Journal of Psychosomatic Research 188 (2025) 111968

Contents lists available at ScienceDirect

Journal of Psychosomatic Research

journal homepage: www.elsevier.com/locate/jpsychores

Network structure of functional somatic symptoms

Alexandra Litzenburger [a], Yannick Rothacher [b], Kay-Uwe Hanusch [a], Ulrike Ehlert [c], Urs M. Nater [d], Susanne Fischer [c,*]

[a] Bern University of Applied Sciences, Department of Health Sciences, Berne, Switzerland
[b] University of Zurich, Institute of Psychology, Psychological Methods, Evaluation and Statistics, Switzerland
[c] University of Zurich, Institute of Psychology, Clinical Psychology and Psychotherapy, Switzerland
[d] University of Vienna, Department of Psychology, Clinical Psychology, Austria

ARTICLE INFO

Keywords:
Chronic fatigue syndrome
Fibromyalgia
Functional somatic syndromes
Irritable bowel syndrome
Network

ABSTRACT

Objective: The overlap among functional somatic syndromes (FSS) is substantial, which is why various empirical attempts at an improved understanding of related symptoms have been undertaken. Network analyses are particularly valuable from a clinical point of view, since they focus on the extent to which symptoms expression is co-dependent. The aim of this study was to provide the first estimation of the network structure of symptoms in 17 FSS.

Methods: $N = 3054$ young adults participated in an online survey. The Questionnaire on Functional Somatic Syndromes (FSSQ) was used to diagnose FSS and to assess related symptoms. The Patient Health Questionnaire (PHQ-9) was used to assess (comorbid) depression. Various R packages were used for network analysis, which yielded correlations between symptoms (edges), symptom groups (communities), and measures of centrality for individual symptoms (e.g., node strength).

Results: The final network had a relatively small number of edges, with small (46.5 %) or small- to medium-sized (47.1 %) correlations. Ten communities were identified: cognitive problems/fatigue/depression, sensory problems, facial pain, head/neck/upper back pain, dizziness/nausea, throat pain/problems with swallowing, chest pain, widespread pain, abdominal pain/problems with digestion, and genital pain. The highest node strength in the network was found for the symptoms "tired", "down, depressed, or hopeless", and "tired after minimal exertion".

Conclusions: The network analyses pointed to ten distinct groups of moderately associated symptoms in individuals with FSS. Fatigue and depression emerged as important symptoms connecting groups. Future studies should test whether (transdiagnostic) interventions specifically targeting these symptoms are particularly potent in alleviating FSS.

1. Introduction

Medically unexplained symptoms or functional somatic symptoms are highly abundant in the general population [1] as well as in primary [2] and secondary healthcare settings [3]. In specific constellations, they have received labels such as "chronic fatigue syndrome" [4], "fibromyalgia" [5], and "irritable bowel syndrome" [6], which can be found as exclusionary diagnoses in various somatic disease chapters within the International Classification of Diseases [ICD] [7]. However, the overlap among at least some of these functional somatic syndromes (FSS) is substantial [8,9]. This has led some researchers to question the necessity of several distinct FSS [10], of which at least 17 have been described in the literature [11].

In response to this conceptual criticism, various empirical attempts at an improved understanding of the structure of functional somatic symptoms have been undertaken in the past. As recently reviewed by Senger et al. [12], these have included factorial and latent class analyses, which assume that latent constructs (or causes) underlie the expression of clusters of specific symptoms. For instance, one line of research has supported a bifactor model, according to which functional somatic

* Corresponding author at: University of Zurich, Institute of Psychology, Clinical Psychology and Psychotherapy, Binzmuehlestrasse 14/Box 26, 8050 Zurich, Switzerland.
E-mail addresses: alexandra.litzenburger@students.bfh.ch (A. Litzenburger), yannick.rothacher@psychologie.uzh.ch (Y. Rothacher), kay.hanusch@bfh.ch (K.-U. Hanusch), u.ehlert@psychologie.uzh.ch (U. Ehlert), urs.nater@univie.ac.at (U.M. Nater), s.fischer@psychologie.uzh.ch (S. Fischer).

https://doi.org/10.1016/j.jpsychores.2024.111968
Received 3 July 2024; Received in revised form 23 October 2024; Accepted 29 October 2024
Available online 1 November 2024

symptoms are best explained by one general factor related to all symptoms and four factors related to specific groups of symptoms (i.e., fatigue, pain, gastrointestinal, and cardiopulmonary) [13,14].

More recently, network analyses, which represent yet another method to understand symptom structure, have attracted researchers' attention [15]. Whereas factorial and latent class analyses aim to shed light on aetiology, these analyses focus on the extent to which symptom expression is co-dependent (e.g., to what extent fatigue and pain mutually reinforce one another). This renders network analyses highly valuable from a clinical point of view. For instance, in depressive and anxiety disorders, network models have empirically identified central symptoms of these disorders as well as symptoms bridging the two disorders [16]. Prioritising such symptoms in subsequent pharmacological or psychological treatments could lead to more rapid treatment success and, hence, to more efficient treatments. Pioneer work by Senger et al. [12] has recently applied network analyses to patients with somatoform disorders, the predecessor of somatic symptom disorder. The authors found five symptom groups to best represent their data: neurological, cardiovascular, musculoskeletal, gastrointestinal, and urogenital. Moreover, Melidis et al. [17] and Hyland et al. [18] have undertaken the first attempts at estimating the network structure of FSS, identifying up to eleven symptom groups which best reflected their data. However, their sample only included individuals with the most prominent FSS, namely chronic fatigue syndrome, fibromyalgia, and irritable bowel syndrome, although at least 17 FSS have been described in the extant empirical literature [11]. Nevertheless, these findings are highly valuable, as, upon replication, they might allow more nuanced insights into symptom interplay, whether specific groups of symptoms are related to treatment response, and how they change over the course of treatment.

The aim of this study was to provide the first estimation of the network structure of symptoms pertaining to 17 different FSS. Given the high comorbidity between FSS and depression [19], a second aim was to identify "bridge symptoms" between FSS and depressive disorders. Finally, we wanted to explore to what extent the network structure found in individuals with FSS differed from the one observed in individuals with (less severe levels) of somatic symptoms that were not part of any FSS.

2. Methods

2.1. Participants and procedures

Details about the original study from which the current data set was extracted can be found elsewhere [20–22]. In brief, $N = 3054$ young adults residing in Switzerland were recruited via college and university mailing lists between 2009 and 2010 and participated in an online survey on functional somatic syndromes. Mean age was 24.6 ± 5.6 years, 2042 (73.4 %) of the participants were women and 812 (26.6 %) were men. In total, $n = 289$ individuals fulfilled research diagnostic criteria for at least one of 17 FSS, including chronic fatigue syndrome, fibromyalgia, and irritable bowel syndrome (see also next section). The study design was approved by the ethics committee of the University of Zurich and all participants provided electronic informed consent.

2.2. Measures

The Questionnaire on Functional Somatic Syndromes [FFSS; see [23] for the full German version] was used to diagnose FSS, which comprises of five subsequent sets of questions that are connected via a complex algorithm. First, screening questions on 51 somatic symptoms are presented (see also Table 1), which are rated according to their frequency of occurrence ("never/rarely", "frequently", "almost always/always"). If a participant endorses cardinal symptoms of a specific FSS (e.g., if they report frequent fatigue for chronic fatigue syndrome), they are forwarded to the next set of questions covering the research diagnostic

Table 1
Item descriptives of the Questionnaire for Functional Somatic Syndromes (FFSS; score range 0–2) and the depression module of the Patient Health Questionnaire (PHQ-9; score range 0–3). Descriptives are presented as means (standard deviations).

