ARTICLE IN PRESS
SCHRES-08847; No of Pages 8
Schizophrenia Research xxx (xxxx) xxx
Contents lists available at ScienceDirect
Schizophrenia Research
journal homepage: www.elsevier.com/locate/schres

Virtual reality based cognitive behavioral therapy for paranoia: Effects on mental states and the dynamics among them

Chris N.W. Geraets [a,*], Evelien Snippe [b], Marije van Beilen [a], Roos M.C.A. Pot-Kolder [c,d], Marieke Wichers [b], Mark van der Gaag [c,d], Wim Veling [a,c,e]

[a] University of Groningen, University Medical Center Groningen, Department of Psychiatry, the Netherlands
[b] University of Groningen, University Medical Center Groningen, Department of Psychiatry, Interdisciplinary Center Psychopathology and Emotion regulation (ICPE), the Netherlands
[c] Parnassia Psychiatric Institute, The Hague, the Netherlands
[d] VU University and Amsterdam Public Mental Health research institute, Department of Clinical Psychology, Amsterdam, the Netherlands
[e] Maastricht University, Department of Psychiatry and Neuropsychology, Maastricht, the Netherlands

ARTICLE INFO

Article history:
Received 6 November 2019
Received in revised form 31 March 2020
Accepted 18 May 2020
Available online xxxx

Keywords:
Schizophrenia
Psychosis
Experience sampling method
Momentary assessment
Network analysis
Emotion processing

ABSTRACT

Background: Negative affective processes may contribute to maintenance of paranoia in patients with psychosis, and vice versa. Successful treatment may break these pathological symptom networks. This study examined whether treatment with virtual reality based cognitive behavioral therapy (VR-CBT) for paranoia influences momentary affective states, and whether VR-CBT changes the adverse interplay between affective states and paranoia.
Methods: Patients with a psychotic disorder ($n = 91$) were randomized to 16-session VR-CBT or treatment as usual (TAU). With the experience sampling method (structured diary technique) mental states were assessed for 6–10 days at baseline, posttreatment and 6-month follow-up. Multilevel analysis were performed to establish treatment effects and time-lagged associations between mental states, that were visualized with networks of mental states.
Results: Average levels of paranoia (feeling suspicious [b = −032., p = .04], disliked [b = −49., p < .01] and hurt [b = −0.52, p < .01]) and negative affect (anxious [b = −0.37, p = .01], down [b = −0.33, p = .04] and insecure [b = −0.17, p = .03) improved more after VR-CBT than TAU, but positive affect did not. Baseline mental state networks had few significant connections, with most stable connections being autocorrelations of mental states. The interplay between affective states and paranoia did not change in response to treatment. A trend reduction in average intranode connections (autocorrelations) was found after VR-CBT (b = −0.07, p = .08), indicating that mental states reinforce themselves less after treatment.
Conclusions: VR-CBT reduced paranoid symptoms and lowered levels of negative affect in daily life, but did not affect the extent to which mental states influenced each other. Findings do suggest that as a result of treatment mental states regain flexibility.

1. Introduction

Patients with a psychotic disorder often suffer from anxiety and depressed mood in addition to psychotic symptoms such as paranoid ideations. Negative affective states such as feeling lonely, anxiety and depressed mood may foster the maintenance of paranoia (Freeman, 2007; Freeman et al., 2002; Garety and Freeman, 2013; Van Os et al., 2014), suggesting that disrupting the pathological interplay between negative emotional states and paranoia, may be key components of paranoia treatment. In this study, we investigated the effects of virtual reality based cognitive behavioral therapy (VR-CBT) for paranoia on affect in daily life. Further, the effects of VR-CBT on the dynamic temporal associations between feelings of anxiety, depression, loneliness, safety and paranoia were explored using a network approach.

