ARTICLE IN PRESS

Schizophrenia Research xxx (xxxx) xxx

Contents lists available at ScienceDirect

Schizophrenia Research

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

A time-series network approach to auditory verbal hallucinations: Examining dynamic interactions using experience sampling methodology

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A R T I C L E I N F O

Article history:
Received 16 July 2019
Received in revised form
23 October 2019
Accepted 29 October 2019
Available online xxx

Keywords:
Psychosis
Auditory verbal hallucinations
Voice hearing
Network analysis
Experience sampling method

A B S T R A C T

Background: Identifying variables that influence daily-life fluctuations in auditory verbal hallucinations (AVHs) provides insight into potential mechanisms and targets for intervention. Network analysis, that uses time-series data collected by Experience Sampling Method (ESM), could be used to examine relations between multiple variables over time.
Methods: 95 daily voice-hearing individuals filled in a short questionnaire ten times a day for six consecutive days at pseudo-random moments. Using multilevel vector auto-regression, relations between voice-hearing and negative affect, positive affect, uncontrollable thoughts, dissociation, and paranoia were analysed in three types of networks: between-subjects (between persons, undirected), contemporaneous (within persons, undirected), and temporal (within persons, directed) networks. Strength centrality was measured to identify the most interconnected variables in the models.
Results: Voice-hearing co-occurred with all variables, while on a 6-day period voice-hearing was only related to uncontrollable thoughts. Voice-hearing was not predicted by any of the factors, but it did predict uncontrollable thoughts and paranoia. All variables showed large autoregressions, i.e. mainly predicted themselves in this severe voice-hearing sample. Uncontrollable thoughts was the most interconnected factor, though relatively uninfluential.
Discussion: Severe voice-hearing might be mainly related to mental state factors on the short-term. Once activated, voice-hearing appears to maintain itself. It is important to assess possible reactivity of AVH to triggers at the start of therapy; if reactive, therapy should focus on the triggering factor. If not reactive, Cognitive Behavioural interventions could be used first to reduce the negative effects of the voices. Limitations are discussed.

1. Introduction

Auditory verbal hallucinations (AVHs) are characterised by the perception of voices in the absence of external stimuli (Slade and Bentall, 1988). These experiences are common across a number of psychiatric conditions such as schizophrenia, bipolar disorder and borderline personality disorder, and can be highly distressing and disabling (de Leede-Smith and Barkus, 2013; Johns et al., 2014). The frequency and intensity of AVHs differ greatly between individuals, and typically fluctuate within people's daily life depending on contextual variables and mental states (Delespaul et al., 2002). Uncovering the variables that influence daily-life fluctuations in AVHs may offer insight into the mechanisms which drive them, as well as targets for intervention.

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https://doi.org/10.1016/j.schres.2019.10.055
0920-9964/© 2019 Published by Elsevier B.V.

Most studies have explored the relations between AVHs and mental states by correlations or prediction analyses whereby the direction of the effect is specified *a priori*. Most studies used cross-sectional data (e.g. Morrison and Baker, 2000; Smith et al., 2006), but increasingly Experience Sampling Methodology (ESM) is used (e.g. Hartley et al., 2014; Oorschot et al., 2012a,b). ESM involves the assessment of momentary experiences in daily life via questionnaires that are completed multiple times a day over several days, thereby producing time-series data (de Vries, 1992; Delespaul, 1995; Myin-Germeys et al., 2009). ESM data is considered more reliable and ecologically valid as experiences are captured in real-time, real-world contexts, and can be analysed to reveal temporal relationships between variables over time (Shiffman et al., 2008). Until recently, this type of data was mainly analysed by (multilevel) regression analysis; hence, analyses were performed with only one outcome, thereby ignoring other possible (inter)connections between variables. Nowadays, it is possible to include multiple factors as both predictor and outcome in a network model, enabling analysis of multiple relations and mutual associations (Borsboom, 2016; Borsboom and Cramer, 2013).

The traditional factorial medical approach to psychopathology assumes that symptoms are manifestations of an underlying latent factor (i.e. a mental disorder). Recently, there has been a shift towards network approaches which conceptualise symptoms as dynamic, interconnected networks that interact with each other over time, without the necessity of an underlying latent construct like a disorder (Borsboom and Cramer, 2013; Fried et al., 2017; Nelson et al., 2017). Within this framework, a network is a visual model consisting of elements ("*nodes*"), such as symptoms, mental states and contextual factors, and connections between the elements ("*edges*"), indicating strength and direction of relations. By analyzing timelagged ESM data using the network framework (Sacha Epskamp et al., 2018), it is possible to graph complex dynamic connections to elucidate the pattern of temporal relations between nodes. An other important advantage of network analysis is that it may identify factors that are central, i.e. influential, in the time-series models.

