary material online). More information about the strongest edges as well as the correlation matrix that contains all the partial correlation coefficients is presented in Table S1.

<insert figure A1 and figure A2>
Symptom centrality
The nodes with the highest EI in both the pre-treatment and the post-treatment network were anhedonia, fatigue, and feeling depressed (See figure S3 and S4). In addition, bootstrapped difference tests of EI for the baseline network showed that anhedonia showed a significantly higher EI than sleeping problems, suicidal ideation, feeling worthless or excessive guilt, decreased concentration, and psychomotor agitation or retardation. At post-treatment, anhedonia and feeling depressed showed a significantly higher EI than sleeping problems, suicidal ideation, and decreased concentration. Fatigue showed a significantly higher EI than sleeping problems, suicidal ideation, feeling worthless or excessive guilt, and decreased concentration. Sleeping problems showed a significantly lower EI than decreased concentration, a change in weight or appetite, psychomotor agitation or retardation, feeling depressed, fatigue, and anhedonia (figure S6).

Stability Centrality
The CS-coefficients for EI were .365 at baseline and .521 at post-treatment, indicating moderate to strong stability; Epskamp et al., 2018). With respect to the graphical LASSO network, the CS-coefficients for EI were .208 at baseline and .438 at post-treatment, indicating moderate stability. Given that the partial correlation network yielded higher stability values, we solely reported results for the partial correlation network.

Network structure and connectivity
The network comparison test (NCT) examined significant differences between the pre-treatment and the post-treatment networks. No significant differences in the overall network structures were found (M = .313, p = .146), suggesting that the overall organization of symptoms remained broadly consistent from pre- to post-BA. Given the non-significance of the network invariance test and the lack of hypotheses about specific edges, it was not investigated whether there were differences across specific edges (Van Borkulo et al., 2022).

Interestingly, the global EI was significantly higher in the post-treatment network (3.67) compared to the pre-treatment network (.78), S = 2.88, p < .001. Thus, the post-treatment network showed significantly higher connectivity than the pre-treatment network. In the post-treatment network, all nodes were significantly more central than in the pre-treatment
network (all $p$’s $\leq .010$). See Table S2 for a complete overview of significant differences in centralities.

**Relative importance network**

To complement the aforementioned centrality inferences, a relative importance analysis was conducted (figure S7 and S8). At pre-treatment, anhedonia was strongly predictive of feeling worthless or excessive guilt ($\text{lmg} = .49$) and feeling depressed ($\text{lmg} = .43$). In addition, the predictive influence of anhedonia severity on all symptoms was stronger than the reverse influences on anhedonia severity. Moreover, decreased concentration was strongly predictive of psychomotor agitation or retardation ($\text{lmg} = .46$), feeling worthless or excessive guilt was strongly predictive of suicidal ideation ($\text{lmg} = .37$), and fatigue was strongly predictive of a change in weight or appetite ($\text{lmg} = .35$). At post-treatment, anhedonia remained strongly predictive of feeling depressed ($\text{lmg} = .36$) and feeling worthless or excessive guilt ($\text{lmg} = .32$). Moreover, fatigue remained strongly predictive of a change in weight or appetite ($\text{lmg} = .35$), but a change in weight or appetite was also strongly predictive of fatigue ($\text{lmg} = .31$). Psychomotor agitation or retardation were strongly predictive of decreased concentration ($\text{lmg} = .30$).

**Symptom centrality for the relative importance network**

These relationships are further reflected in the centrality indices. At both pre- and post-treatment, anhedonia, feeling depressed, and fatigue showed the highest level of out-strength in the network (figure S9 and figure S10). The CS-coefficient was .281 at pre-treatment and .438 at post-treatment highlighting a moderate to strong stability (Epskamp et al., 2018).

**Discussion**

This is the first study investigating change in symptomatology of older adults following a psychotherapeutic intervention, by focusing on the change in symptom networks following BA. The severity of all depressive symptoms significantly decreased after eight weeks of BA. Moreover, the symptoms of feeling depressed, changes in weight and appetite, decreased concentration, and psychomotor agitation or retardation showed a stronger decrease in the BA group than in the TAU group. BA-theory or previous studies do not provide explanations on why these specific symptoms reduced more in BA than in TAU.

