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Relating ASD symptoms to well-being: moving across different construct levels

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Abstract

Background. Little is known about the specific factors that contribute to the well-being (WB) of individuals with autism spectrum disorder (ASD). A plausible hypothesis is that ASD symptomatology has a direct negative effect on WB. In the current study, the emerging tools of network analysis allow to explore the functional interdependencies between specific symptoms of ASD and domains of WB in a multivariate framework. We illustrate how studying both higher-order (total score) and lower-order (subscale) representations of ASD symptomatology can clarify the interrelations of factors relevant for domains of WB.

Methods. We estimated network structures on three different construct levels for ASD symptomatology, as assessed with the Adult Social Behavior Questionnaire (item, subscale, total score), relating them to daily functioning (DF) and subjective WB in 323 adult individuals with clinically identified ASD (aged 17–70 years). For these networks, we assessed the importance of specific factors in the network structure.

Results. When focusing on the highest representation level of ASD symptomatology (i.e. a total score), we found a negative connection between ASD symptom severity and domains of WB. However, zooming in on lower representation levels of ASD symptomatology revealed that this connection was mainly funnelled by ASD symptoms related to insistence on sameness and experiencing reduced contact and that those symptom scales, in turn, impact different domains of WB.

Conclusions. Zooming in across construct levels of ASD symptom severity into subscales of ASD symptoms can provide us with important insights into how specific domains of ASD symptoms relate to specific domains of DF and WB.

Adults with autism spectrum disorder (ASD) often report an alarmingly low well-being (WB) on various life domains, such as social environment, physical health, leisure, affective and sexual relationships when compared with individuals without ASD (Nordin & Gillberg, 1998; Bastiaansen *et al.* 2004; Jennes-Coussens *et al.* 2006; Cottenceau *et al.* 2012; Ikeda *et al.* 2014). A meta-analysis has recently shown the robustness of this phenomenon in a broad range of studies on WB and later outcome in ASD (Magiati *et al.* 2014; Van Heijst & Geurts, 2015). However, the factors contributing to WB of ASD individuals, as well as the mechanisms through which they operate, remain obscure.

One plausible hypothesis is that ASD symptom severity has a direct negative effect on WB. However, the literature reports no consistent relationship between ASD symptom severity and indices of WB (Eaves & Ho, 2008; Kuhlthau *et al.* 2010, 2013; Kamp-Becker *et al.* 2011; Van Heijst & Geurts, 2015). In response to this finding, researchers have highlighted the need to investigate how variations in the combination of potential factors contribute to individual differences in separate domains of WB (Diener, 1994; Myers & Diener, 1995; Ryff & Keyes, 1995; Woodman *et al.* 2016). In this regard, it has been suggested that future studies should (a) assess different domains of WB instead of using an overall score, reflecting a higher order construct (see Fig. 1*a* for a corresponding example; Woodman *et al.* 2016), and (b) study their interaction with multifactorial determinants (e.g., Diener *et al.* 2000). We will, therefore, study *different domains* of WB (Fig. 1*b*) instead of treating it as a monolithic entity (Fig. 1*a*; Diener, 1994).

Along a similar line of reasoning, a growing body of work is evolving around the question whether or not it is useful to use a total score as a proxy for symptom severity of mental disorders (Borsboom, 2008; Fried *et al.* 2016). Particularly, when interested in how certain variables differentially influence different symptoms of mental disorders, studying individual symptoms promises important insights (Lux & Kendler, 2010; Hieronymus *et al.* 2015). In the field of depression research, this approach has gained support from a recent study that reported four common depression rating scales to be highly multifactorial and, hence, unlikely to reflect a single underlying construct, such as depression (Fried *et al.* 2016). Similarly, different symptoms feature different associations with other disorders (Lux & Kendler, 2010), are differently influenced by stress (Fried *et al.* 2015), display different responses to adverse

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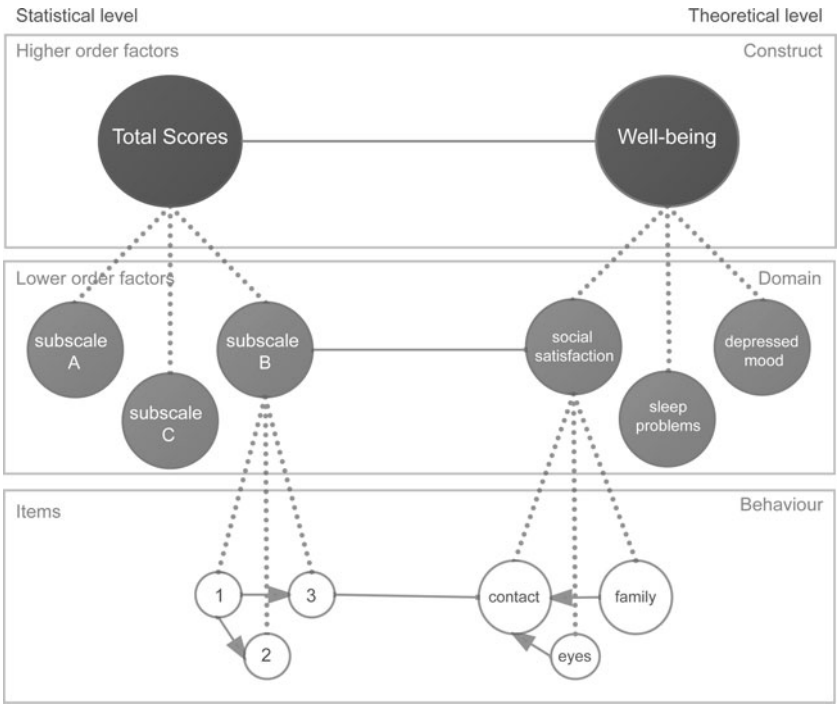

Fig. 1. This graph shows the three different statistical levels and their correspondent theoretical level one can choose to investigate the relationship between psychological constructs.

life events (Keller *et al.* 2007; Cramer *et al.* 2012), and have a differential predictive value for onset of the disorder (Boschloo *et al.* 2016). Given its heterogeneous nature (Geschwind, 2009; Herbert, 2010), a similar situation may well obtain for ASD. Although two recent reports have shown that there are important insights to be gained when studying symptom-to-symptom relations in ASD (Anderson *et al.* 2015; Ruzzano *et al.* 2015), the application of this approach (Fig. 1*c*) in the ASD realm has been limited.