Network models are increasingly used to study psychiatric disorders, including psychosis (Isvoranu et al., 2017; Levine and Leucht, 2016; Van Rooijen et al., 2017, 2018). These studies, that relied on cross-sectional data, identified (shortest) pathways between variables, strong links between factors, and clusters of symptoms. In addition, temporal networks can be used to identify interactions between nodes over time, thereby producing indications for the direction of relations (Epskamp et al., 2018). Klippel et al. (2017) analysed timelagged data by network analysis in a population with psychosis, and found that minor daily life stress preceded positive and negative affect, paranoia, loss of control, and tiredness. In an n = 1 study (Bak et al., 2016), temporal models of resting and relapsing states, consisting of voice-hearing, feeling down, feeling relaxed, loss of control, and paranoia, were calculated and compared. In both stable state and full relapse, voice-hearing was preceded by all variables. It might be valuable to study the dynamics of AVHs by both correlational and temporal models. Our aim was to discover novel insights about the dynamic relations between AVHs and key variables, such as generating new hypotheses about causal relations and potential treatment targets.

The aim of the current study was to conduct time-series network analysis on an ESM dataset that included a number of key variables that have previously been found to influence fluctuations in AVHs, i.e.: positive and negative affect (Delespaul et al., 2002; Hartley et al., 2013; Oorschot et al., 2012a,b), intrusions (Jones and Fernyhough, 2006; Morrison and Baker, 2000), rumination (Hartley, Haddock, Vasconcelos e Sa, Emsley and Barrowclough, 2014), dissociation (Dorahy et al., 2009; Escudero-Pérez et al., 2016; Varese et al., 2011), paranoia (Oorschot et al., 2012a,b; Palmier-Claus et al., 2014), and self-esteem (Smith et al., 2006).

To study how these mental state factors were associated with AVHs and whether there were indications for temporal relations in this sample, we:

a) examined the between-persons relations between AVHs and the mental state variables by a between-subjects network, and;
b) examined the concurrent relations between AVHs and mental state variables by a contemporaneous network; and
c) examined the consecutive (lagged) relations between AVHs and mental state variables by a temporal network; and
d) identified the most central nodes in the models, i.e. what nodes are the most strongly connected to other nodes.

2. Method

2.1. Participants

Data were collected as part of a larger randomized controlled trial (RCT) testing the effects of a smartphone application (Temstem) in participants with persistent, frequent and distressing AVHs (see Jongeneel et al., 2018). Participants were recruited from 12 specialized mental healthcare institutions in the Netherlands. Inclusion criteria required the presence of AVHs for longer than one month, for at least four days a week in three of the last four weeks, irrespective of diagnosis. Exclusion criteria were inadequate competence of the Dutch language, current involuntary hospitalization in a closed ward, limited cognitive abilities (estimated IQ < 70), change of antipsychotics and/or antidepressants in the last month, currently receiving CBT for AVHs, not willing or capable to learn to use a smartphone, and intensive previous or current use of the Temstem application.

The present study included participants who had completed at least 25 out of 60 ESM questionnaires in the baseline ESM week before randomization; this is considered to be a sufficient number of measurement moments to capture a range of experiences over the sampling period (Palmier-Claus et al., 2011). 123 Participants started the baseline ESM week. 28 Participants were not able to fill in enough questionnaires. Data of in total 95 participants were included in analyses.

All procedures in this study complied with the ethical standards of the relevant national and institutional committees on human experimentation, and with the Helsinki Declaration as revised in 2008. The study was approved by the medical Ethics Committee of the VU University Medical Centre (METC number: 2015.435/NL53684.029.15).

2.2. Measures

ESM questionnaires were collected using PsyMate, an experience sampling application for smartphones (www.psymate.eu; Myin-Germeys et al., 2011). For six consecutive days, PsyMate prompted participants ten times a day to complete a brief electronic questionnaire. All prompts appeared at a pseudo-random moment in every 90-min time window between 7.30 a.m. and 10.30 p.m. Participants were required to complete assessments within 15 min following the prompt. Time intervals between two consecutive beeps (*t-1* and *t*) ranged from 15 min to 3 h. This study only focused on lag-1 (*t-1*) intervals, not lag-2 or larger intervals (e.g. *t-2*, *t-3* etc.).