Item	Symptom	Individuals with FSS	Individuals without FSS	*p* value	95 % CI
fss1	Headache	0.61 (0.60)	0.45 (0.54)	< 0.001	[0.1, 0.2]
fss2	Neck pain	0.75 (0.66)	0.53 (0.60)	< 0.001	[0.1, 0.3]
fss3	Facial pain	0.06 (0.25)	0.02 (0.16)	0.012	[0.0, 0.1]
fss4	Mouth pain	0.12 (0.36)	0.08 (0.29)	0.071	[−0.0, 0.1]
fss5	Jaw pain	0.19 (0.47)	0.08 (0.30)	< 0.001	[0.1, 0.2]
fss6	Sore throat	0.30 (0.51)	0.20 (0.42)	0.002	[0.1, 0.2]
fss7	Chest pain	0.16 (0.38)	0.09 (0.30)	0.004	[0.0, 0.1]
fss8	Back pain	0.73 (0.67)	0.59 (0.63)	< 0.001	[0.1, 0.2]
fss9	Upper back pain	0.55 (0.69)	0.38 (0.57)	< 0.001	[0.1, 0.3]
fss10	Lower back pain	0.51 (0.63)	0.45 (0.60)	0.107	[−0.0, 0.1]
fss11	Abdominal pain	0.63 (0.59)	0.25 (0.45)	< 0.001	[0.3, 0.5]
fss12	Upper abdominal pain	0.36 (0.57)	0.09 (0.30)	< 0.001	[0.2, 0.3]
fss13	Lower abdominal pain	0.51 (0.57)	0.22 (0.44)	< 0.001	[0.2, 0.4]
fss14	Genital pain	0.05 (0.22)	0.02 (0.13)	0.013	[0.0, 0.1]
fss15	Pain during sexual intercourse	0.09 (0.33)	0.07 (0.27)	0.287	[−0.0, 0.1]
fss17	Pain in several lymph nodes	0.07 (0.26)	0.03 (0.18)	0.032	[0.0, 0.7]
fss18	Pain in several joints	0.23 (0.48)	0.16 (0.42)	0.033	[0.0, 0.1]
fss19	Pain in several muscles	0.15 (0.37)	0.14 (0.36)	0.526	[−0.0, 0.1]
fss20	Pain in the left side of my body	0.11 (0.36)	0.04 (0.23)	0.004	[0.0, 0.1]
fss21	Pain in the right side of my body	0.09 (0.33)	0.04 (0.20)	0.007	[0.0, 0.1]
fss22	Pain above the waist	0.18 (0.41)	0.12 (0.34)	0.015	[0.0, 0.1]
fss23	Pain below the waist	0.12 (0.34)	0.07 (0.26)	0.018	[0.0, 0.1]
fss24	Pain/discomfort swallowing	0.05 (0.23)	0.03 (0.17)	0.092	[−0.0, 0.1]
fss25	Sensation of a lump in the throat	0.15 (0.37)	0.11 (0.33)	0.133	[−0.0, 0.1]
fss26	Discomfort empty swallowing	0.05 (0.23)	0.03 (0.16)	0.136	[−0.0, 0.1]
fss27	Discomfort swallowing food	0.03 (0.19)	0.01 (0.13)	0.139	[−0.0, 0.0]
fss28	Pain/discomfort during digestion	0.65 (0.64)	0.35 (0.53)	< 0.001	[0.2, 0.4]
fss29	Abdominal bloating	0.77 (0.62)	0.58 (0.56)	< 0.001	[0.1, 0.3]
fss30	Nausea	0.33 (0.53)	0.14 (0.36)	< 0.001	[0.1, 0.3]
fss31	Vomiting	0.04 (0.22)	0.02 (0.14)	0.079	[−0.0, 0.1]
fss32	Pain/discomfort during excretion	0.25 (0.48)	0.15 (0.39)	0.001	[0.0, 0.2]
fss33	Pain/discomfort in the bowel	0.34 (0.54)	0.20 (0.44)	< 0.001	[0.1, 0.2]
fss34	Pain/discomfort in the bladder	0.08 (0.29)	0.05 (0.23)	0.062	[−0.0, 0.1]

(continued on next page)

Table 1 (*continued*)

Item	Symptom	Individuals with FSS	Individuals without FSS	*p* value	95 % CI
fss35	Insomnia	0.37 (0.59)	0.24 (0.49)	< 0.001	[0.1, 0.2]
fss36	Hypersomnia	0.65 (0.71)	0.50 (0.63)	0.001	[0.1, 0.2]
fss37	Tired after minimal exertion	0.40 (0.60)	0.26 (0.48)	< 0.001	[0.1, 0.2]
fss38	Constantly tired and exhausted	0.72 (0.67)	0.53 (0.61)	< 0.001	[0.1, 0.3]
fss39	Memory problems	0.24 (0.49)	0.20 (0.42)	0.130	[−0.0, 0.1]
fss40	Concentration problems	0.55 (0.64)	0.45 (0.56)	0.015	[0.0, 0.2]
fss41	Balance problems	0.18 (0.40)	0.11 (0.33)	0.004	[0.0, 0.1]
fss42	Dizziness	0.35 (0.50)	0.24 (0.45)	0.001	[0.0, 0.2]
fss43	Numbness/ tingling in arms/ legs	0.24 (0.45)	0.17 (0.39)	0.007	[0.0, 0.1]
fss44	Eye problems	0.25 (0.48)	0.21 (0.44)	0.258	[−0.0, 0.1]
fss45	Visual disorders	0.12 (0.34)	0.13 (0.37)	0.423	[−0.1, 0.0]
fss46	Light sensitivity	0.27 (0.50)	0.18 (0.41)	0.006	[0.0, 0.2]
fss47	Ears	0.13 (0.36)	0.07 (0.30)	0.007	[0.0., 0.1]
fss48	Auditory disorders	0.08 (0.29)	0.05 (0.26)	0.153	[−0.0, 0.1]
fss49	Noise sensitivity	0.22 (0.48)	0.12 (0.36)	0.001	[0.0, 0.2]
fss50	Problems with sense of touch	0.02 (0.17)	0.01 (0.10)	0.223	[−0.0, 0.0]
fss51	Heart problems	0.10 (0.30)	0.05 (0.23)	0.009	[0.0, 0.1]
fss52	Respiratory problems	0.22 (0.46)	0.13 (0.36)	0.003	[0.0, 0.1]
phq2a	Little interest or pleasure	0.98 (0.77)	0.93 (0.72)	0.295	[−0.1, 0.2]
phq2b	Down, depressed, or hopeless	0.98 (0.85)	0.82 (0.77)	0.003	[0.1, 0.3]
phq2c	Trouble sleeping	1.26 (1.00)	1.03 (0.91)	< 0.001	[0.1, 0.4]
phq2d	Tired or having little energy	1.45 (0.91)	1.29 (0.81)	0.008	[0.0, 0.3]
phq2e	Poor appetite or overeating	1.06 (0.93)	0.89 (0.87)	0.005	[0.1, 0.3]
phq2f	Feeling bad about oneself	0.74 (0.93)	0.62 (0.79)	0.045	[0.0, 0.2]
phq2g	Trouble concentrating	0.87 (0.86)	0.75 (0.78)	0.034	[0.0, 0.2]
phq2h	Moving slowly or being fidgety	0.39 (0.66)	0.29 (0.57)	0.009	[0.0, 0.2]
phq2i	Self-harm or suicidal thoughts	0.21 (0.50)	0.17 (0.47)	0.186	[−0.0, 0.1]

criteria of chronic fatigue syndrome (in this case the Fukuda criteria [4]). These questions are built on established instruments to diagnose FSS wherever they exist and are scored according to existing instructions. In the case that no established instruments exist, each diagnostic criterion is answered on a dichotomous scale ("not present" vs. "present"). If a participant fulfils research diagnostic criteria, they are subsequently surveyed about health care visits (e.g., 'Have you ever visited a doctor about your fatigue/post-exertional malaise?'). If a participant responds with "yes", they are consequentially directed to a list of items addressing frequent medical exclusionary diagnoses ("What diagnosis did your doctor give you?"). Finally, if a participant does not have any somatic diseases which might account for their symptoms (e.g., meningitis), they are considered fulfilling criteria for a specific FSS (e.g., chronic fatigue syndrome).

Depressive symptoms were measured by the depression module of the Patient Health Questionnaire [PHQ-9]; [24], which asks about impairment caused by nine symptoms of depression ("not at all", "several days", "more than half of the days", "nearly every day").