Past studies investigating the inconsistent interacting nature of ASD symptom severity and routes to outcome and WB have often included higher order representations (i.e., total scores, Fig. 1*a*) of ASD symptomatology in their analyses (e.g., Renty & Roeyers, 2006; Eaves & Ho, 2008; Tilford *et al.* 2012; Kuhlthau *et al.* 2013). Few studies, in contrast, have included subscales of ASD traits (Fig. 1*b*) to explore their relation to WB (e.g., Kuhlthau *et al.* 2010; De Vries & Geurts, 2015). For example, the more socially impaired and restricted in behaviour, the lower the reported quality of life (Kuhlthau *et al.* 2010). Yet, no study has explored the underlying network of *individual symptoms* and aspects of WB and daily functioning. The question of which specific ASD symptoms may impact domains of WB and DF thus remains open. The analysis of lower-order factors (i.e. subscales; Fig. 1*b*) and even specific items (Fig. 1*c*) that represent concrete feelings, thoughts, or behaviours, instead of higher-order factors (i.e. total scores; Fig. 1*a*) could advance our understanding of WB in the ASD population.

This paper aims to advance such an analysis. We investigate the network structure of ASD symptom profiles and domains of WB for ASD adults. WB can be assessed with distinct concepts reflecting the affective and cognitive evaluation of one's life (Bartels & Boomsma, 2009). In this regard, we focus on both the individuals' subjective appraisal of their lives and the objective evaluation of the individual's daily functioning. We aim to study the interplay of ASD symptoms and separate components of subjective WB and DF by applying network analysis techniques in an exploratory fashion. We identify the network structure by applying state of the art statistical methodology for solving high-dimensional regression problems (based on penalized regression; Tibshirani, 1996; Meinshausen & Bühlmann, 2006); the subsequent analysis of that network structure then uses exploratory network analysis techniques taken from the emerging science of complex networks (Kolaczyk, 2009; Barabási, 2012) to determine the centrality of variables in the network. Thus, the first step in this data-driven analysis is based on well-known and validated statistical techniques, and involves extensions of existing approaches rather than a qualitatively different one. However, the approach does go beyond standard approaches in the second order analysis of the network structure, in which the centrality of variables in that structure is analyzed.

Methods

Participants[1]

A total of 323 adult participants aged completed three questionnaires relevant for this study. All participants were clients in the period 2013–2015 taking part in routine outcome measurements of the Dr. Leo Kannerhuis, a tertiary mental health clinic specialized in ASD assessment and treatment across the life-span. Participants were diagnosed following the official Dutch Guidelines for ASD assessment in adulthood (Trimbos, 2013), which are developed alongside the UK guidelines (National Institute for Health and Clinical Excellence, 2012). The extensive diagnostic procedure included clinical (non-standardized) psychiatric interviews and thorough developmental and psychological history from one or both parents, guardians or another close relative. All DSM-IV[2] (APA, 2000) classifications were based on a consensus meeting by a team of professionals including at least a psychiatrist and a psychologist working independently from the current study.

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Outcome measures[3]

Subjective WB

Subjective WB was measured with the Dutch version of the Manchester Short Assessment of Quality of Life (MANSA; Priebe *et al.* 1999; Dutch translation: Van Nieuwenhuizen *et al.* 2000), a brief version of the Lancashire Quality of Life Profile (Oliver *et al.* 1997). The MANSA is a self-report questionnaire that has been shown to be a viable instrument to obtain condensed and accurate quality of life data (Priebe *et al.* 1999). For 12 of the 14 MANSA items, participants indicated *how satisfied* they were with different domains of their lives. The response scale ranged from 1 ('could not be worse') to 7 ('could not be better'). The 12 continuous MANSA items covered participants' satisfaction with their life in general (*lifWB*), their job (*worWB*), not having a job (*nworWB*), their financial situation (*finWB*), the quality of their friendships (*socWB*), their leisure time (*leiWB*), their living situation (*livWB*), their personal safety (*safeWB*), their cohabitants (*cohWB*), living alone (*livWB*), their sex life (*sexWB*), their family relations (*famWB*), their physical health (*phyWB*) and their psychological health (*psyWB*); for an overview of these abbreviations please see Table 1. The remaining two of the 14 MANSA items were dichotomous (yes/no) and participants indicated whether they had a (good) friend (*onefWB*) and whether they had seen a (good) friend in the past week (*visWB*).

Daily functioning

DF was assessed with the Dutch translation of the Health of the Nation Outcome Scales (HoNOS; Wing *et al.* 1998; Dutch translation Mulder *et al.* 2004), a reliable instrument designed to measure behavioural problems, impairments, symptoms and social problems (Mulder *et al.* 2004). All patients were administered the 12 HoNOS items by their psychiatrist. These items include: (1) problems resulting from overactive, aggressive, disruptive or agitated behaviour (*agrDF*), (2) suicidal thoughts or behaviour, or non-accidental self-injury (*sharDF*), (3) problem drinking or drug taking (*drugDF*), (4) cognitive problems involving memory, orientation or understanding (*cogDF*), (5) problems associated with physical illness (*phyDF*), (6) problems associated with hallucinations and delusions (*delDF*), (7) depressed mood (*depDF*), (8) other behavioural problems (*comDF*), (9) problems making supportive social relationships (*relDF*), (10) problems associated with daily life (*adlDF*), (11) problems associated with living situation (*livDF*), (12) opportunities for using and improving abilities (occupational and recreational; *skiDF*). The consulted psychiatrists were asked to rate each of the 12 items on a five-point Likert scale (ranging from 1 ['no problem'] to 5 ['severe to very severe problem']) indicating how problematic their client's recent situation has been in the respective area.