A recent perspective on the onset and maintenance of psychiatric disorders is the network approach. In brief, it states that mental states may activate each other, like nodes in a network (Cramer et al., 2010). It has been theorized that, in psychiatric disorders, a dysfunctional cascade may exist of mental states triggering other mental states in the next moment, which in turn reinforce each other (Cramer et al., 2010; Nelson et al., 2017; Wigman et al., 2013). For example, in psychosis, feeling lonely may cause someone to feel more anxious, which in turn can make someone more susceptible for paranoid thoughts, which can

* Corresponding author at: University of Groningen, University Medical Center Groningen, Department of Psychiatry, PO Box 30.001, 9700 RB Groningen, the Netherlands.
E-mail address: c.n.w.geraets@umcg.nl (C.N.W. Geraets).

https://doi.org/10.1016/j.schres.2020.05.047
0920-9964/

Please cite this article as: C.N.W. Geraets, E. Snippe, M. van Beilen, et al., Virtual reality based cognitive behavioral therapy for paranoia: Effects on mental states and the dy..., Schizophrenia Research, https://doi.org/10.1016/j.schres.2020.05.047

increase anxiety again. If mental states strongly trigger each other continuously, an inflexible vicious circle of mental states may occur.

Cognitive models also support the idea that negative affective states contribute to the maintenance of psychotic symptoms (Bentall et al., 2001; Freeman, 2007; Freeman et al., 2002; Garety et al., 2001; Garety and Freeman, 1999; Howes and Murray, 2014; Smith et al., 2006). Freeman et al. (2002) propose that anxiety facilitates the creation of paranoid thoughts, and that anxiety-related processes contribute to the maintenance and distress of paranoia. Moreover, they argue that paranoid delusions are a direct reflection of emotional concerns.

Indeed, cross-sectional as well as experimental research with virtual reality (VR) has repeatedly found that paranoia is associated with anxiety, negative affect, depressed mood and stress in people with psychosis (Fowler et al., 2012; Freeman et al., 2015; Veling et al., 2016). Studies using the experience sampling method (ESM), an extensive diary method which measures mental states and experiences multiple times a day in the flow of daily life, also support this. ESM research shows that negative affect levels are higher in individuals with psychosis compared to healthy people, while positive affect levels tend to be lower (Cho et al., 2017; Myin-Germeys et al., 2018; Oorschot et al., 2012).

In addition, ESM research has taught us that not only symptom levels are elevated in psychosis, but that also dynamic moment-to-moment interactions between mental states differ from healthy individuals (Klippel et al., 2017; Wigman et al., 2015). For example, Thewissen et al. (2011) found that higher anxiety levels preceded paranoid experiences. Moreover, higher levels of paranoia were preceded by elevated negative affective states in terms of feeling down, angry and anxious. Recently, Klippel et al. (2017) found that feeling down predicted feeling suspicious in the next moment, which in turn predicted anxiety in patients with psychosis. In family members and healthy controls such relations were not present.

While relationships between negative affective states and paranoia are well documented, little is known about the interplay between affective states and paranoia in relation to the effects of treatment. To our knowledge, no trials have yet compared pre and posttreatment dynamic interactions between mental states in psychosis patients. One case study did show that the dynamic temporal associations within a network of mental states of an individual with psychosis differed during different levels of symptom severity (stable, impending relapse and full relapse) of the illness (Bak et al., 2016). During (impending) relapse, connections grew stronger and clustering of symptoms changed between mental states, indicating qualitative changes in the network, as would be expected based on the network approach to psychopathology.

Recently, we developed VR-CBT for paranoia and social activity. We previously reported that VR-CBT indeed did reduce paranoid ideations (Pot-Kolder et al., 2018). To extend our previous findings, in the present study we studied the effects of VR-CBT on negative and positive affect in everyday life, and explored whether the bidirectional temporal associations among paranoia and several negative affective states change in response to treatment. To this end, we used ESM diaries that were completed before and after the intervention, and at 6-month follow-up.

It was hypothesized that in individuals with a psychotic disorder 1] VR-CBT results in lower levels of negative affect and higher levels of positive affect than treatment as usual (TAU), 2] at baseline temporal associations are present between negative emotional states (feeling safe, anxious, down, and lonely) and paranoia (feeling suspicious) that activate each other, and that 3] VR-CBT results in changes in the temporal associations between mental states.

2. Method

2.1. Design

This was a multi-center randomized controlled trial (ISRCTN registration: 12929657). Assessments were completed at baseline, posttreatment (three months after baseline) and follow-up (six months after baseline). After baseline, participants were randomized to VR-CBT or TAU. Researchers were blind to treatment allocation. Participants in the TAU group had access to the usual treatment, consisting of antipsychotic medication, and consultation and/or supportive counselling by psychiatrists, psychiatric nurses or social workers. The TAU group was not allowed to receive any psychological therapy aimed at improving social participation during the trial.