2.3. Statistical analyses

The analysis was conducted using R and Studio Version 4.2.2 and closely followed the procedures outlined by Senger et al. [12]. The packages bootnet [25], qgraph [26], igraph [27], NetworkComparisonTest [28], and Networktools [29] were used.

Two network models, one for individuals with FSS and individuals without FSS, were calculated. The symptoms were represented as circles (nodes) and the correlations between the symptoms as lines (edges) [25]. In the graphs, thicker edges (edge weights) indicated greater correlations between nodes, green edges indicated positive correlations between nodes, and red edges indicated negative correlations between nodes. As our data was ordinal, a Gaussian graphic model [30] with partial Spearman correlations was used [31]. To minimise the risk of false positive edges, a graphical least absolute shrinkage and selection operator (graphical lasso) [32,33] was used. To avoid calculating edges where none exist, small edges were set to exactly zero, which in turn makes for a sparser network and helps to ensure only true relationships between nodes are displayed.

By setting small edges to exactly zero, this ensured that only the true relationships between symptoms were displayed and made for a sparser network. For the graphical lasso, the tuning parameter λ was estimated, which regulated sparsity within a network. A high λ indicates that many edges are removed, possibly even true edges, resulting in a sparser network. By contrast, a low λ is more conservative, but might leave false positive edges within in the network, resulting in a denser network. To select the most appropriate network model for our data, the Extended Bayesian Information Criterion was used [31]. For this purpose, γ was set to a recommended 0.5 [34]. A small γ accepts more models with higher numbers of connections and therefore γ should be selected carefully. The stability and accuracy of the edge weights within each network was estimated by 1000 sample bootstrapping [25,31].

To identify symptoms clusters (communities), that is, symptoms that form a dense subgraph within the network, the Walktrap algorithm was used [35]. The algorithm performs random walks between two nodes, whereby fewer steps indicate a closer relationship between symptoms. To obtain a measure of centrality, that is, to estimate the relative importance of symptoms within a given network, the three most commonly used centrality measures were used: node strength, defined as the absolute sum of edge weights for each node [25], closeness, defined as the average distance from one node to all other nodes in the network [36], and betweenness, defined as the frequency of a node being on the shortest way from one node to another [36,37]. To assess the stability of the centrality measures, we used non-parametric bootstrapping [25,38], which yields a correlation stability coefficient. The correlation stability coefficient shows how many cases of the sample can be dropped whilst keeping the correlation of the centrality measures above $r = 0.70$ between the sample and the bootstrapped samples. This coefficient should be above 0.25, preferably above 0.50, which indicates that, even when 50 % of the sample are dropped, the correlation remains above 0.70.

When symptoms of a given community have strong relations not only within a community, but to symptoms of other communities, they are called bridge symptoms [29]. We calculated those bridge centralities, wherein bridge strengths is the sum of the absolute value of all edges from a given node to nodes outside one's community and bridge expected influence (1-step) is the sum of the values of those edges.

To test whether the two networks differed significantly from each other, we used the Network Comparison Test [39]. This permutation test estimates differences of relevant test statistics such as the invariance of the network structures, the strength discrepancy of one or more edges, and the invariance of global strength, which is the absolute sum of edge

weights [40]. As recommended, we applied a Holm-Bonferroni correction [39]. Additionally, we calculated a coefficient of similarity by correlating the edge weight across both networks [41].

3. Results

3.1. Sample characteristics

The final network of individuals with FSS consisted of $n = 222$ participants, of whom 73 % were female. The mean age was 25 (± 5.5) years and the symptom severity score was 22.38 (maximum: 102). The network of individuals without FSS consisted of $n = 1722$ participants, of whom 78 % were female. The mean age was 24 (± 5.5) years and the symptom severity score was 16.23 (maximum: 102). The means and standard deviations of all 51 items of the FFSS and 9 items of the PHQ are listed in Table 1.

3.2. Network of symptoms in individuals with FSS

The network of individuals with FSS is illustrated in Fig. 1. The network had a relatively small number of edges, with small (46.5 %) or small- to medium-sized (47.1 %) correlations. Twenty-one edges (1.2 %) were greater than 0.5 (see Supplement 1). This points to distinct groups of weakly to moderately associated symptoms.

A community analysis of the individuals with FSS yielded 14 communities as the best solution. Excluding communities which only consisted of one item, ten relevant communities remained: *cognitive problems/fatigue/depression* (purple, 16 items, e.g., "tired after minimal exertion"), *sensory problems* (light blue, 6 items, e.g., "sensitive to light"), *facial pain* (black, 3 items, e.g., "jaw pain"), *head/neck/upper back pain* (dark green, 5 items, e.g., "headaches"), *dizziness/nausea* (orange, 4 items, e.g., "vomiting"), *throat pain/problems with swallowing* (light green, 5 items, e.g., "feeling of a lump in the throat"), *chest pain* (dark red, 2 items, e.g., "heart problems"), *widespread pain* (blue, 6 items, e.g., "pain in several joints"), *abdominal pain/problems with digestion* (white, 7 items, e.g., "lower abdominal pain"), and *genital pain* (light pink, 2 items, e.g., "pain in the genitals").

The measures of centrality are depicted in Fig. 2. Regarding node strength, the highest strength in the network was found for the items "tired or little energy", "down, depressed, or hopeless", and "tired after