Autism spectrum disorder

The Dutch self-report version of the Adult Social Behaviour Questionnaire (ASBQ-SR; Horwitz *et al.* 2016) was used to yield a score profile of all individuals among six ASD problem domains from the perspective of the adult with ASD. The questions are line with the ASD DSM-5 criteria and the ASBQ-SR has been shown to have good discriminant properties and (APA, 2013; Horwitz *et al.* 2016). In the network, we included the six subscales identified within the ASBQ-SR: reduced contact (*rconAS;* $N_{items} = 7$; e.g. 'You have little or no interest in socializing with others.'), reduced empathy (*rempAS*; $N_{items} = 7$; e.g. 'You find it hard to sense what someone else will like or think is nice.'), reduced interpersonal insight (*rsiAS*; $N_{items} = 8$; e.g. 'You take everything literally, for example, you don't understand certain expressions.'), violation of social conventions (*vscAS*; $N_{items} = 6$; e.g. 'You seek contact with anyone and everyone; you show no reserve.'), insistence on sameness (*inssAS*; $N_{items} = 8$; e.g., 'You don't like a lot of things happenings at once.') and sensory stimulation/motor stereotypies (*ssmsAS*; $N_{items} = 8$; e.g. 'You feel the urge to flap your hands or arms about when you are excited.'). Participants were asked to respond to each of the 44 items indicating whether the described behaviour 'clearly applies to you' (2), 'infrequently applies to you' (1) or 'does not apply to you' (0) (Table 2).

Statistical analysis

To identify potential paths through which ASD related behaviour may influence an individual's functioning and subjective WB, we computed graphical lasso networks with the R-package *qgraph* (Epskamp *et al.* 2012). The advantage of network analysis is that it visualizes the multivariate dependencies among variables that otherwise remain hidden. In addition, this dependency structure can be analyzed with techniques taken from network analysis, in which for instance the centrality of variables in the network can be assessed (Barrat *et al.* 2004; Opsahl *et al.* 2010). In our network representation, nodes represent questionnaire items while edges represent a statistical measure of association, such as a correlation or estimated causal effect. Here, we used the graphical lasso procedure to estimate partial correlations between all nodes in the network. Since we included both ordinal and continuous variables, analyses were based on polychoric correlations.

Because of the large number of partial correlations assessed, it is important to control the rate of false positive connections. To this aim, the graphical lasso uses the least absolute shrinkage and selection operator (lasso) (Tibshirani, 1996). This operator, which sets very small edges to zero, converges upon the generating network structure if the generating network is sparse (Foygel

Table 1. Descriptives for the participants ($N = 2341$)

Variable	M (s.d.)	Range
Age (in years)	32.43 (13.36)	17–70
Gender	71% male	
	29% female	
Health of the nation outcome scale (HoNOS)	13.75 (8.18)	1–54
Adult social behaviour questionnaire (ASBQ-SR)	30.57 (14.9)	1–88
Manchester short assessment of quality of life (MANSA)	48.05 (12.47)	12–71

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Table 2. List of abbreviations of the 32 nodes in the network. The extension of the node name indicates that the item is either concerned with daily functioning (DF), well-being (WB), or or autism spectrum disorder.

Abbreviation	Meaning in the network	Scale
adlDF	Problems with activities of daily life	0 (none) – 4 (serious problems)
agrDF	Agressive behaviour	0 (none) – 4 (serious problems)
cogDF	Cognitive problems	0 (none) – 4 (serious problems)
comDF	Comorbid problems	0 (none) – 4 (serious problems)
drugDF	Problematic drug use	0 (none) – 4 (serious problems)
delDF	Problems due to delusions	0 (none) – 4 (serious problems)
depDF	Problems due to depressive mood	0 (none) – 4 (serious problems)
livDF	Problems with living situation	0 (none) – 4 (serious problems)
phyDF	Physical problems	0 (none) – 4 (serious problems)
relDF	Problems with relationships	0 (none) – 4 (serious problems)
sharDF	Self mutilation	0 (none) – 4 (serious problems)
cohWB	Satisfaction about cohabitants	0 (=could not be worse) – 7 (could not be better)
famWB	Satisfaction about family relationships	0 (=could not be worse) – 7 (could not be better)
finWB	Satisfaction about financial situation	0 (=could not be worse) – 7 (could not be better)
leiWB	Satisfaction about leisure time activities	0 (=could not be worse) – 7 (could not be better)
lifWB	Life in general	0 (=could not be worse) – 7 (could not be better)
livWB	Satisfaction about living situation	0 (=could not be worse) – 7 (could not be better)
nworWB	Satisfaction about not working	0 (=could not be worse) – 7 (could not be better)
onefWB	Having a (good) friend	0 (=YES) – 1 (=NO)
phyWB	Satisfaction about physical health	0 (=could not be worse) – 7 (could not be better)
psyWB	Satisfaction about psychological health	0 (=could not be worse) – 7 (could not be better)
safeWB	Satisfaction about personal safety	0 (=could not be worse) – 7 (could not be better)
sexWB	Satisfaction about sex life	0 (=could not be worse) – 7 (could not be better)
skiWB	Opportunities to develop & use skills	0 (none) – 4 (serious problems)
socWB	Satisfaction about quality of friendships	0 (=could not be worse) – 7 (could not be better)
visWB	Having met a (good) friend in the past week	0 (=YES) – 1 (=NO)
sumAS	Total score indicating ASD symptom severity	Total score of all ASBQ items
inssAS	Subscale: Insistence on sameness	Sum of items that are coded as 0 (does not apply), 1 (somewhat applies) or 2 (clearly applies)
rconAS	Subscale: reduced contact	See above
rempAS	Subscale: reduced empathy	See above
rsiAS	Subscale: reduced social insight	See above
ssmsV	Subscale: sensory stimulation & motor stereotypies	See above
vscAS	Subscale: violations of social conventions	See above
comNR	No. of co-occurring diagnoses	Continuous

& Drton, 2011). The resulting procedure has close to perfect specificity (Van Borkulo *et al.* 2014), which means that, if an edge is present in the estimated network, it is virtually certain to exist in the population. However, sensitivity is markedly lower, which means that there are likely more edges in the population than are present in the estimated network. Overall, one can think of our lasso graphs as a precise estimate of the true network architecture, correcting for Type 1 errors. But one should keep in mind that the small values have become exactly zero for reasons of model simplification. Thus, absent edges in the presented network are not necessarily absent in the true network but might just have a very small value and are, therefore, shrunken by the applied regularization.