Each ESM questionnaire comprised 45 items (for an overview of these items, see Jongeneel et al., 2018). For the present study, only the items assessing AVHs, negative affect, positive affect, intrusions, rumination, dissociation, paranoia, and self-esteem were used. Intrusions and rumination showed strong partial correlations in both the contemporaneous and between-persons networks (respectively $r = .572$ and $r = 972$), indicating multicollinearity (Daoud, 2017). Therefore, these items were combined into one *uncontrollable thoughts* factor. Self-esteem and positive affect also showed strong partial correlations in mainly the between-persons network ($r = 628$). We choose to delete self-esteem because positive affect was measured with three items, making it possibly a more reliable variable (Shrout and Lane, 2012). Hence, our final model consisted of six variables: AVHs, negative affect, positive affect, uncontrollable thoughts, dissociation, and paranoia. These variables were derived from 16 items in total − see Table 1. All items were rated on a 7-point Likert scale ranging from *not at all* (1) to *very* (7). With the exception of paranoia and AVHs, which were measured using single items, other constructs included multiple items which formed part of a broader factor. In these cases the average of these items formed the final variable. Items were developed based on previous ESM studies in psychosis (e.g. Delespaul, 1995; Delespaul et al., 2002; Thewissen et al., 2011; Thewissen et al., 2008), with further details available in Jongeneel et al. (2018).

2.3. Statistical analysis

For analyses, we used R version 3.5.1 and R packages mlVAR (Epskamp et al., 2016), RColorBrewer (Neuwirth, 2011), and qgraph (Epskamp et al., 2012).

2.3.1. Assumption checks

Kolmogorov-Smirnov tests and visual inspection of histograms were performed to assess the multivariate normality assumption of the statistical model we estimated in our main analyses (i.e., multilevel vector auto-regression [VAR]). According to the Kolmogorov-Smirnov tests, residuals of the multilevel VAR model were normally distributed for all variables ($p > .05$). Furthermore, we used the Kwiatkowksi-Phillips-Schmidt-Shin unit root test (KPSS; Kwiatkowski et al., 1992) to test whether all variables in all participants met the assumption of stationarity (i.e. whether means and variances of all items remained stable over time) (following Bringmann, 2016). For the majority of participants, this assumption was met. For the few participants for which the assumption was violated, detrending of their data was applied. For details and more information about the detrending procedure, see Online Supplementary Materials.

2.3.2. Descriptive statistics

For each participant, we calculated the mean (i.e., intra-individual mean) and standard deviation (i.e. intra-individual standard deviation) of each variable. We repeated this for all variables in all participants to generate a set of intra-individual means of all variables. From these values, we calculated the mean, standard deviation, and range for each variable (Table 2). Using the same procedure, we calculated the mean, standard deviation, and range of intra-individual standard deviations (Table 3).

2.3.3. Network estimation

We estimated three types of networks: a between-subjects network to investigate between subjects associations; a contemporaneous network to research concurrent relations, and a temporal network to investigate timelag associations.

The undirected between-subjects model uses the participants' mean of each variable over time (Epskamp et al., 2018), and can therefore best be compared to cross-sectional studies (Greene et al., 2018); for instance, the mean scores of AVHs and paranoia in a one week ESM period. A positive connection between AVHs and paranoia in this analysis would indicate that people with higher scores on AVHs during a week tend to have higher scores on paranoid ideation during this same week and vice versa.

The contemporaneous network, including all separate datapoints per variable, investigates concurrent relations between nodes. These relations are controlled for temporal effects and all other variables at the same timepoint to compute a partial (i.e. unique) correlations network (Epskamp et al., 2018; Wild et al., 2010). A contemporaneous network differs from a correlational network, for the contemporaneous network does not violate the independence of measurements assumption and takes the temporal relationship into account whereby the relationships within a timepoint can be separately analysed from relationships between timepoints (as in temporal models) (Epskamp et al., 2018).

In the directed temporal network, time series data are analysed including timelags (Epskamp et al., 2018; Epskamp et al., 2018; Van der Krieke et al., 2015). A variable at a certain timepoint (t) is predicted by the same variable (autoregressive effects) and all other variables (cross-lagged effects) at the previous timepoint (t-1). This results in partial correlations. When a variable at t-1 predicts a variable at t, this indicates that one item precedes the other. An advantage of the temporal network over conceptually simpler prediction models is that predictions are bidirectional: all variables are simultaneously predictors and outcome (Van der Krieke et al., 2015). This provides information about the temporal multivariate relations in the data.

2.3.4. Network centrality

Centrality measures can identify which node in a network is the most central, i.e. how well connected a node is to other variables (e.g. Costantini et al., 2015). We calculated the *strength* of the nodes for all networks, using the R package *qgraph* (Epskamp et al., 2012). The temporal network indicates both in-strength and out-strength of nodes. A high in-strength means the node is well influenced by other nodes. In the contrary, a node with high out-strength is a good predictor of other nodes.

2.4. Network visualization

Using the R package *qgraph* (S. Epskamp et al., 2012), we visualized all aforementioned associations as networks. Networks consist of circles, which represent variables, and lines between the circles representing associations between the variables. Positive

Table 1
ESM items.

Construct	Item
AVHs	"I hear voices"
Paranoia	"I am suspicious"
Negative affect	"I feel insecure/sad/lonely/anxious/irritated/relaxed (reversed)"
Positive affect	"I feel cheerful/satisfied/enthusiastic"
Uncontrollable thoughts	"I have intrusive thoughts"; "My thoughts won't let go"
Dissociation	"I feel unreal"; "The environment feels unreal, as if I'm not part of it"; "I feel absent, without a sense of time"

Note: Items have been translated into English from Dutch.