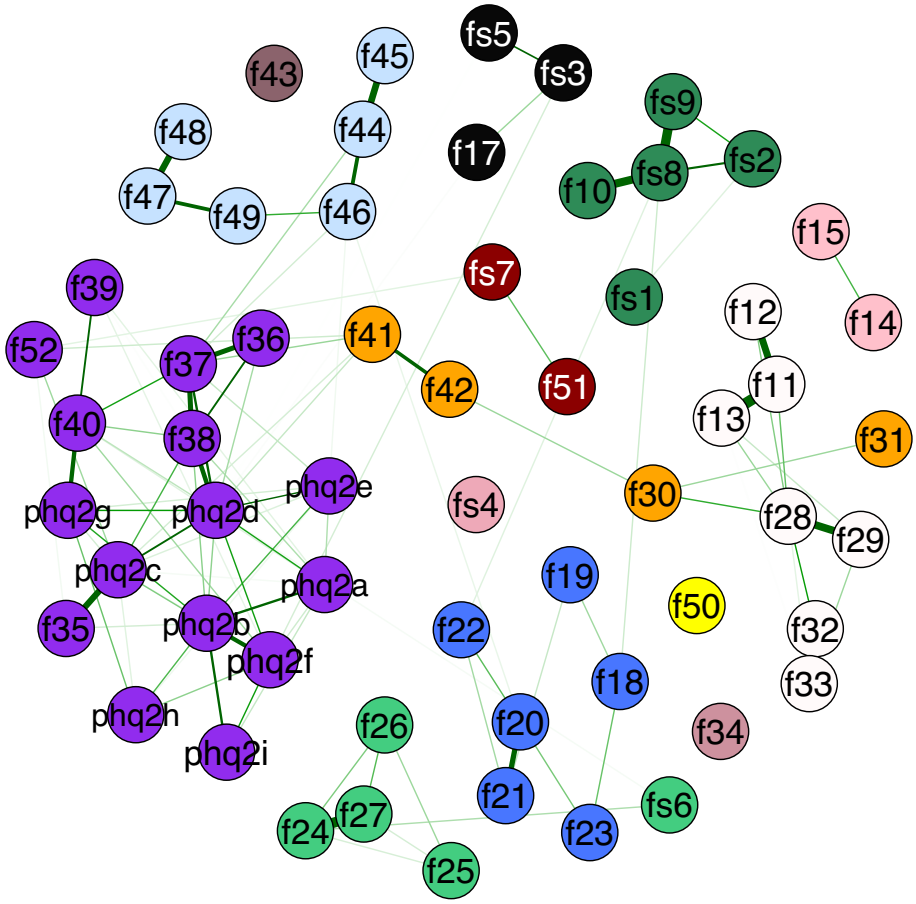

Fig. 1. Network model of symptoms in n = 222 individuals with functional somatic syndromes (FSS).
fss1 = headache, fss2 = neck pain, fss3 = facial pain, fss4 = mouth pain, fss5 = jaw pain, fss6 = sore throat, fss7 = chest pain, fss8 = back pain, fss9 = upper back pain, fss10 = lower back pain, fss11 = abdominal pain, fss12 = upper abdominal pain, fss13 = lower abdominal pain, fss14 = genital pain, fss15 = pain during sexual intercourse, fss17 = pain in several lymph nodes, fss18 = pain in several joints, fss19 = pain in several muscles, fss20 = pain in the left side of the body, fss21 = pain in the right side of the body, fss22 = pain above the waist, fss23 = pain below the waist, fss24 = pain/discomfort swallowing, fss25 = sensation of a lump in the throat, fss26 = discomfort empty swallowing, fss27 = discomfort swallowing food, fss28 = pain/discomfort during digestion, fss29 = abdominal bloating, fss30 = nausea, fss31 = vomiting, fss32 = pain/discomfort during excretion, fss33 = pain/discomfort in the bowel, fss34 = pain/discomfort in the bladder, fss35 = insomnia, fss36 = hypersomnia, fss37 = tired after minimal exertion, fss38 = constantly tired and exhausted, fss39 = memory problems, fss40 = concentration problems, fss41 = balance problems, fss42 = dizziness, fss43 = numbness/tingling in arms/legs, fss44 = eye problems, fss45 = visual disorders, fss46 = light sensitivity, fss47 = ears, fss48 = auditory disorders, fss49 = noise sensitivity, fss50 = problems with sense of touch, fss51 = heart problems, fss52 = respiratory problems, phq2a = little interest or pleasure, phq2b = down, depressed, or hopeless, phq2c = trouble sleeping, phq2e = tired or having little energy, phq2f = feeling bad about oneself, phq2g = trouble concentrating, phq2h = moving slowly or being fidgety, phq2i = self-harm or suicidal thoughts.

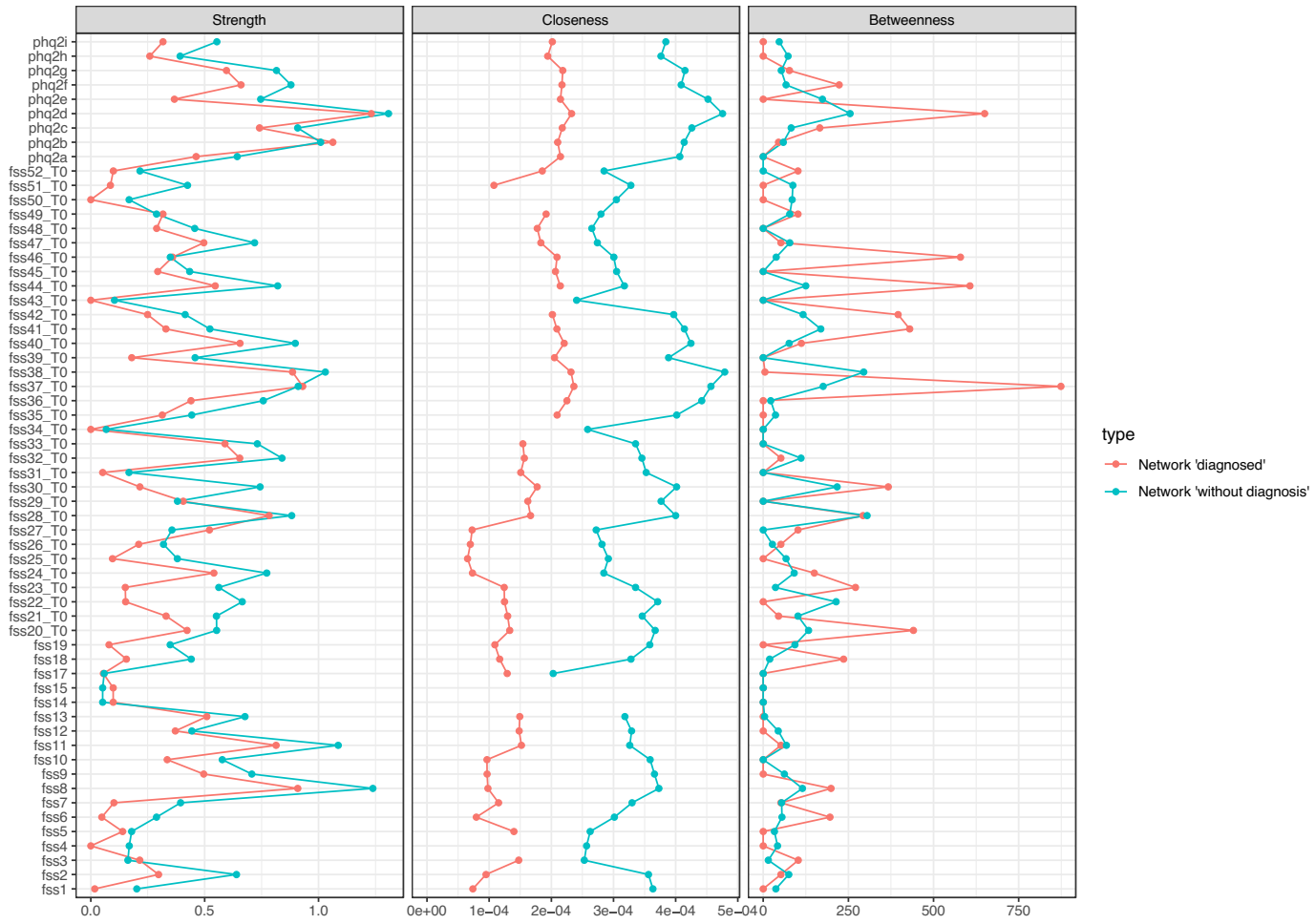

Fig. 2. Centrality measures of the networks of individuals with functional somatic syndromes (FSS) ("diagnosed") and without FSS ("without diagnosis").
fss1 = headache, fss2 = neck pain, fss3 = facial pain, fss4 = mouth pain, fss5 = jaw pain, fss6 = sore throat, fss7 = chest pain, fss8 = back pain, fss9 = upper back pain, fss10 = lower back pain, fss11 = abdominal pain, fss12 = upper abdominal pain, fss13 = lower abdominal pain, fss14 = genital pain, fss15 = pain during sexual intercourse, fss17 = pain in several lymph nodes, fss18 = pain in several joints, fss19 = pain in several muscles, fss20 = pain in the left side of the body, fss21 = pain in the right side of the body, fss22 = pain above the waist, fss23 = pain below the waist, fss24 = pain/discomfort swallowing, fss25 = sensation of a lump in the throat, fss26 = discomfort empty swallowing, fss27 = discomfort swallowing food, fss28 = pain/discomfort during digestion, fss29 = abdominal bloating, fss30 = nausea, fss31 = vomiting, fss32 = pain/discomfort during excretion, fss33 = pain/discomfort in the bowel, fss34 = pain/discomfort in the bladder, fss35 = insomnia, fss36 = hypersomnia, fss37 = tired after minimal exertion, fss38 = constantly tired and exhausted, fss39 = memory problems, fss40 = concentration problems, fss41 = balance problems, fss42 = dizziness, fss43 = numbness/tingling in arms/legs, fss44 = eye problems, fss45 = visual disorders, fss46 = light sensitivity, fss47 = ears, fss48 = auditory disorders, fss49 = noise sensitivity, fss50 = problems with sense of touch, fss51 = heart problems, fss52 = respiratory problems, phq2a = little interest or pleasure, phq2b = down, depressed, or hopeless, phq2c = trouble sleeping, phq2e = tired or having little energy, phq2f = feeling bad about oneself, phq2g = trouble concentrating, phq2h = moving slowly or being fidgety, phq2i = self-harm or suicidal thoughts.

minimal exertion". Regarding betweenness, the nodes with the highest betweenness were "tired after minimal exertion", "tired or little energy", and "eye problems". Between the top ten items of node strength and betweenness only two items overlapped ("tired after minimal exertion" and "tired or little energy"). Network stability was sufficient for edge weights (0.52) and node strength (0.52), but stayed below the cut off of 0.5 for closeness (0) and betweenness (0.05). As the network contained nodes with no edges, closeness contained no variance (0).