The created networks then allow for identification of influential focal points of the network (Opsahl *et al.* 2010) through analysis of *node centrality* indices: *strength*, *betweenness*, and *closeness*. For the WB networks, we were interested which correlates are most central, i.e., most relevant in the network in terms

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of impact on other nodes in the system. In a weighted network, the node *strength* is the sum of number and strength of direct connections. Node *betweenness* measures how often a node lies on the shortest path between two randomly chosen other nodes in the graph, acting as a bridge between those nodes. Node *closeness* quantifies the average distance from a node to all other nodes in the network (for more elaborate definitions, see Costantini *et al.* 2014). We performed additional stability checks to assess how stable the centrality indices in these networks are under observing subsets of participants. We used the R-package *bootnet* (Epskamp *et al.* 2017) and appended the results in the supplementary material of this paper. Since the CS-coefficient indicated good stability for strength, we limit our report to strength centrality.

Results

Sample descriptives

We included data from a cohort of 323 AS adults [231 (71%) males; 92 (29%) females] aged 17–70 years (M = 32.4, S.D. = 13.36). All participants were Dutch-speaking, non-institutionalized, and able to fill in questionnaires themselves. Of these individuals 38% had been diagnosed with PDD-NOS, 37% with Asperger's syndrome and 25% with Autistic disorder (see Table 1). Almost 20% of the cohort also met criteria for a mood disorder (mainly Major Depressive Episode) and 1% for Attention Deficit Hyperactivity Disorder (ADHD). ASBQ scores reflecting self-reported ASD symptomatology ranged from 1 to 88 (M = 30.58; S.D. = 14.91). The reported sample statistics resemble the sample mean and standard deviation of the ASBQ scores found in Horwitz *et al.* (2016). Missing data percentages across nodes ranged from 0% to 44.41% (satisfaction with not having a job) with M = 5.72 S.D. = 10.27. Note that we computed all networks employing pairwise deletion of missing data.

ASD symptoms and WB networks[4]

Figures 2, 3, and 4 visualize the network structure of WB domains and different representations of ASD symptoms: the total score of the ASBQ-SR, the six subscales of the ASBQ-SR and the unpacked subscales (i.e., single items). The colour of the node refers to used questionnaires: green nodes reflect questions about subjective WB from the MANSA, while blue nodes reflect the ASD symptom subscales (AS) from the ASBQ-SR and red nodes are items about DF from the HoNOS. Each edge represents bidirectional partial relations between questions, controlling for all other associations in the network.

Higher-order representation network (construct)

From the first network (Fig. 2), featuring the ASBQ-SR total score, it becomes evident that, in general, more severe ASD symptoms (sumAS) are associated with reduced psychological satisfaction (psyWB), which in turn features the strongest positive

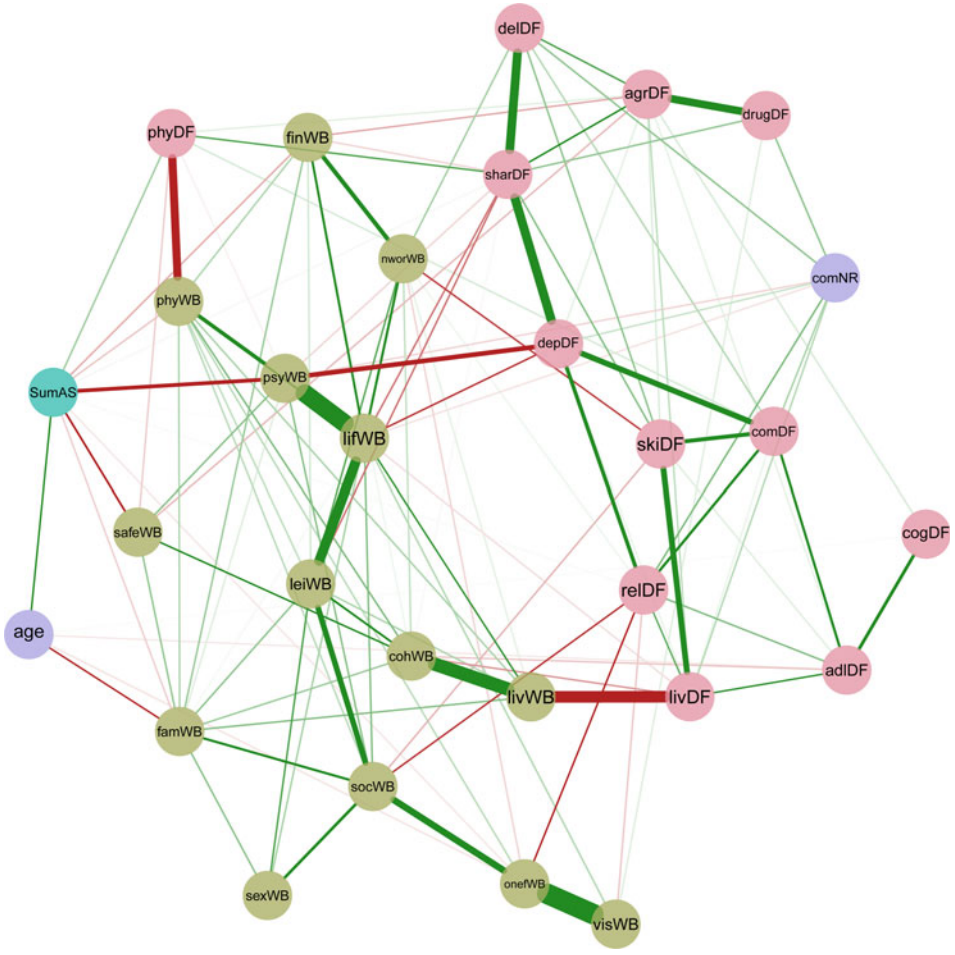

Fig. 2. Graphical LASSO network with a higher-order representation (Fig. 1*a*), i.e., the ASBQ-SR total score, for ASD symptom severity (AS, blue node). The brown nodes refer to self-report items of a well-being (WB) questionnaire, while the rosy nodes reflect psychiatrist-reported items of a daily functioning (DF) questionnaire. Thickness of the edge indicates the strength of the respective pairwise connection and colour indicates the size of the partial correlation (green for positive; red for negative connections).