Even though symptom severity decreased, the network connectivity significantly increased. The relationships between symptoms thus became more densely connected after
treatment. The overall network structure did not differ significantly between the two timepoints. This indicates that there is no difference between the network organization before and after treatment. However, there were differences in centrality across the two time-points. All symptoms were significantly more central at post-treatment. Moreover, anhedonia was the most central symptom in the network at both time-points, followed by fatigue, and feeling depressed. The relative importance network indicated that anhedonia was predictive of the severity of all other symptoms. Interestingly, the predictive influence of anhedonia severity on these symptoms was stronger than the reverse influences on anhedonia severity.

The finding of increased connectivity after BA contradicts the connectivity hypothesis, which suggests that a strong interconnectedness of symptoms could accelerate the progression from mild to severe depressive symptoms, thereby creating a ‘negative spiral’ (Cramer et al., 2016). This increased connectivity, however, is in line with the growing body of research suggesting that psychotherapy increases, rather than decreases, relationships between symptoms (e.g., Berlim et al., 2021; Bos et al., 2018; McElroy et al., 2019). This is further supported by the finding that, in the current study, all symptoms increased in centrality at post-treatment, meaning that all symptoms were more strongly connected to other depressive symptoms at post treatment. McElroy et al (2019) have explained such an increase in connectivity as a ‘positive spiral’ where improvement in one symptom leads to improvement in other symptoms. Possibly, increased connectivity in a sample of people at risk for depression, may indicate that deterioration in one symptom can lead to a deterioration of other symptoms, whereas the increase in connectivity during or after treatment in a clinical sample may indicate the opposite (Cramer et al., 2016; McElroy et al., 2019). That is, improvement in one symptom may spread to improvements in other symptoms. As such, the goal of psychotherapy would be to initiate and maintain a positive spiral. This notion shares similarities with BA theory, which specifically postulates that the interaction between behavioral avoidance and depressed feelings can create a downward spiral exacerbating depressive feelings, and that the key mechanism to disrupt this spiral is to increase positively reinforcing behavior. In turn, this would lead to enhanced feelings of reward, thereby creating a positive spiral (Lewinsohn, 1974). However, even though a strongly connected network after treatment does not imply that these symptoms meet clinically relevant cut-offs indicative of a depressive disorder, it is possible that, due to this increased connectivity, the risk for activation of other symptoms remains high (Cramer et al., 2010).

As such, according to the connectivity hypothesis, individuals with a highly connected symptom network after treatment may have an increased risk for relapse when they start to
experience symptoms again. While these findings align with the ‘positive spiral’ model (McElroy et al; 2019), the design of our study prevents us from drawing causal inferences on whether heightened connectivity can be explained by a positive spiral. Future studies with a temporal design should thus investigate whether and how an increase of connectivity during treatment is related to a reduction of depressive symptoms, and whether increased connectivity after treatment is indeed a risk factor for relapse.

Combining connectivity results with centrality indices informs us that anhedonia was more central at post-treatment compared to pre-treatment. In addition, anhedonia was the most central symptom in the network and was more strongly connected to other depressive symptoms than sleeping problems, suicidal ideation, and decreased concentration. The relative importance network additionally illustrated that anhedonia was more strongly predictive of all depressive symptoms than vice versa and the out-strength index indicated that anhedonia mostly influenced the network by activating other symptoms. Altogether, when seen in light of the aforementioned ‘positive spiral’ theory (McElroy et al., 2019), anhedonia might be the most connected symptom in the network to activate improvement in other symptoms, which could initiate a positive spiral. Neurobiological studies indeed suggest that depressed patients generally underestimate the pleasure they will experience from an activity and thus tend to be less motivated in trying to obtain it (Dichter et al., 2009; Martin-Soelch, 2009). In other words, in depression, a continued feeling of anhedonia seems to be expected when planning an activity, while engaging in an activity might actually generate a pleasant experience (Dichter et al., 2009; Martin-Soelch, 2009). BA theory is based on the theoretical premise that repeated planning of possibly rewarding activities will eventually result in a feeling of pleasure that is linked to these activities (Lewinsohn, 1974). The observed decrease in anhedonia hence might be a motivator to continuously plan mood-boosting behaviors, thereby increasing the likelihood that other depression related symptoms will improve as well. Even though current results do not allow causal inferences because of the lack of temporality in the design, our study suggests that anhedonia may play a central role in the symptom network of older adults. To further understand BA and its mechanisms, future studies could focus on the temporal relationship between rewarding activities, anhedonia, and other depressive symptoms.