The bridge item analyses regarding FSS and depression are depicted in Fig. 3. The highest expected influence was found for the symptoms "balance", "tired after minimal exertion", "nausea", and "pain/discomfort during digestion".

3.3. Network of symptoms in individuals without FSS

The network of individuals without FSS is illustrated in Fig. 4. In comparison with the individuals with FSS, the network of individuals without FSS had a larger number of edges, whereas the correlations were mostly very small and small (72.5 %), with fewer medium-sized edges (24.3 %). Only nine edges (0.5 %) were greater than 0.5 (see Supplement 2). This points to widespread, but weak associations among the symptoms.

Community analysis of the individuals without FSS yielded twelve communities as the best solution. Three of these were identical to the ones identified in individuals with FSS: *head/neck/upper back pain*, *throat pain/problems with swallowing*, and *genital pain*. Four communities were almost identical: *cognitive problems/fatigue/depression*, *facial pain*, *chest problems*, and *widespread pain*. However, in individuals without FSS, the item "difficulties with breathing" belonged to the *chest problems* rather than to the *depression, fatigue, and cognitive problems* community. Moreover, the item "pain in lymph nodes" belonged to the *widespread pain* rather than to the *facial pain* community. The five remaining communities were: *neurological problems/nausea* (white, 6 items, e.g., "vomiting"), *eye problems* (dark pink, 3 items, e.g., "sensitive to light"), *ear problems* (orange, 3 items, e.g., "sensitive to noise"), *abdominal pain* (medium pink, 3 items, e.g., "lower abdominal pain"), and *problems with*

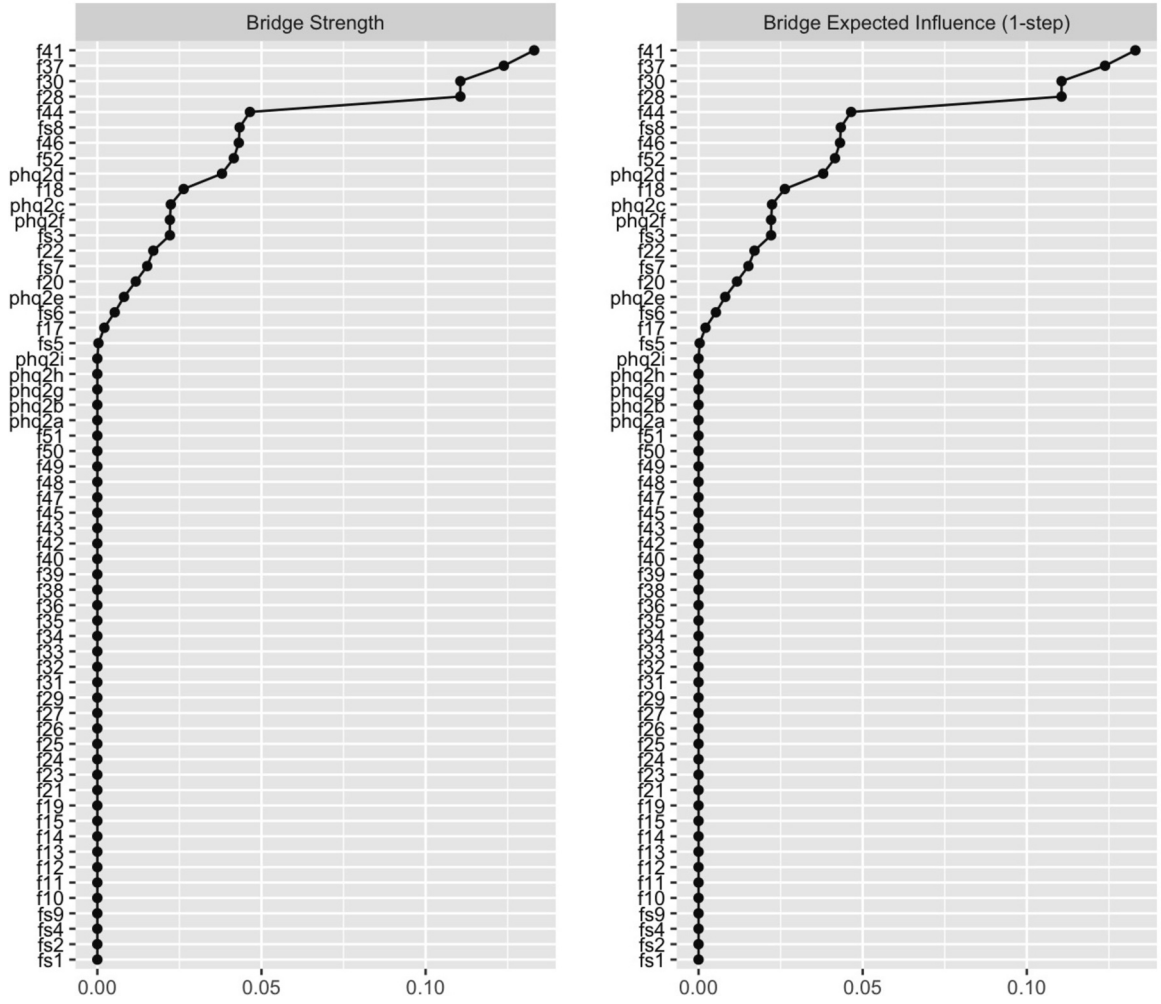

Fig. 3. Bridge strength and bridge expected influence between functional somatic syndromes (FSS) and depression.
fss1 = headache, fss2 = neck pain, fss3 = facial pain, fss4 = mouth pain, fss5 = jaw pain, fss6 = sore throat, fss7 = chest pain, fss8 = back pain, fss9 = upper back pain, fss10 = lower back pain, fss11 = abdominal pain, fss12 = upper abdominal pain, fss13 = lower abdominal pain, fss14 = genital pain, fss15 = pain during sexual intercourse, fss17 = pain in several lymph nodes, fss18 = pain in several joints, fss19 = pain in several muscles, fss20 = pain in the left side of the body, fss21 = pain in the right side of the body, fss22 = pain above the waist, fss23 = pain below the waist, fss24 = pain/discomfort swallowing, fss25 = sensation of a lump in the throat, fss26 = discomfort empty swallowing, fss27 = discomfort swallowing food, fss28 = pain/discomfort during digestion, fss29 = abdominal bloating, fss30 = nausea, fss31 = vomiting, fss32 = pain/discomfort during excretion, fss33 = pain/discomfort in the bowel, fss34 = pain/discomfort in the bladder, fss35 = insomnia, fss36 = hypersomnia, fss37 = tired after minimal exertion, fss38 = constantly tired and exhausted, fss39 = memory problems, fss40 = concentration problems, fss41 = balance problems, fss42 = dizziness, fss43 = numbness/tingling in arms/legs, fss44 = eye problems, fss45 = visual disorders, fss46 = light sensitivity, fss47 = ears, fss48 = auditory disorders, fss49 = noise sensitivity, fss50 = problems with sense of touch, fss51 = heart problems, fss52 = respiratory problems, phq2a = little interest or pleasure, phq2b = down, depressed, or hopeless, phq2c = trouble sleeping, phq2e = tired or having little energy, phq2f = feeling bad about oneself, phq2g = trouble concentrating, phq2h = moving slowly or being fidgety, phq2i = self-harm or suicidal thoughts.

digestion (light blue, 5 items, e.g., "bloating").

The measures of centrality are depicted in Fig. 2. Regarding node strength, the findings were identical to individuals with FSS: The highest strength in the network was found for the items "tired or little energy", "down, depressed, or hopeless", and "tired after minimal exertion". Regarding betweenness, six out of ten items were identical to the ones identified in the individuals with FSS. The nodes with the highest betweenness were "problems with digestion", "tired and exhausted all the time", and "tired or having little energy". Between the top ten items of node strength and betweenness only four items overlapped ("tired and exhausted all the time", "tired or little energy", "tired after minimal exertion", and "problems with concentration"). Network stability was strong for edge weights (0.75) and node strength (0.75), but stayed below the cut off of 0.5 for closeness (0) and betweenness (0.21). As the network contained nodes with no edges, closeness contained no variance (0).