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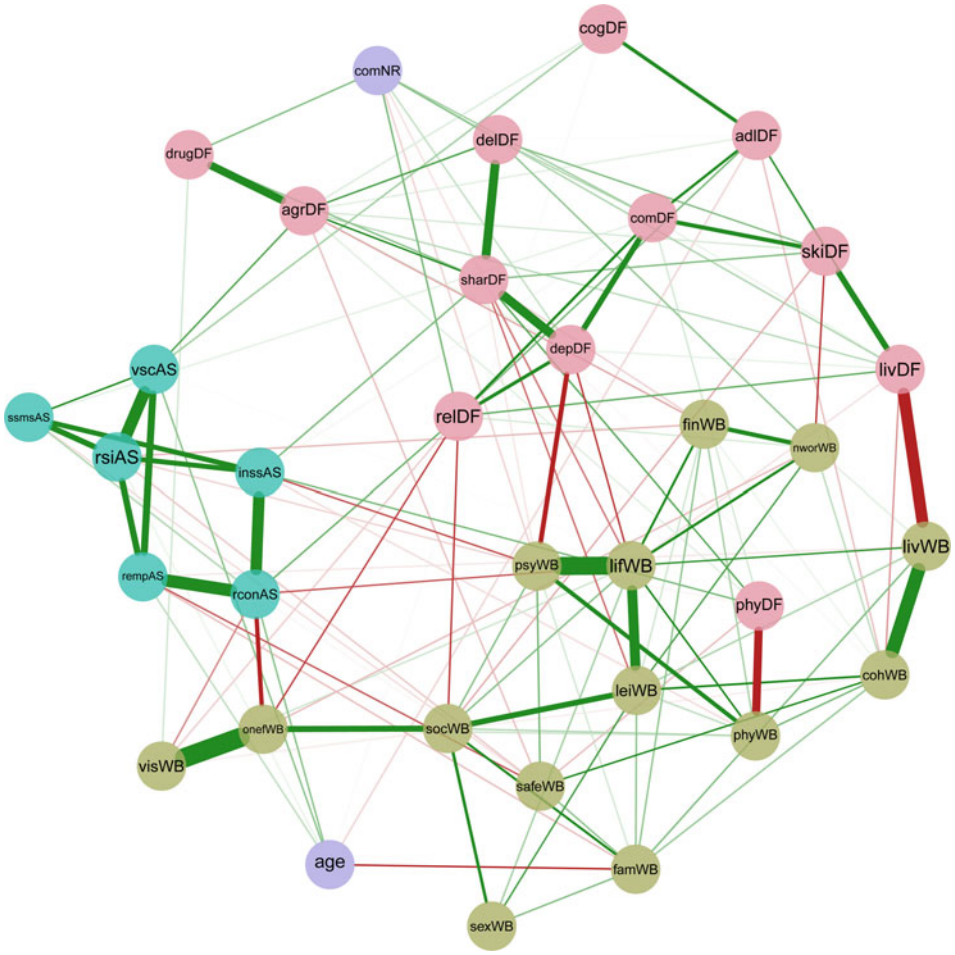

Fig. 3. Graphical LASSO network with a lower-order representation (Fig. 1*b*), i.e., ASBQ-SR subscales, for ASD symptom severity (blue nodes). The brown nodes refer to self-report items of a well-being questionnaire, while the rosy nodes reflect psychiatrist-reported items of a daily functioning questionnaire. The thickness of the edge indicates the strength of the respective pairwise connection and the colour indicates the size of the correlation (green for positive; red for negative connections).

connection with general life satisfaction (lifWB). Other positive connections with life satisfaction include items related to social factors, such as satisfaction with leisure time (leiWB) or satisfaction with one's living situation (livWB). Moreover, the network shows that there is a second gateway from ASD severity to WB variables, a direct connection between ASD symptoms (sumAS) and satisfaction with one's personal safety (safeWB) which in turn is directly, but weakly, related to how satisfied one is with the people one lives with (cohWB).

We find another weak direct connection from ASD symptoms to the cluster of DF indicators (e.g. self-harming behaviour, aggressive behaviour, and delusions) passes through physical problems (phyDF) and physical WB (phyWB), which is, in turn, directly related to psychological satisfaction (psyWB). The strongest direct negative path to general life satisfaction is its connection with depressive mood (depDF).

Centrality analyses for this network reveal that cognitive problems (cogDF) have the lowest centrality on the strength index. It is important to note that the item about cognitive problems (cogDF) was asked in relation to the salient diagnosis (here: ASD) and not just any cognitive problems. We found that general life satisfaction ranks as the most central factor in the network, implying that this factor provides the most information when one is interested in how a person will score on all other variables in the network. One could interpret from this result that life satisfaction is a common effect of the other WB domains in the network.

Lower-order representation network (domain)

To explore the unique patterns of interaction for different ASD characteristics, we estimated a second network featuring all six subscales of the ASBQ-SR as separate nodes. In this section we report how the results of the lower-order network extend the results of the higher-order network reported above. Figure 3 depicts the pattern of interrelations for the six ASD symptom subscales and domains of WB. We found that the strong negative connection from ASD symptom total score to psychological satisfaction in Fig. 2 is mainly funnelled by insistence on sameness (inssAS) and that reduced contact (rconAS) directly relates to general life satisfaction (lifS).