Please cite this article as: Jongeneel, A et al., A time-series network approach to auditory verbal hallucinations: Examining dynamic interactions using experience sampling methodology, Schizophrenia Research, https://doi.org/10.1016/j.schres.2019.10.055

relations are green and negative relations are red. The relations are weighted, with thicker edges indicating stronger connections.

2.5. Sensitivity analyses

In 17 participants, we observed one or several variables to be constant across time ($SD = 0$). To examine if these non-fluctuating time series (4.56% in total) influenced results, we excluded all participants with at least one constant variable, and re-ran analyses on this sample ($n = 78$).

2.6. Stability analyses

To examine the stability of the networks, 100 networks were estimated that included randomly selected data of 76 participants (i.e. 80%). We calculated the Spearman rank correlation between the centrality measures of our main model and the 100 N = 76 models. These 100 correlations were plotted in a histogram. To ensure full transparency, we discuss differences between the sensitivity analyses, stability analyses, and the main analyses in the results and discussion section and report all R-code and model output in the Online Supplementary Materials.

3. Results

3.1. Descriptive statistics

The initial dataset consisted of 4130 datapoints. Data with time intervals larger than 3 h, due to a missed beep or transition between days (night), were excluded from analysis (1830 beeps). Our final dataset consisted of 2300 measurement occasions with a mean time lag of 92.97 min and a standard deviation of 39.45 min.

Table 2 shows the characteristics of the sample. Table 3 presents the means, standard deviations, and range of intra-individual means and intra-individual standard deviations for each variable. Participants reported to hear voices (i.e. scoring at least a 2 on a 7-point Likert scale) in 83% of the ESM questionnaires, and indicated severe voice-hearing (i.e. scoring a 6 or 7) on 48% of the reports.

3.2. Network analyses

3.2.1. Between-subjects network

The between-subjects partial correlations network in Fig. 1 (left top panel) presents the pair-wise associations among the mean levels of variables over all beeps, when controlling for the mean levels of all other variables in the network. In the network, AVHs only connected to the rest of the network by a direct and positive association with uncontrollable thoughts ($r = 0.32$, $p < .01$). The network further showed positive associations between negative affect and uncontrollable thoughts ($r = 0.33$, $p < .001$), dissociation ($r = 0.27$, $p < .05$), and paranoia ($r = 0.29$, $p < .01$), and a negative association between negative affect and positive affect ($r = -0.21$, $p < .05$). Uncontrollable thoughts and dissociation were positively connected ($r = 0.33$, $p < .01$). According to Cohen, who considers a standardized partial correlation (r) of .1 to be small, .3 moderate, and .5 large, all significant effects had a moderate effect size.

Table 2
Sample characteristics (n = 95).

Variable	Mean (SD)
Female, no. (%)	51 (53.7)
Age in years: mean (SD)	43 (11.5)
Primary DSM-IV-TR chart diagnosis, no. (%)[a]	
Schizophrenia	40 (44.4)
Psychotic disorder NOS	18 (20.0)
Schizoaffective disorder	10 (11.1)
Post-traumatic stress disorder	8 (8.9)
Borderline personality disorder	5 (5.6)
Mood disorder[b]	5 (5.6)
Other[c]	4 (4.4)
Voice-hearing duration, in years: mean (SD)	15.9 (11.6)
Amount of completed ESM assessments: mean (SD)	43.47 (12.30)

Note: [a] Only diagnoses of those who completed the Temstem Trial were reported. [b] Mood disorders consists of: mood disorder with psychotic characteristics, depressive disorder, and bipolar disorder. [c] Other consists of: anxiety disorders, dissociative identity disorder, and other personality disorders. NOS = not otherwise specified.

Table 3
Mean, standard deviation, and range of intra-individual means and intra-individual standard deviations per variable. All variables have a potential score range from 1 to 7.

	Intra-individual means				Intra-individual SDs			
	M*	SD	Min	Max	M**	SD	Min	Max
AVHs	4.60	1.89	1.11	7	1.06	0.59	0	2.60
NA	3.10	0.96	1.38	5.56	0.56	0.23	0.15	1.22
PA	3.91	1.25	1.35	6.68	0.83	0.39	0.22	2.02
Paranoia	2.81	1.60	1	6.64	0.90	0.57	0	2.58
Dissociation	2.75	1.61	1	6.98	0.75	0.48	0	2.22
UT	3.70	1.70	1.10	7	1.03	0.46	0.	2.28

Note: AVHs = Auditory Verbal Hallucinations; NA = Negative Affect; PA = Positive Affect; UT = Uncontrollable thoughts. * Each participant has a mean value for the variable, and over all participants the mean of that variable is the score in this column. ** Each participant has a standard deviation of their mean of each variable, and over all participants the mean of the standard deviations for that variable is the score in this column.