3.4. Network comparison

The test for invariance of network structure indicated a similar network structure between networks ($M = 0.26$, $p = 0.7$). The invariance of global strength also showed a very similar sum of absolute edge weights ($S = 7.26$, $p = 0.95$) and most edge weights differences (95 %) stayed below the threshold of 0.05 %. After applying the Holm-Bonferroni correction, only 5 % of all edges differed significantly ($n = 59$). The coefficient of similarity was 0.54, indicating a moderate fit of the two networks.

4. Discussion

The present study yielded three main findings: First, the network structure of FSS was characterised by ten distinct groups of symptoms, which were moderately associated, and central symptoms within the network included being tired after minimal exertion, fatigue, and

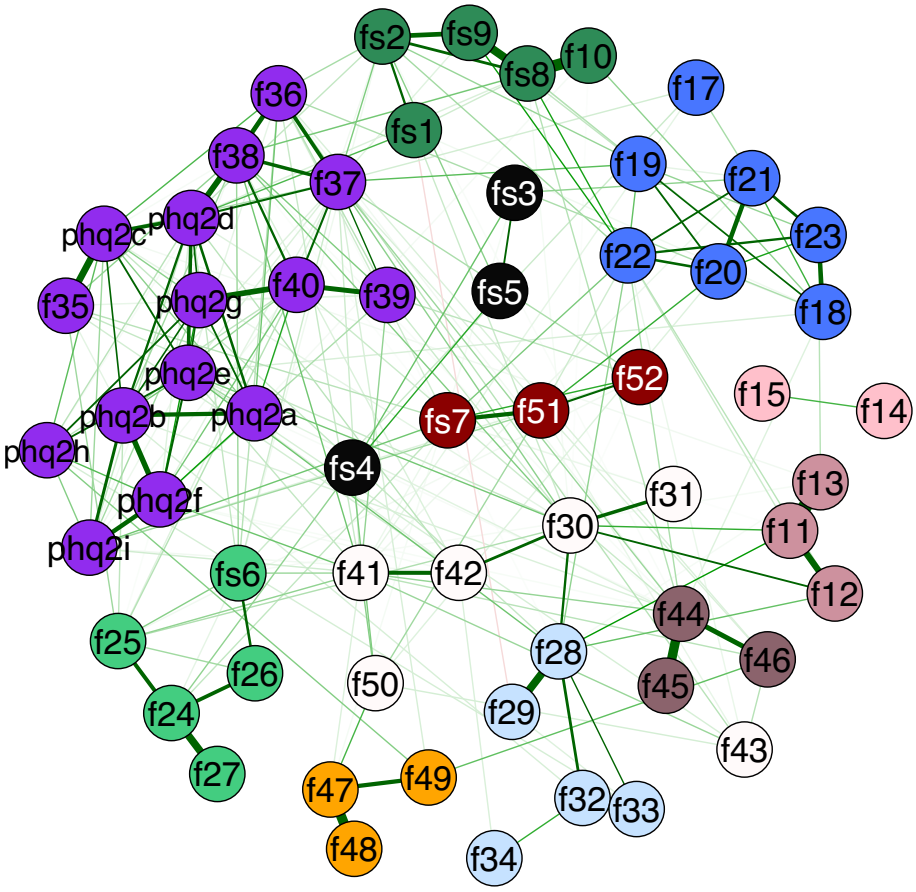

Fig. 4. Network model of symptoms in $n = 1722$ individuals without functional somatic syndromes (FSS).
fss1 = headache, fss2 = neck pain, fss3 = facial pain, fss4 = mouth pain, fss5 = jaw pain, fss6 = sore throat, fss7 = chest pain, fss8 = back pain, fss9 = upper back pain, fss10 = lower back pain, fss11 = abdominal pain, fss12 = upper abdominal pain, fss13 = lower abdominal pain, fss14 = genital pain, fss15 = pain during sexual intercourse, fss17 = pain in several lymph nodes, fss18 = pain in several joints, fss19 = pain in several muscles, fss20 = pain in the left side of the body, fss21 = pain in the right side of the body, fss22 = pain above the waist, fss23 = pain below the waist, fss24 = pain/discomfort swallowing, fss25 = sensation of a lump in the throat, fss26 = discomfort empty swallowing, fss27 = discomfort swallowing food, fss28 = pain/discomfort during digestion, fss29 = abdominal bloating, fss30 = nausea, fss31 = vomiting, fss32 = pain/discomfort during excretion, fss33 = pain/discomfort in the bowel, fss34 = pain/discomfort in the bladder, fss35 = insomnia, fss36 = hypersomnia, fss37 = tired after minimal exertion, fss38 = constantly tired and exhausted, fss39 = memory problems, fss40 = concentration problems, fss41 = balance problems, fss42 = dizziness, fss43 = numbness/tingling in arms/legs, fss44 = eye problems, fss45 = visual disorders, fss46 = light sensitivity, fss47 = ears, fss48 = auditory disorders, fss49 = noise sensitivity, fss50 = problems with sense of touch, fss51 = heart problems, fss52 = respiratory problems, phq2a = little interest or pleasure, phq2b = down, depressed, or hopeless, phq2c = trouble sleeping, phq2e = tired or having little energy, phq2f = feeling bad about oneself, phq2g = trouble concentrating, phq2h = moving slowly or being fidgety, phq2i = self-harm or suicidal thoughts.

depression. Second, bridge symptoms between FSS and depression included being tired after minimal exertion, balance problems, and nausea. Third, the network structure of FSS was similar to the network structure of somatic symptoms that were not part of any FSS, although the latter network was characterised by weaker associations between symptoms.

Our first finding was that the network structure of FSS enclosed ten communities of symptoms: cognitive problems/fatigue/depression, sensory problems, facial pain, head/neck/upper back pain, dizziness/nausea, throat pain/problems with swallowing, chest pain, widespread pain, abdominal pain/problems with digestion, and genital pain. This finding is similar to the findings revealed by Melidis et al. [17] and Hyland et al. [18], who identified up to eleven symptom groups among individuals with chronic fatigue syndrome, fibromyalgia, and irritable bowel syndrome. However, the symptom groups per se are not identical. For instance, in the Melidis et al. [17] study, fatigue and cognitive problems fell into the same cluster, whereas mood was a cluster of its own. This finding might be explained by the fact that our sample contained 14 FSS in addition to chronic fatigue syndrome, fibromyalgia, and irritable bowel syndrome. Our finding is also both similar and different to the finding of Senger et al. [12], who studied patients with somatoform disorders. On the one hand, their five symptom groups, namely neurological, cardiovascular, musculoskeletal, gastrointestinal, and urogenital were also identified in the present study. On the other hand, our study found five additional groups of symptoms. For instance, our neurological group was further divided into a group of cognitive problems/fatigue/depression and a group of sensory problems, and different groups of pain in various body regions were identified. This discrepancy may be due to fact that our individuals with FSS were recruited from the general population, whereas Senger et al. [12] had recruited outpatients and inpatients suffering from more severe symptoms (see also the discussion of our third finding further below). Apart from the communities, our network analysis also revealed central symptoms of FSS, namely post-exertional tiredness, fatigue and depression. These findings are in line with one previous study in chronic fatigue syndrome [42] and with the Senger et al. [12] study and could mean that these complaints are particularly powerful in potentially influencing and being influenced by other functional somatic symptoms. One underlying mechanism might be that both fatigue and depression can lead to physical inactivity, which fosters pain and other functional somatic symptoms by means of physiological deconditioning [e.g., [43]]. Another mechanism might be that, due to their chronic and

debilitating nature [e.g., [11]], several somatic symptoms frequently cause secondary fatigue and depression.

Our second finding was that bridge symptoms between FSS and depression included post-exertional tiredness, balance problems and nausea, and pain/discomfort during digestion. This means that individuals with atypical depression, who are characterised by hypersomnia and hyperphagia, may be particularly likely to develop FSS. Conversely, patients with FSS characterised by post-exertional tiredness, balance problems, nausea, and/or pain/discomfort during digestion might be more prone to develop depression. This finding aligns well with pathophysiological findings in FSS and atypical depression. For instance, hypocortisolism is frequently found in chronic fatigue and irritable bowel syndrome as well as in atypical depression, which is distinct from the hypercortisolaemic pattern associated with melancholic depression (which is characterised by the inverse neurovegetative pattern, insomnia and hypophagia) [44–46].