In addition, reduced contact acts as a bridge to relational problems (relDF), which in turn funnels the shortest paths from the ASD symptom scales to nodes indicating comorbidity, i.e. depressive mood (depDF), comorbid problems (comDF) and the number of co-occuring diagnoses one has (comNR). Insistence on sameness (inssAS) is related to more physical problems (phyDF) and more problems with self-harming behaviour. Another interesting link from the ASD symptom cluster (blue) to the DF cluster (red) suggests that having an ASD symptom profile featuring violations of social conventions (vscAS) is associated with more aggressive behaviour (agrDF). Also, there is a negative link between reduced empathy (rempAS) and satisfaction with one's personal safety (safeWB). These results suggest different routes to domains of WB and daily functioning, depending on

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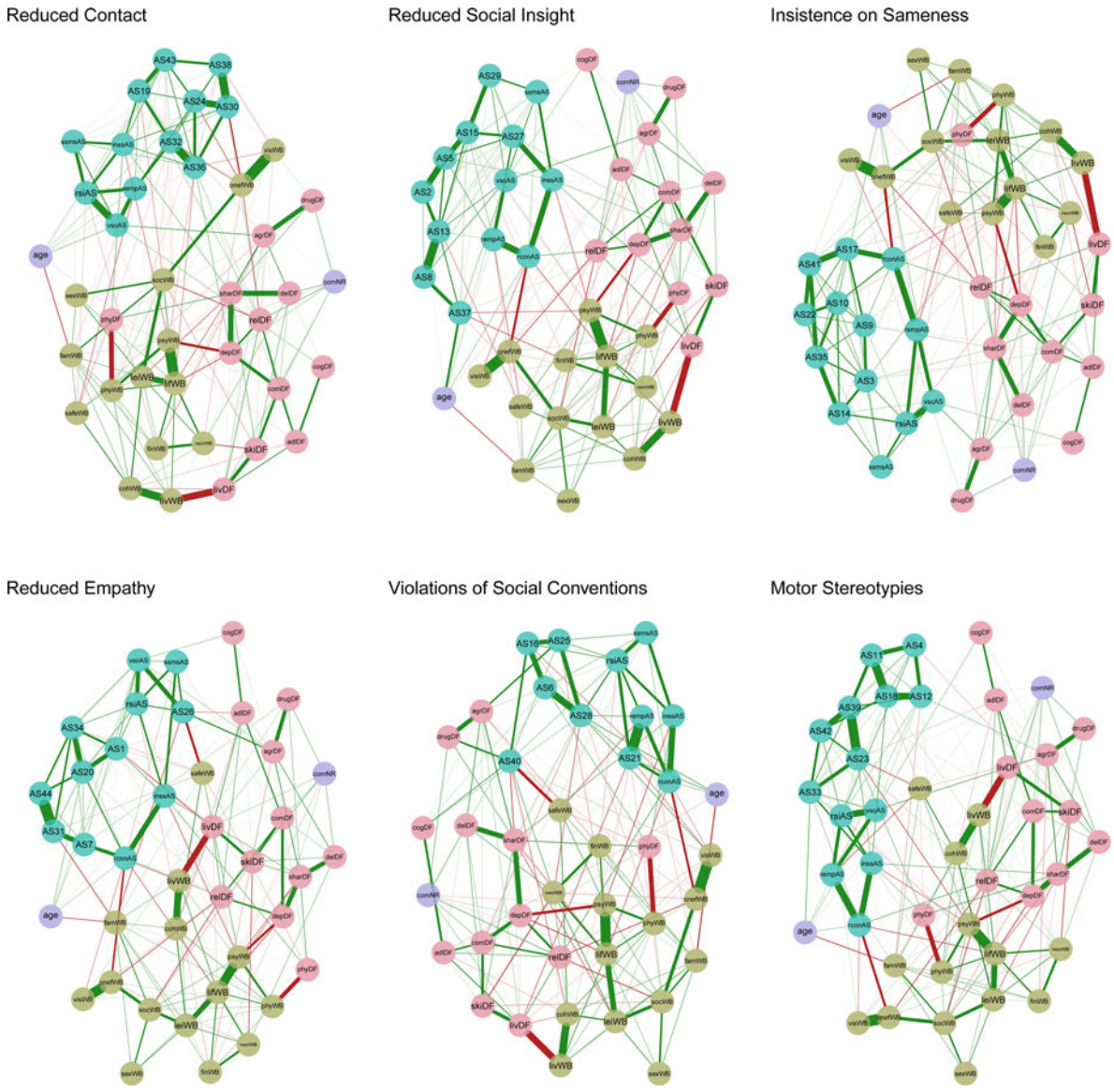

Fig. 4. Graphical LASSO networks with each individual subscales of the ASBQ-SR unpacked into its behavioural elements (Fig. 1c). From left to right: Reduced Contact, Reduced Social Insight, Insistence on Sameness, Reduced Empathy, Violation of Social Conventions and Motor Stereotypies. The brown nodes refer to self-report items of a well-being questionnaire, while the rosy nodes reflect psychiatrist-reported items of a daily functioning questionnaire. The thickness of the edge indicates the strength of the respective pairwise connection and the colour indicates the size of the correlation (green for positive; red for negative connections).

ASD symptom profiles. On a more general note, the network also reveals that older individuals are likely to be less satisfied with their family context but report less problems with daily living. In terms of ASD characteristics, older adults score higher on reduced contact, violations of social conventions and reduced empathy.

The estimates of strength centrality[5] for this network are presented in Fig. 1 of the supplement. The pattern of centrality is similar to the higher-order representation network, with life satisfaction being the most central node in the network. But here, reduced contact (rconAS) appears as the second most central node in the network in terms of degree centrality, highlighting its important role in the network connecting the cluster of symptom scales (blue) and the WB variables in the network (rosy & brown). Again, we found cognitive problems (cogDF) to be the least central node in the network. In both networks, this node lies in the periphery of the network, suggesting that the other nodes in the network cannot explain most of its variance, and that it does not explain much variance itself. However, in contrast to Fig. 2, this network reveals a direct connection between cognitive problems (cogDF) and ASD symptomatology, which is a positive link between violations of social conventions (vscAS) and cognitive problems.