3.2.2 Contemporaneous network. The network in Fig. 1 (left center panel) shows how variables tended to co-occur at the same moment, controlling for all other variables at the same moment and for all temporal relations among variables. As this visualization shows, AVHs were positively associated to uncontrollable thoughts ($r = 0.22$, $p < .001$), paranoia ($r = 0.11$, $p < .01$), dissociation ($r = 0.10$, $p < .01$), negative affect ($r = 0.05$, $p < .05$), and negatively to positive affect ($r = -0.09$, $p < .001$). Some other notable associations were observed between negative affect and uncontrollable thoughts ($r = 0.15$, $p < .001$), dissociation ($r = 0.12$, $p < .001$), paranoia ($r = 0.12$, $p < .001$), and negatively to positive affect ($r = -0.12$, $p < .01$) and between dissociation and paranoia ($r = 0.12$, $p < .001$) and uncontrollable thoughts ($r = 0.11$, $p < .001$). All significant effects were small or small to moderate. Of all the possible associations, only paranoia and positive affect showed no significant partial correlation.

3.2.2. Temporal network

The left bottom panel in Fig. 1 shows how variables predicted themselves (i.e. autoregressions) and each other across time (i.e. partial predictions). All variables had significant and moderate autoregression coefficients, for instance AVHs at time *t-1* predicted AVHs at time *t* ($r = 0.21$, 95% CI = 0.14, 0.28, $p < .001$). None of the pairs of variables were bidirectionally associated. AVHs predicted uncontrollable thoughts and paranoia (respectively $r = 0.07$, 95% CI = 0.01, 0.14, $p < .05$ and $r = 0.06$, 95% CI = 0.01, 0.11 $p < .05$). Conversely, however, none of the variables in the network predicted AVHs, neither direct nor indirect. Furthermore, negative affect predicted paranoia ($r = 0.06$, 95% CI = 0.01, 0.11, $p < .05$), and negatively predicted positive affect ($r = -0.05$, 95% CI = −.11, 0, $p < .05$). Finally, dissociation predicted negative affect ($r = 0.11$, 95% CI = 0.05, 0.17, $p < .001$) and uncontrollable thoughts ($r = 0.08$, 95% CI = 0.01, 0.14, $p < .05$). It should be noted that all effects were (very) small.

3.2.3. Strength centrality

The centrality plots in Fig. 1 present 'raw' strength sum scores. A node with high strength centrality is well connected to other nodes