Our third finding, which was based on a comparison between individuals with FSS vs. individuals without FSS, suggested fewer symptom groups in the more severely affected subsample. This finding echoes the study of Melidis et al. [17], in which they found that the greater the symptom severity the stronger the symptom connections. It is equally in line with Senger et al.'s [12] comparison of inpatients and outpatients. It is, however, contrary to the finding by Hyland et al. [18], who found higher connectivity in healthy individuals as compared to individuals with FSS. However, their healthy controls were not sampled from the same population as patients and might have contained individuals with FSS or other disorders. Should our finding and the findings by Melidis et al. [17] and Senger et al. [12] be confirmed by future studies, this might mean that, as symptoms aggravate, they become more interconnected. This interpretation is clinically intuitive and builds on psychological learning processes, such as classical conditioning. However, as a hypothesis, it warrants testing in longitudinal studies, in which individuals with functional somatic symptoms are followed up over several years.

The finding that post-exertional tiredness was both a central symptom of FSS and a symptom bridging FSS and depression speaks to it high clinical relevance. Concretely, interventions specifically targeting post-exertional tiredness could be key to a more rapid symptomatic improvement of various functional somatic symptoms, while at the same time providing a means to prevent an onset of comorbid depression. Current evidence-based treatment approaches for chronic fatigue syndrome, which prominently features this symptom, include graded exercise [47,48] and cognitive behaviour therapy [48,49]. Whereas the former specifically targets post-exertional tiredness and aims at slowly increasing physical activity to counteract physiological deconditioning, the latter includes cognitive interventions aiming at modifying dysfunctional cognitions related to physical activity (e.g., catastrophising). Importantly, however, networks might differ across individuals and post-exertional tiredness might not be a key symptom of all patients with FSS. Indeed, the study by Hyland et al. [18] produced networks specific to individual FSS, such as chronic fatigue syndrome, fibromyalgia, or irritable bowel syndrome. In the future, networks could/should be calculated for each individual patient before treatment to tailor interventions to their specific symptom profile. Ideally, these individual networks would be based on ecologically valid data [e.g., [50]] and their trajectories would be followed over the course of treatment [e.g., [51]].

The present study presents with a number of strengths. It is the first study investigating the network structure of 17 FSS. Second, it complements the prior literature by identifying bridge symptoms between functional somatic symptoms and depression and by comparing networks between individuals with clinically relevant and irrelevant somatic symptoms. Third, the total sample size was relatively large and sampled from the general population rather than from primary, secondary, or tertiary care settings, which are subject to healthcare seeking bias. However, a number of limitations also deserve mentioning. First, although this was a large sample free of healthcare bias, its representativeness was limited by the fact that it mainly consisted of young adults with a high socioeconomic status. Indeed, symptom severity was rather low even in individuals with manifest FSS, which likely affects network structure. Indeed, as evident from the comparison between individuals with and without FSS and the Melidis et al. [17] and Senger et al. [12] studies, it appears that the lower the symptom severity, the weaker the symptom connections, which could indicate that symptoms become more interconnected as FSS develop. Second, although medical explanations for FSS were carefully excluded by means of a stepwise algorithm, diagnoses were not validated by means of physical examinations or laboratory testing. Third, the present study used a cross-sectional design, which means that the temporal order in which symptoms are co-expressed cannot be determined. Fourth, given their high import in FSS, it would have been interesting to also investigate bridge symptoms between FSS and anxiety disorders, and we recommend that future studies continue to investigate the co-expression of somatic and anxiety symptoms by means of network analysis. Finally, as evident from the above discussion, group-level network analysis has produced some inconsistent results across studies, which means that its findings need to be interpreted with caution and that, as outlined above, individual-level analyses might hold promise to illuminate symptom interplay in a clinical context.

In conclusion, our network analyses pointed to ten distinct groups of moderately associated symptoms in individuals with various FSS. Post-exertional tiredness emerged as a particularly important symptom connecting the identified symptom groups and as a potential bridge symptom between FSS and depression. Should the present findings be replicated, future studies should test whether interventions specifically targeting post-exertional tiredness are particularly potent in alleviating FSS.

CRediT authorship contribution statement

Alexandra Litzenburger: Writing – review & editing, Writing – original draft, Visualization, Formal analysis. **Yannick Rothacher:** Writing – review & editing, Formal analysis. **Kay-Uwe Hanusch:** Writing – review & editing. **Ulrike Ehlert:** Writing – review & editing, Resources. **Urs M. Nater:** Writing – review & editing, Resources, Project administration, Methodology, Investigation, Conceptualization. **Susanne Fischer:** Writing – review & editing, Writing – original draft, Supervision, Project administration, Methodology, Investigation, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jpsychores.2024.111968.

References

[1] W. Hiller, W. Rief, E. Brahler, Somatization in the population: from mild bodily misperceptions to disabling symptoms, Soc. Psychiatry Psychiatr. Epidemiol. 41 (9) (2006) 704–712.
[2] T. Toft, P. Fink, E. Oernboel, K. Christensen, L. Frostholm, F. Olesen, Mental disorders in primary care: prevalence and co-morbidity among disorders. Results from the functional illness in primary care (FIP) study, Psychol. Med. 35 (8) (2005) 1175–1184.
[3] C. Nimnuan, M. Hotopf, S. Wessely, Medically unexplained symptoms: an epidemiological study in seven specialities, J. Psychosom. Res. 51 (1) (2001) 361–367.
[4] K. Fukuda, S.E. Straus, I. Hickie, M.C. Sharpe, J.G. Dobbins, A. Komaroff, The chronic fatigue syndrome: a comprehensive approach to its definition and study.