Item networks (behaviour)

To uncover whether specific behavioural elements of the ASD symptom domains provide more information about their interaction with domains of WB, we estimated networks for each unpacked subscale separately. Figure 4 depicts the six estimated networks for each unpacked subscale. For the three symptom scales that had strong direct connections to domains of WB the

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unpacked networks reveal that some items are more important than others. First, the upper left graph in the panel shows that the strong negative connection we found between reduced contact (rconAS) and psychological satisfaction (psyWB) is mainly funnelled by the item representing whether an individual avoids people who try to make contact with them (AS36). Second, when unpacking the subscale of insistence on sameness (upper right panel graph), the connection between insistence on sameness (inssAS) and self-harm (sharDF) we found before does not result in a single pronounced connection between a subscale item and self-harm. Both, the item representing panicking when things turn out differently than one is used to (AS3), the item representing not liking when a lot of things happen at once (AS22) and the item representing needing a lot of time getting used to somewhere new (AS9) are connected to self-harm. Third, the connection we found in the subscale network between violations of social conventions (vscAS) and aggressive behaviour (agrDF) goes through the item representing whether one is too personal when approaching other people (AS25). Another strong connection appears between satisfaction with one's safety (safeWB) to the item representing whether individuals asks strangers for things they need (food or drinks when hungry or thirsty; AS40), suggesting that this characteristic can put ASD individuals at risk for unsafe situations.

Discussion

To our knowledge, this study is the first to illuminate the complex interaction pattern of ASD symptom profiles, daily functioning, and WB in a large group of individuals with ASD. We found that, in general, ASD symptoms do not directly relate to general life satisfaction, but their influence on WB is funnelled by psychological satisfaction and feeling safe in one's personal environment. Moreover, the current study is the first to assess these factors on three different construct levels for ASD symptoms using network analyses: a higher-order representation, lower-order representations, and separate items. Evaluating three different construct levels for ASD symptoms revealed different (clinically) relevant insights with respect to WB in adults with ASD.[6] For each of the three levels, we will discuss core findings of the study.

First, results of our total score network reveal that ASD symptom severity has a direct influence on psychological WB, which is, in turn, the most important factor for general life satisfaction of individuals with ASD. However, domains of daily functioning, such as self-harming behaviour and depressed mood, and domains of WB, such as living situation and leisure time, are *directly* connected to general life satisfaction of individuals with ASD. These results might suggest that interventions directed at improving the quality of life of people with ASD could very well target feelings of depression, loneliness, and one's personal environment instead of ASD symptom severity, which is in line with common ASD guidelines (National Institute for Health and Clinical Excellence, 2012). One possible explanation could be a mutual relationship between social skills and experiencing depression related to social interactions: individuals experiencing depression may be less likely to employ their social skills in daily life interactions and, vice versa, individuals who do not practice their social skills might be more likely to experience loneliness (Bellini, 2004; Lever & Geurts, 2016).

Relatedly, in the literature one often encounters the notion that co-occurring psychiatric problems are assumed to be a prognostic factor for ASD (APA, 2013) and that they are assumed to intensify the core symptoms of ASD (Wood & Gadow, 2010). Yet, the resulting networks of this study do not feature a direct mutual influence between ASD symptom severity and comorbid problems. Specifically, the relation between depressed mood and ASD symptoms seems to be funnelled by many other domains of daily functioning. Moreover, the number of co-occurring diagnoses does not appear to have a strong influence on both WB and daily functioning. This is in line with our recent study in a large ASD cohort where the number of comorbid diagnoses did not seem to have a significant impact on subjective WB (Deserno *et al.* 2016), suggesting that this factor might have a largely indirect effect on WB. In addition, the results of the current study highlight the importance of physical WB, including self-harm and aggressive behaviour, for general life satisfaction of ASD individuals. This is consistent with studies suggesting that behavioural disturbance, too, plays an important role in individual developmental trajectories (Totsika *et al.* 2011). A focus on improving aggressive and self-harming behaviours might also benefit later outcome in adulthood (Howlin *et al.* 2004; Magiati *et al.* 2014).

Second, when moving to the lower-level representations of ASD, i.e., the subscale network, we found that the widespread notion that higher ASD symptom severity is related to lower WB is mainly funnelled by three of the assessed six ASD domains: insistence on sameness, violations of social conventions, and reduced contact. The only domain of ASD symptomatology that appears to have a direct link to general life satisfaction is the degree to which one experiences reduced social contact. This finding is in line with earlier research showing that the lack of social responsiveness can partly explain low reported WB scores of children with ASD (Kuhlthau *et al.* 2010). A recent study found that quality of life is negatively correlated with severity of repetitive behaviour in children with ASD (Moss *et al.* 2017), which is in line with the direct connection we found between insistence on sameness and domains of WB. In addition, results of our recent report on WB predictors across the lifespan suggested that resources that allow the individual to engage in social relations have a huge impact on WB (Deserno *et al.* 2016). Our network provides additional information on these factors, as it shows what other direct interrelations these factors have. For example, insistence on sameness does not only funnel the influence of ASD symptoms on psychological WB, but also on levels of self-harm and physical WB. We show that investigating these factors on different construct levels replicates earlier findings from the ASD and WB literature, but provides additional information on the multicausal system in which they operate.

Third, results of our item-level analysis showed that a specific behavioural aspect of ASD related social impairment influences general life satisfaction directly, namely the degree to which individuals avoid contact. It is imperative, however, not to overinterpret absent connections in these graphs, as these may be due to limited power. At the same time, one can be fairly sure that the connections present in the networks are structural elements of the network architecture. It is, therefore, interesting that our networks suggest that cognitive functioning is not crucial for WB since it is often hypothesized that higher cognitive capacities predict better outcome on many life domains. However, also the opposite has been hypothesized as higher cognitive functioning could lead to increased awareness of dysfunction in daily life. That we did not observe a relationship could stem from the questionnaire used in the current study, where cognitive problems are not equivalent to level of intelligence. Rather, in this

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questionnaire, clinicians are asked to rate a client's cognitive problems such as memory problems and learning problems. Another explanation of this result could be related to the nature of our sample, which includes only participants with a normal to high intelligence level resulting in insufficient variance on this variable. In the current study, however, the latter was not the case. Future studies could investigate what specific factors funnel the impact of cognitive functioning on an individual's WB.