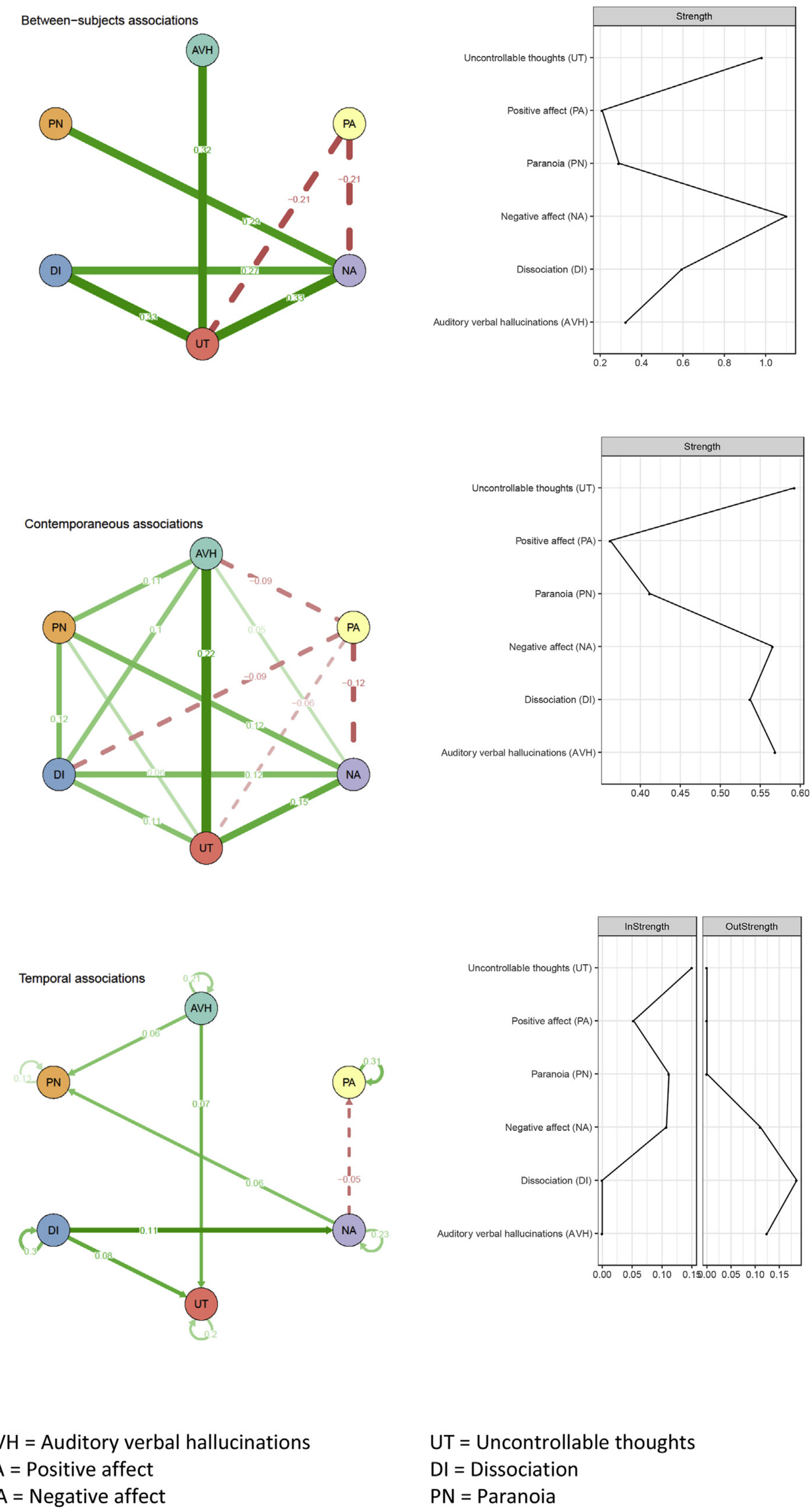

Fig. 1. Between-subjects (top left panel), contemporaneous (center left panel), and temporal associations (bottom left panel) visualized as networks using *qgraph*. Circles represent the variables. Lines between circles represent partial correlations. Thickness of the lines corresponds to the strength of the partial correlation (i.e., the numeric value in the middle of the lines). Green lines between circles represent positive partial correlations, while red disrupted lines represent negative partial correlations. The between-subjects associations in the center left panel represent how intra-individual means are connected by partial correlations. In the bottom left panel, arrows visualize temporal partial correlations. For instance, the arrow from AVHs to uncontrollable thoughts represents that AVHs at a previous time-point predicted uncontrollable thoughts at the subsequent time-point. To enhance visibility of the temporal effects we were interested in, we adjusted the autoregression coefficients by multiplying them by .2; those are interpretable in relation to each other, but not in relation to the cross lagged effects. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

(Costantini et al., 2015). In the between-persons network (right top panel), AVHs, which was one of the least strong nodes, was less well connected to other nodes in the model than negative affect and uncontrollable thoughts, which were the strongest nodes in this model. In the contemporaneous network (right center panel), strength was highest in uncontrollable thoughts, negative affect and AVHs, but as all variables had multiple connections, the difference between the strongest and least strongest nodes was not large and therefore unlikely to be influential. Additionally, in the temporal network (right bottom panel), uncontrollable thoughts scored highest on in-strength, which shows that this variable was most strongly predicted by other variables across time (i.e., the sum of incoming temporal associations). Dissociation and AVHs had relatively high out-strength, meaning that their sum of outgoing temporal associations were relatively high (compared to other variables in the network). However, considering the small edge weights, it appears that none of the nodes are strong predictors of other nodes on an absolute scale.

3.3. Sensitivity analysis

The visualization of the network models whereby the participants with non-fluctuating time series ($n = 17$) were excluded from analysis, are added in the Supplementary files. Only a few visible differences occurred when these participants were removed, with no changes in AVH in any model.

3.4. Stability analysis

The histograms containing the Spearman rank correlations between centrality measures of the N = 95 and the 100 n = 76 networks, are added in the Supplementary files. A few low correlations were found for all models, indicating that data of a subgroup of 76 participants differed relatively from the N = 95 data; however, the majority (>70%) of the correlations were above .7.

4. Discussion

In a clinical sample of 95 participants with frequent, distressing AVHs, we used time-series network models to investigate whether negative affect, positive affect, uncontrollable thoughts, dissociation, and paranoia were associated with daily life fluctuations of AVHs, and to examine the direction of relations between these variables and AVHs. The between-persons network, that analysed how variables were mutually connected over a period of 6 days, showed that AVHs was only related to uncontrollable thoughts. The contemporaneous model, that indicated undirected concurrent associations between the variables, showed that AVHs co-occurred with all other variables. In contrast, the temporal network that analysed the direction of relations over time, showed that AVHs was not predicted by any of the other factors. However, AVHs did predict uncontrollable thoughts and paranoia at subsequent timepoints. All variables showed large autoregression rates, which might indicate that all factors mainly predicted themselves.