Further centrality indices showed that sleeping problems was the least central symptom both before as well as after treatment. This suggests that this symptom is the least connected to other depressive symptoms. Sleeping problems were less strongly connected to other depressive symptoms than decreased concentration, a change in weight or appetite,
psychomotor agitation or retardation, feeling depressed, fatigue, and anhedonia. This is in line with research in younger depressed patients (i.e., age \( \leq 65 \) years; Bringmann et al., 2015). Univariate statistics revealed that even though sleeping problems improved over time, it remained the most prevalent symptom in both treatment groups (i.e., the highest mean symptom scores among all symptoms both before and after treatment). Current results indicate that while depression treatment (both BA and TAU) might slightly improve sleeping problems, sleeping problems may not be a central symptom of depression in older adults, but rather a more general consequence of physical illness or problems related to old age such as the desynchronization of biological rhythms (Costa et al., 2013). However, a previous study (Bao et al., 2017) illustrated that sleep disturbances and depression often co-occur at old age and suggest that treatments that tackle underlying mechanisms, such as light therapy and chronotherapy may improve treatment results. It might therefore be useful to focus on circadian rhythm and early day light exposure within BA. Given that sleeping problems are less central and thus less connected to other depressive symptoms, it can be expected that these interventions do not strongly change other depressive symptoms. However, given the fact that sleeping problems are the most severe symptom both at baseline and at post-treatment, and are common and debilitating in older adults, the integration of sleep related treatment tools, such as early day light exposure and chronotherapy into BA, might improve quality of life and therefore the overall usefulness of BA for this population (Bao et al., 2017).

Further, the high centrality values of anhedonia, feeling depressed, and fatigue are in line with previous findings in various age groups (Belvederi Murri et al., 2020; Berlim et al., 2021; Guineau et al., 2022; Wichers et al., 2021). Thus, for both younger and older adults, similar symptoms appear to be central before and after treatment. That is, these symptoms are mostly connected to other symptoms in the network. However, future studies that directly compare symptom networks between younger adults and older adults are needed to confirm this.

This study has several strengths. First, this study used data of a pragmatic trial with a relatively old group of home dwelling older adults with moderate to severe clinically relevant depressive symptoms. This group has never been studied in the context of network change during psychotherapy. Second, the sample included participants with moderate to severe clinically relevant depressive symptoms (i.e., a PHQ-9 score > 9) rather than the presence of major depressive disorder (MDD). In other words: participation in the study was not a function of presence of the core symptoms of MDD. This approach provided variability among all symptoms, thereby reducing the impact of ‘Berkson’s bias’ on centrality estimates.
Third, our focus on clinically relevant depressive symptoms is in line with the Research Domain Criteria (RDoC) framework that aims to investigate the mechanisms pertaining to mental health dysfunctions from a dimensional point of view (Cuthbert, 2014; Insel et al., 2010). By focusing on this group as seen in general practice, we obtained ecologically valid results. Fourth, this study used state of the art network analysis techniques such as the use of multiple indicators per node (de Ron et al., 2022). By combining symptoms of two depression questionnaires into one node, measurement error has been reduced and node reliability improved. Fifth, in contrast to most cross-sectional network analysis studies (e.g., Belvederi Murri et al., 2020; Guineau et al., 2022; Wichers et al., 2021), we compared networks at two time points to gain more insight into the longitudinal impact of BA on a depression symptom network.

Nevertheless, our findings should be interpreted in the light of some limitations. First, even though our sample size was comparable to other studies that compared networks before and after treatment (e.g., Berlim et al., 2021; Roca et al., 2019) a sample of 96 participants is modest for network analyses. While we did find significant differences between the networks, it is important to recognize that the NCT requires sufficient power to detect network differences. Therefore, there might be more differences between the networks, which may not have been detected due to the relatively modest sample size (Van Borkulo et al., 2022). This stresses the importance of replications across larger datasets before definitive clinical inferences can be made. Nevertheless, our study had moderate to strong stability (Epskamp et al., 2018). Second, the small subsample of the TAU group (n = 65) rendered powerful network analysis impossible. Finally, we solely analyzed differences between symptom networks before and after BA. With this approach, we get closer to suggest causal connections, but we cannot confirm them (Bos et al., 2017). In addition, our cross-sectional networks allow for inferences at the group level and cannot directly be translated to the individual. Therefore, future studies should include intensive idiographic longitudinal designs to facilitate inferences on directionality and causality of the networks. This enables the investigation of symptom dynamics within individuals over time.