The exercise of unpacking the higher-order construct of ASD symptom severity into subscales of ASD symptoms has provided us with important insights on how specific domains of ASD symptoms relate to specific domains of DF and WB. However, the networks that zoom in on the items that are nested in the subscales, do not necessarily reveal a pattern of interrelations that the subscale network did miss out on.

Limitations and future directions

A few points related to the data our networks are based on, deserve mention. First, this study was limited by the available data from one specific mental health clinic, resulting in an inability to verify exact IQ scores and lack of generalizability to those with intellectual disabilities. Relatedly, the age diversity of the clients included in the Treatment Monitor resulted in a broad age range (17–70 years) in this sample. Second, data included both self-report and proxy-report information. In general, self-reported and proxy-reported evaluations of WB reflect very distinct types of information (Ruggeri *et al.* 2001). A focus on, either only subjective information (i.e., self-report), or only proxy information about WB and DF would likely lead to different results. However, recent literature has highlighted the need to use multiple informants when assessing behavioural and emotional functioning in individuals with ASD (Stratis & Lecavalier, 2015). In the current study we, therefore, combined the subjective evaluation of one's WB with the more objective proxy evaluation of someone's daily functioning. Third, the questionnaire that was used to assess WB was not specifically developed for individuals with ASD. The ASD population could, for example, differ from typically developed adult in how they value aspects of DF and WB (Tavernor *et al.* 2013). Future research could investigate the association patterns of ASD symptoms and WB with a validated measure of WB for the ASD population. Fourth, although there is more and more attention for gender specific profiles in ASD, we decided not to add sex as a covariate as our male-female ratio was perfectly representative of the population, as recent large-scale epidemiological studies suggest (from Baio, 2014; Jensen *et al.* 2014; Lai *et al.* 2015). Moreover, in our recent paper on the multifactorial structure of factors for WB in another large ASD sample ($N = 2341$), sex did not appear to have a significant impact on WB (Deserno *et al.* 2016). Also, a recent study suggested that the factor structure of ASD symptoms is similar across gender (Grove *et al.* 2016). Future studies could investigate gender-related profiles in WB but this was beyond the scope of the current study. Fifth, from the data and analyses in this report, we cannot determine the direction of the reported associations. However, researchers are currently developing and testing techniques that work with directed graphs based on both time series data and cross-sectional data. Directed networks consist of pointing arrows, pointing in the direction of prediction, and perhaps causation (directed acyclic graphs, DAGs; McNally, 2016). Also, a future research avenue would be to apply the Perceived Causal Relations method (Frewen *et al.* 2012) to the subscale graph reported in this paper. In such a project, ASD adults and/or clinicians could be asked to rate the strength and direction of each relation between two variables. However, both investigations are beyond the scope of the current paper.

Despite these limitations, our findings provide a first mapping of WB networks moving across three construct levels of ASD to illuminate the multivariate pattern of associations. There are a few promising avenues for future study of later outcome in ASD. While it was hypothesized for some time that symptoms have differential impact on WB, our results additionally suggest that different symptom profiles may result in different correlation networks of WB domains. For example, symptom profiles that mainly feature problems with social contact directly impact another set of WB domains than symptom profiles that also include rigid behaviour. When interested in taking this scientific quest beyond mechanistic explanations, our finding has interesting implications. For example, examining variance of human development from a network perspective might point us towards the toolbox of dynamic systems approaches to the study of complex systems (Borsboom & Cramer, 2013). This approach facilitates an examination of how human behaviours might arise from the dynamic interaction of relevant factors over time. Thus, when interested in symptom profiles and their influence on developmental trajectories, the examination of longitudinal data is warranted (Van de Leemput *et al.* 2014). In this context, future longitudinal studies should investigate whether differences in developmental trajectories can be explained by underlying differences at the level of a latent variable (i.e., ASD) or whether developmental outcomes can be explained by the spontaneous emergence of coherent higher-order forms through interactions among simpler components. Eventually, it is anticipated that several pathways to and from different symptom profiles are identified, allowing for a precise investigation of the highways to happiness.

Notes

[1] All participants included in this study took part in the Treatment Monitoring Program of the Dr. Leo Kannerhuis. When they enter this program, they sign a care agreement of the clinic informing them (amongst other things) that their anonymized dossiers will be used for scientific purposes. In addition, the research reported in this paper has been approved by the Ethics Committee of the University of Amsterdam (2015-BC-4586).

[2] In the Netherlands, the official introduction of the fifth edition of the DSM is scheduled in 2017 (NVGzP, 2015).

[3] The items of all three questionnaires with corresponding abbreviations can be found in Table 1 of the supplementary material.

[4] Please find our parameter matrix for the Subscale network in the online supplement of this paper.

[5] Since we mainly interpret the Subscale network, we checked the stability of our inferences regarding this network with the R-package *bootnet*. We computed the centrality stability (CS) coefficient, quantifying the maximum proportion of cases that can be dropped for a correlation higher than 0.7 with the original centrality. The centrality stability coefficient indicated good stability of the node strength index, $CS > 0.5$ (Epskamp *et al.* 2017). Confidence intervals of the edge-weights indicated good accuracy, in line with what we would expect with the current study's sample size and number of nodes (see Supplementary Figs S2–S5).

[6] To improve the interpretation of the reported results we evaluated the obtained network structures with help of a feedback panel consisting of ASD adults and professionals working with people with ASD.

Supplementary material. The supplementary material for this article can be found at https://doi.org/10.1017/S0033291717002616

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Declaration of Interest. None.

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