International chronic fatigue syndrome study group, Ann. Intern. Med. 121 (12) (1994) 953–959.
[5] F. Wolfe, D.J. Clauw, M.A. Fitzcharles, D.L. Goldenberg, R.S. Katz, P. Mease, A. S. Russell, I.J. Russell, J.B. Winfield, M.B. Yunus, The American College of Rheumatology preliminary diagnostic criteria for fibromyalgia and measurement of symptom severity, Arthritis Care Res. 62 (5) (2010) 600–610.
[6] B.E. Lacy, F. Mearin, L. Chang, W.D. Chey, A.J. Lembo, M. Simren, R. Spiller, Bowel disorders, Gastroenterology 150 (6) (2016) 1393–1407.
[7] WHO, The ICD-10 classification of mental and behavioural disorders - clinical descriptions and diagnostic guidelines, World Health Organization, Geneva, 1992.
[8] L.A. Aaron, D. Buchwald, A review of the evidence for overlap among unexplained clinical conditions, Ann. Intern. Med. 134 (9 Pt 2) (2001) 868–881.
[9] M.A. Rodriguez, N. Afari, D.S. Buchwald, Evidence for overlap between urological and nonurological unexplained clinical conditions, J. Urol. 182 (5) (2009) 2123–2131.
[10] S. Wessely, P.D. White, There is only one functional somatic syndrome, Br. J. Psychiatry 185 (2004) 95–96.
[11] S. Fischer, U.M. Nater, Functional somatic syndromes – conceptualization, epidemiology, and treatment, Z. Med. Psychol. 21 (2012) 148–160.
[12] K. Senger, J. Heider, M. Kleinstauber, M. Sehlbrede, M. Witthoft, A. Schroder, Network analysis of persistent somatic symptoms in two clinical patient samples, Psychosom. Med. 84 (1) (2022) 74–85.
[13] M. Witthoft, S. Fischer, F. Jasper, F. Rist, U.M. Nater, Clarifying the latent structure and correlates of somatic symptom distress: a bifactor model approach, Psychol. Assess. 28 (1) (2016) 109–115.
[14] M. Witthöft, W. Hiller, N. Loch, F. Jasper, The latent structure of medically unexplained symptoms and its relation to functional somatic syndromes, Int. J. Behav. Med. 20 (2) (2013) 172–183.
[15] D. Borsboom, A network theory of mental disorders, World Psychiatry 16 (1) (2017) 5–13.
[16] H. Cai, M.Y. Chen, X.H. Li, L. Zhang, Z. Su, T. Cheung, Y.L. Tang, M. Malgaroli, T. Jackson, Q. Zhang, Y.T. Xiang, A network model of depressive and anxiety symptoms: a statistical evaluation, Mol. Psychiatry 29 (2024) 767–781.
[17] C. Melidis, S.L. Denham, M.E. Hyland, A test of the adaptive network explanation of functional disorders using a machine learning analysis of symptoms, Biosystems 165 (2018) 22–30.
[18] M.E. Hyland, Y. Antonacci, A.M. Bacon, Comparison of the symptom networks of long-COVID and chronic fatigue syndrome: from modularity to connectionism, Scand. J. Psychol. (2024).
[19] P. Henningsen, T. Zimmermann, H. Sattel, Medically unexplained physical symptoms, anxiety, and depression: a meta-analytic review, Psychosom. Med. 65 (4) (2003) 528–533.
[20] S. Fischer, J. Gaab, U. Ehlert, U.M. Nater, Prevalence, overlap, and predictors of functional somatic syndromes in a student sample, Int. J. Behav. Med. 20 (2) (2013) 184–193.
[21] S. Fischer, G. Lemmer, M. Gollwitzer, U.M. Nater, Stress and resilience in functional somatic syndromes - a structural equation modeling approach, PLoS ONE 9 (11) (2014).
[22] S. Fischer, U.M. Nater, Functional somatic syndromes: asking about exclusionary medical conditions results in decreased prevalence and overlap rates, BMC Public Health 14 (2014).
[23] U.M. Nater, S. Fischer, S. Latanzio, D. Ruoss, J. Gaab, FFSS – Fragebogen zur Erfassung funktioneller somatischer syndrome [FFSS - questionnaire on functional somatic syndromes], Verhaltenstherapie 21 (4) (2011) 263–265.
[24] R.L. Spitzer, K. Kroenke, J.B. Williams, Validation and utility of a self-report version of PRIME-MD: the PHQ primary care study. Primary care evaluation of mental disorders. Patient health questionnaire, JAMA 282 (18) (1999) 1737–1744.
[25] S. Epskamp, D. Borsboom, E.I. Fried, Estimating psychological networks and their accuracy: a tutorial paper, Behav. Res. Methods 50 (1) (2018) 195–212.
[26] S. Epskamp, A.O.J. Cramer, L.J. Waldorp, V.D. Schmittmann, D. Borsboom, Qgraph: network visualizations of relationships in psychometric data, J. Stat. Softw. 48 (4) (2012) 1–18.
[27] G. Csardi, T. Nepusz, The igraph software package for complex network research, InterJournal Complex Syst. (2006) 1695.
[28] C.D. van Borkulo, R. van Bork, L. Boschloo, J.J. Kossakowski, P. Tio, R. A. Schoevers, D. Borsboom, L.J. Waldorp, Comparing network structures on three aspects: a permutation test, Psychol. Methods 28 (6) (2023) 1273–1285.
[29] P. Jones, Tools for Identifying Important Nodes in Networks, 2024.
[30] S.L. Lauritzen, Graphical Models, Oxford University Press, Oxford, 1996.
[31] S. Epskamp, E.I. Fried, A tutorial on regularized partial correlation networks, Psychol. Methods 23 (4) (2018) 617–634.
[32] J. Friedman, T. Hastie, R. Tibshirani, Sparse inverse covariance estimation with the graphical lasso, Biostatistics 9 (3) (2008) 432–441.
[33] R. Tibshirani, Regression shrinkage and selection via the lasso, J. R. Stat. Soc. B 58 (1) (1996) 267–288.
[34] R. Foygel, M. Drton, Extended Bayesian information criteria for Gaussian graphical models, Adv. Neural Inf. Proces. Syst. 23 (2010) 604–612.
[35] P. Pons, M. Latapy, Computing communities in large networks using random walks, Lect. Notes Comput. Sci. 3733 (2005) 284–293.
[36] S. Boccaletti, V. Latora, Y. Moreno, M. Chavez, D.U. Hwang, Complex networks: structure and dynamics, Phys. Rep. 424 (4–5) (2006) 175–308.
[37] R.J. McNally, Can network analysis transform psychopathology? Behav. Res. Ther. 86 (2016) 95–104.
[38] E. Costenbader, T.W. Valente, The stability of centrality measures when networks are sampled, Soc. Networks 25 (4) (2003) 283–307.
[39] C.D. van Borkulo, S. Epskamp, A. Millner, NetworkComparisonTest: Statistical Comparison of Two Networks Based on Three Invariance Measures. https://cran.rproject.org/web/packages/, 2021.
[40] T. Opsahl, F. Agneessens, J. Skvoretz, Node centrality in weighted networks: generalizing degree and shortest paths, Soc. Networks 32 (3) (2010) 245–251.
[41] M. Rhemtulla, E.I. Fried, S.H. Aggen, F. Tuerlinckx, K.S. Kendler, D. Borsboom, Network analysis of substance abuse and dependence symptoms, Drug Alcohol Depend. 161 (2016) 230–237.
[42] S. Kujawski, J. Slomko, J.L. Newton, N. Eaton-Fitch, D.R. Staines, S. Marshall-Gradisnik, P. Zalewski, Network analysis of symptoms co-occurrence in chronic fatigue syndrome, Int. J. Environ. Res. Public Health 18 (20) (2021).
[43] J.A. Verbunt, H.A. Seelen, J.W. Vlaeyen, G.J. van de Heijden, P.H. Heuts, K. Pons, J.A. Knottnerus, Disuse and deconditioning in chronic low back pain: concepts and hypotheses on contributing mechanisms, Eur. J. Pain 7 (1) (2003) 9–21.
[44] L.M. Tak, A.J. Cleare, J. Ormel, A. Manoharan, I.C. Kok, S. Wessely, J.G. Rosmalen, Meta-analysis and meta-regression of hypothalamic-pituitary-adrenal axis activity in functional somatic disorders, Biol. Psychol. 87 (2) (2011) 183–194.
[45] C. Stetler, G.E. Miller, Depression and hypothalamic-pituitary-adrenal activation: a quantitative summary of four decades of research, Psychosom. Med. 73 (2) (2011) 114–126.
[46] K. Markopoulou, S. Fischer, A. Papadopoulos, L. Poon, L.J. Rane, A. Fekadu, A. J. Cleare, Comparison of hypothalamo-pituitary-adrenal function in treatment resistant unipolar and bipolar depression, Transl. Psychiatry 11 (1) (2021) 244.
[47] L. Larun, K.G. Brurberg, J. Odgaard-Jensen, J.R. Price, Exercise therapy for chronic fatigue syndrome, Cochrane Database Syst. Rev. 4 (4) (2017) CD003200.
[48] P. Whiting, A.M. Bagnall, A.J. Sowden, J.E. Cornell, C.D. Mulrow, G. Ramirez, Interventions for the treatment and management of chronic fatigue syndrome: a systematic review, JAMA 286 (11) (2001) 1360–1368.
[49] J.R. Price, E. Mitchell, E. Tidy, V. Hunot, Cognitive behaviour therapy for chronic fatigue syndrome in adults, Cochrane Database Syst. Rev. 2008 (3) (2008) CD001027.
[50] A.R. Smith, L.N. Forrest, S.S. Kinkel-Ram, W. Grunewald, S.D. Tubman, A. Esche, C. Levinson, A longitudinal network analysis of suicide risk factors among service members and veterans sampled for suicidal ideation or attempt, Psychol. Med. (2024) 1–11.
[51] L. Schumacher, J.P. Klein, M. Elsaesser, M. Harter, M. Hautzinger, E. Schramm, L. Kriston, Implications of the network theory for the treatment of mental disorders: a secondary analysis of a randomized clinical trial, JAMA Psychiatry 80 (11) (2023) 1160–1168.