In conclusion, this study offers unique insights on differences in depressive symptom networks before and after BA in older adults that merit further study. This study showed that symptom severity decreased after both BA and TAU, that some symptoms showed a stronger decrease in the BA group, and that network connectivity and centrality of all symptoms increased after treatment, which might indicate a positive spiral (McElroy et al., 2019). This study indicates that important features of symptom networks of older adults, such as centrality
and connectivity, are comparable to those in younger populations (Berlim et al., 2021; Bringmann et al., 2015; Guineau et al., 2022). We believe that this application of network analysis leads to an improved understanding of depressive symptomatology in older adults that in turn might impact future therapeutic interventions.

References


Bos, F. M., Fried, E. I., Hollon, S. D., Bringmann, L. F., Dimidjian, S., DeRubeis, R. J., &


Cuthbert, B. N. (2014). The RDoC framework: facilitating transition from ICD/DSM to


psychopathological network theory and methodology. Perspectives on Psychological
Journal of statistical software, 17, 1-27. https://doi.org/https://doi.org/10.18637/jss.v017.i01
Guineau, M. G., Ikani, N., Rinck, M., Collard, R., van Eijndhoven, P., Tendolkar, I., Schene,
https://doi.org/https://doi.org/10.1017/S0033291722000575
reported depression treatment and future treatment preferences: an observational study
Holvast, F., Massoudi, B., Oude Voshaar, R. C., & Verhaak, P. F. M. (2017). Non-
pharmacological treatment for depressed older patients in primary care: A systematic
review and meta-analysis. PLoS one 12(9), e0184666.
Holvast, F., van Hattem, B. A., Sinnige, J., Schellevis, F., Taxis, K., Burger, H., & Verhaak,
P. F. (2017). Late-life depression and the association with multimorbidity and
https://doi.org/https://doi.org/10.1093/fampra/cmx018
Insel, T., Cuthbert, B., Garvey, M., Heinssen, R., Pine, D. S., Quinn, K., Sanislow, C., &
framework for research on mental disorders. In (Vol. 167, pp. 748-751): American
Psychiatric Association.
Janssen, N., Huibers, M. J. H., Lucassen, P., Voshaar, R. O., Marwijk, H., Bosmans, J.,
Pijnappels, M., Spijker, J., & Hendriks, G.-J. (2017). Behavioural activation by mental
health nurses for late-life depression in primary care: A randomized controlled trial.
BMC Psychiatry, 17. https://doi.org/https://doi.org/10.1186/s12888-017-1388-x
https://doi.org/10.1159/000509820
Janssen, N. P., Lucassen, P., Huibers, M. J., Ekers, D., Broekman, T. B., Bosmans, J. E., ... &


https://doi.org/https://doi.org/10.3109/02813432.2012.688707


Table A.1. Repeated measures ANOVA analysis of pre-post-measures in depressive symptoms.