The findings from our contemporaneous network are in line with findings of previous studies that reported associations between AVHs and positive and negative affect (Delespaul et al., 2002; Hartley et al., 2013; Oorschot et al., 2012a,b), uncontrollable thoughts (Hartley et al., 2014; Jones and Fernyhough, 2006; Morrison and Baker, 2000), dissociation (Dorahy et al., 2009; Escudero-Pérez et al., 2016; Varese et al., 2011), and paranoia (Oorschot et al., 2012; Palmier-Claus et al., 2014). Similarly, a part of the results of the between-persons network, which can best be compared to cross-sectional studies since it provides insight in how variables are associated when averaged over a period of time (in this study 6 days) (Greene et al., 2018), are in line with previous studies that reported a relation between voice-hearing and intrusions (Jones and Fernyhough, 2006; Morrison and Baker, 2000) and rumination (Hartley, Haddock, Vasconcelos e Sa et al., 2014). However, the between-persons network did not replicate previous findings that voice-hearing was associated with negative affect (Hartley et al., 2013), dissociation (Escudero-Pérez et al., 2016), or paranoia (Oorschot et al., 2012). This might be explained by our use of partial correlations, which depict whether variables are uniquely related to another factor. Investigating correlations without correcting for the other relations, as in previous studies (e.g. Oorschot et al., 2012; Escudero-Pérez et al., 2016), can lead to an over estimation of results and should therefore be interpreted with caution.

The temporal network, which estimates consecutive relations, revealed that none of the variables included in the model predicted changes in AVHs at later time points. Rather, AVHs intensity was found to precede the subsequent intensity of paranoia and uncontrollable thoughts. The fact that this did not occur in the opposite direction is in contrast to prior ESM research, which found that the intensity of rumination (Hartley et al., 2014) and paranoia (Palmier-Claus et al., 2014) can influence subsequent changes in AVHs. This inconsistency could also be accounted for by differences in analytic approach; the current study used time-series network modelling whereby multiple multilevel regressions were analysed, in contrast to Hartley et al., (2014a,b) and Palmier-Claus et al. (2014) who used single multilevel regression analysis. However, a second explanation might be that our results specifically concern this sample of persons with severe AVHs; participants in this study had complex and severe mental health problems, and on average had been hearing voices for 16 years. AVHs were experienced on the majority of the time of measurement occasions (83%), with severe intensity on half of the reports. This sample might be beyond the 'tipping point' of sudden critical transition to more severe illness (Scheffer et al., 2009); they are in a more chronic state wherein symptoms appear to maintain themselves at high frequency, rather than a trigger-dependent oscillating state (Greene et al., 2018). In these aspects, our sample might have been more severely ill than those from prior work identifying different temporal dynamics. Future work should focus on replicating this study in samples of people with AVHs at different levels of severity. It would also be valuable to compare models between samples with different AVHs characteristics, duration of illness, mental disorder diagnoses (Waters and Fernyhough, 2016), and potentially AVHs subtypes (McCarthy-Jones et al., 2014).

Uncontrollable thoughts appeared to be a central node in the association models, suggesting that this variable was connected to most others in the network. In addition, in the temporal model uncontrollable thoughts had highest in-strength, i.e. was most strongly predicted by other factors, and dissociation and AVHs had highest out-strength, i.e. were the strongest predictors. However, centrality measures should not be overestimated, since centrality measures are only point estimates that might not always be estimated reliably (e.g. Epskamp et al., 2018), and it remains unclear whether the central node has predictive power (for an overview of research, see Bringmann et al., 2019).

Sensitivity analyses showed some differences with our results (see Online Supplementary Materials). Removing participants with little temporal variability resulted in small differences in the between-persons network and a lack of one association in the contemporaneous network. Strength centrality differed only between the between-persons networks: uncontrollable thoughts was less strong, while negative affect and dissociation were stronger in our models compared to the sensitivity networks. This might be due to a decrease of power, or the between-persons network structure is somewhat different in this selection of individuals than in the reported model. Notably, the temporal model was not affected. Furthermore, stability analysis showed that

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centrality measures of the main models were highly correlated with the centrality measures in the majority of the subsamples, indicating the models to be stable.

Our overarching interpretation of all networks combined is that severe voice-hearing and other factors might be mainly related on the very short-term. Some stimulus activates a factor that, in turn, activates all other factors very rapidly. Once activated, voice-hearing appears to maintain itself without input from the environment. For clinical practise, this means that it is important to assess at the start of therapy whether voice hearing is still reactive to triggers (e.g. negative affect). If this is the case, interventions may start by targeting these triggers and by that way attempt to prevent voices from occurring. When voices predominantly appear to maintain themselves autoregressively, the focus could be placed on reducing the negative down-stream effects of the voices, for instance by Cognitive Behavioural interventions, e.g. challenging the content of the voices.