<table>
<thead>
<tr>
<th>Symptom</th>
<th>BA</th>
<th>TAU</th>
<th>N</th>
<th>Pre-treatment</th>
<th>Post-treatment</th>
<th>TA</th>
<th>BA</th>
<th>Time</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
<td>SD</td>
<td>F</td>
</tr>
<tr>
<td>Anhedonia</td>
<td>1.70</td>
<td>.73</td>
<td>.98</td>
<td>.92</td>
<td>1.00</td>
<td>.95</td>
<td>1.10</td>
<td>.94</td>
<td>142.7</td>
</tr>
<tr>
<td>Depressed</td>
<td>2.00</td>
<td>.80</td>
<td>1.90</td>
<td>.80</td>
<td>1.10</td>
<td>.80</td>
<td>1.10</td>
<td>.80</td>
<td>138.9</td>
</tr>
<tr>
<td>Sleep</td>
<td>2.10</td>
<td>.60</td>
<td>2.20</td>
<td>.70</td>
<td>1.70</td>
<td>.70</td>
<td>1.70</td>
<td>.70</td>
<td>60.82</td>
</tr>
<tr>
<td>Appetite</td>
<td>1.80</td>
<td>.80</td>
<td>1.60</td>
<td>.80</td>
<td>1.20</td>
<td>.80</td>
<td>1.20</td>
<td>.80</td>
<td>89.42</td>
</tr>
<tr>
<td>Energy</td>
<td>1.60</td>
<td>.80</td>
<td>1.40</td>
<td>.80</td>
<td>.88</td>
<td>.80</td>
<td>.88</td>
<td>.80</td>
<td>77.05</td>
</tr>
<tr>
<td>Self</td>
<td>1.60</td>
<td>.70</td>
<td>1.50</td>
<td>.70</td>
<td>.93</td>
<td>.70</td>
<td>.93</td>
<td>.70</td>
<td>97.14</td>
</tr>
<tr>
<td>esteem</td>
<td>3.80</td>
<td>4.00</td>
<td>4.00</td>
<td>4.00</td>
<td>3.00</td>
<td>3.00</td>
<td>3.00</td>
<td>3.00</td>
<td>52.04</td>
</tr>
<tr>
<td>Concentration</td>
<td>1.50</td>
<td>.70</td>
<td>1.30</td>
<td>.70</td>
<td>1.00</td>
<td>.70</td>
<td>1.00</td>
<td>.70</td>
<td>51.36</td>
</tr>
<tr>
<td>Suicide</td>
<td>.62</td>
<td>.18</td>
<td>.79</td>
<td>.38</td>
<td>.38</td>
<td>.38</td>
<td>.38</td>
<td>.38</td>
<td>69.84</td>
</tr>
</tbody>
</table>

Figure A.1. Partial correlation network before the BA treatment. Nodes represent depressive symptoms. Green lines represent positive partial correlations, whereas red lines represent negative partial correlations. The thickness of an edge reflects the magnitude of the association. Note. Nodes represent symptoms as measured by the used questionnaires (e.g. ‘suicide’ represents ‘suicidal ideation’), but node names are shortened for readability.

Figure A.2. Partial correlation network after the BA treatment. Nodes represent depressive symptoms. Green lines represent positive partial correlations, whereas red lines represent negative partial correlations. The thickness of an edge reflects the magnitude of the association. Note. Nodes represent symptoms as measured by the used questionnaires (e.g. ‘suicide’ represents ‘suicidal ideation’), but node names are shortened for readability.
Author statement

Funding Sources
This work was supported by The Ministry of Health Funding-program for Health Care Efficiency Research ZonMw (843001606). ZonMw had no role in the design, data collection, data analysis, data interpretation, or writing of the report of the study.

Data availability Statement
The data will be made publicly available at DOI https://doi.org/10.34973/1dk9-tj89, after completion of the project, but no later than December 2025, due to ethical considerations, which include ensuring that the release of the data does not interfere with the ongoing analyses of the research group. Until that time, researchers can obtain the data through consultation with the corresponding author.

Author Contributions
NPJ and MG conceptualized the study. NPJ and MG performed the investigation. NPJ and MG curated the data. NPJ, acquired the data. NPJ, MG and NI analyzed and interpreted the data. GJH, PL, and NI supervised the study. NPJ and MG drafted the manuscript. GJH, PL and NI critically revised the manuscript. All authors approved the final version of the manuscript. The corresponding authors attest that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

Acknowledgements
None.
Declaration of Interest

GJH occasionally receives honoraria for lectures at symposia. On a yearly basis it is never more than €1000. All other authors declare: no support from any organization for the submitted work; no financial relationships with any organizations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.
Highlights

- Severity of depressive symptoms decreases after eight weeks of behavioral activation (BA) for older adults.
- Feeling depressed, changes in weight and appetite, decreased concentration, and psychomotor agitation or retardation showed a stronger decrease in the BA group than in the treatment as usual group.
- The most central symptoms at baseline and post-treatment were anhedonia, fatigue, and feeling depressed.
- Behavioral activation enhances connectivity in a symptom network of depressive symptoms.
- Enhanced connectivity indicates a positive spiral wherein symptoms mutually improve each other.