There are several important limitations to consider. A variety of factors, such as several contextual variables (Delespaul et al., 2002; Oorschot et al., 2012), meta-cognitive beliefs (Morrison et al., 2000) and symptom appraisals (Peters et al., 2012) that were previously found to interact with or to be associated with AVHs, were not taken into account in this study. Partly because this was a convenience sample and these variables were not included into the ESM questionnaire, and partly because there is no technique available yet for analysing variables with different measurement levels (e.g. continuous and dichotomous) in multilevel network models, limiting us to continuous variables only.

Both voice-hearing and paranoia were measured with one ESM item while the other variables were multi-item constructs. While some researchers have argued that at least three items per construct is required to ensure reliability (Shrout and Lane, 2012), others suggested that the single-item approach does not raise reliability issues, since repeated questions may serve as multiple questions (Bolger and Laurenceau, 2013; Hektner et al., 2007); thus, answering the question "I hear voices" multiple times complies with filling in three different questions about voice-hearing. In addition, using multiple items decreases the variability of a construct which is disadvantageous when you try to investigate moment-to-moment fluctuations. However, this reflects a broader discussion within ESM research that is beyond the scope of this research.

Our initial model needed to be modified. Self-esteem and positive affect were highly interdependent. Therefore, we had to combine the two factors or remove one (Daoud, 2017). Combining self-esteem with positive affect would result in an uninterpretable factor. Thus, in accordance with another comparable study (Wigman et al., 2016), we choose to remove one of the factors from analyses. Also, a high partial correlation was found between intrusions and rumination, both measured by one item. Therefore, we combined the two variables into one 'uncontrollable thoughts' factor. Literature showed that intrusions and ruminations are closely related (e.g. Guastella and Moulds, 2007) and Jones and Fernyhough (2009) proposed a model whereby ruminations preceded (cognitive) intrusions. However, it could also indicate a lack of validity of the items and it should be investigated further.

The fixed time interval assumption was violated, as the difference in time between measurements was not equal but varied between 15-180 min. It might be expected that some relations that exist within e.g. the 15 min timeframe might not be found because it disappears in all data. But since the network approach is still in its infancy, we cannot specify how problematic this is and there is no appropriate solution for this violation yet.

An inherent limitation of group-level analyses is that it is unclear whether results also account for individuals. Due to the heterogeneity of this sample, it is probable that the network dynamics and symptom processes are individual-specific and in fact differ to some extent from our group-level networks. An $n = 1$ voice-hearing network analysis study (Bak et al., 2016) reported more temporal connections than we did and voice-hearing was predicted best by paranoia. In the full relapse state, existing connections even became stronger. This might imply that this person was not beyond the 'tipping point' of transition to a chronic state, or that the current study missed several important relations. This stresses the importance of investigating several individual networks, to compare them mutually and with the current study results. .

This study has notable strengths. First, the use of network analysis on timelagged data in a sample of individuals with severe voices provides an understanding of the direction and strength of relations between multiple variables simultaneously and over time, as well as how they may mutually interact. Second, we chose to examine a simple model using only five mental state variables, selected on the basis of prior research. This accords with the recommendation by Borsboom (2016), to start by analysing manageable networks that can be modified when more knowledge and data is available, instead of analysing uninterpretable complicated and explorative models.

To conclude, this study was the first to use time-series network analysis to examine concurrent and temporal relations between AVHs and associated variables in a sample of individuals with persistent, frequent and distressing AVHs. Results revealed that AVHs tended to co-occur with all variables, specifically with uncontrollable thoughts, but was not predicted by any other variable. It might be that in this severely ill sample AVHs might have been developed in a trait, rather than a state. An other explanation might be that AVHs and mental state factors are mainly related on the (very) short-term. While there are several limitations to consider, the network approach might increase our knowledge about voice-hearing and other psychopathological phenomena. Research should continue to utilise time-series network analysis to further investigate dynamic processes underlying psychotic symptoms, in samples with a more diverse range of experiences, at different stages of AVHs onset, and across different diagnostic groups.

Declaration of competing interest

None.

Acknowledgements

The authors thank all participants, local researchers, research assistants, and all others who were involved without whom this study would not have been possible. The Temstem trial was funded by a grant awarded to DvdB and MvdG by the 'Innovatie Platform Parnassia' (Monsterseweg 93, 2553 RJ Den Haag).

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.schres.2019.10.055.

Financial support

The Temstem trial is funded by a grant awarded to DvdB and MvdG by the 'Innovatie Platform Parnassia' (Monsterseweg 93, 2553 RJ Den Haag).

Author contributions

All authors contributed to the manuscript. AJ collected the data under supervision of DvdB and MvdG and GA analysed the data under supervision of EF. AJ, GA, EF, PD, MdvG and DvdB interpreted the outcomes.

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