The study was approved by the ethical committee of the Amsterdam University Medical Center. Participants signed informed consent. A €30 compensation was provided per assessment.

2.2. Participants

Participants were recruited from seven mental health centers. Inclusion criteria were: diagnosis of a psychotic disorder, paranoid ideations (Green Paranoid Thought Scalescore>40) (Green et al., 2008), avoidance of public transportation, bars, shops or streets, and age 18–65. Exclusion criteria were a history of epilepsy, IQ < 70, and insufficient command of the Dutch language.

The original sample consisted of 116 patients (Pot-Kolder et al., 2018). In the present study, participants were included only if baseline and posttreatment ESM data were available, and VR-CBT participants had completed minimally three sessions leaving 91 participants for analyses. Excluded patients were significantly younger ($M = 32.2$, $SD = 7.6$) and had a shorter illness duration ($M = 8.5$, $SD = 6.8$) than included patients ($M_{age} = 39.5$, $SD_{age} = 10.1$, $M_{illness} = 15.7$, $SD_{illness} = 10.3$). No other differences were present in sociodemographics or baseline ESM suspiciousness between excluded and included patients.

2.3. Intervention

VR-CBT consisted of maximally 16 one-hour individual therapy sessions given by trained psychologists. Psychologists had completed a basic CBT training. Further, they received two days of training in VR-CBT. The manual described a structured treatment plan for all sessions. Therapists attended 4 h of group supervision each month by MvdG, registered teacher and supervisor of the Dutch Association of Cognitive behavioral therapy. The treatment protocol was aimed at reducing paranoia and improving social participation. The therapy consisted of evidence-based CBT elements such as making treatment goals, exposures, behavioral experiments, reducing safety behavior, and attention strategies. However, instead of in vivo, exercises and behavioral experiments were done in VR. In the first two sessions personal goals were set, and the VR system was introduced. In the following sessions, participants practiced 40 min within VR each session. No homework was given. More details have been published previously (Pot-Kolder et al., 2018).

2.4. Measures

Mental states were assessed using ESM (also ecological momentary assessment), a structured diary technique. During 6–10 days, participants completed short questionnaires on an electronic momentary assessment technology device called PsyMate (Delespaul and Devries, 1987; Myin-Germeys et al., 2011). After general assessments were completed (at baseline, posttreatment and follow-up), the ESM assessment period started (baseline ESM was completed prior to randomization). Ten times daily at semi-random ±90 min intervals between 7.30 AM and 10.30 PM, the device signalled and participants completed the questionnaire. Minimally 20 questionnaires within six consecutive days had to be completed. Prior to the baseline measurement participants received verbal and written information on PsyMate use and completed one 'practice' questionaire. After two days, participants were called to inform on the diary assesments experiences and aswer any questions. All participants had to complete the ESM baseline measurement sufficiently before randomization.

Items were rated on 7-point Likert scales ranging from 0 "not at all" to 7 "very". The following paranoia related items (as confirmed by principle component analysis on all mental state items (Pot-Kolder et al., 2018)) were measured: "I feel suspicious", "I feel that others might hurt me," and "I feel that others dislike me". Negative mental state indicators included: "I feel down", "I feel anxious", "I feel insecure", "I feel disappointed", "I feel lonely", "I feel guilty", "I feel safe" (reverse score, further referred to as "unsafe"), "I feel annoyed". Positive mental state items were: "I feel cheerful", "I feel enthusiastic", "I feel content", "I feel relaxed", and "I like myself".

2.5. Statistical analyses

Data were analysed with SPSS Statistics 24 and R version 3.4.3. Significance was accepted at 0.05. Baseline characteristics were compared with *t*-tests, non-parametric Mann-Whitney *U* tests, or χ^2 tests. As VR-CBT had never been tested previously, and ESM had not been used before as a primary outcome in treatment studies, sample size was estimated conservatively. A moderate effect size of 0·5, power of 0·8, α of 0·05 and a two-sided independent t-test resulted in a sample size of 128.

2.5.1. Mental state levels

Mental state levels were analysed with multilevel analyses on the factors time (baseline vs posttreatment, baseline vs. follow-up), group and the interaction time X group. Multilevel analyses allowed using all available data, under the assumption that data is missing at random. Models included a random intercept for participant and a random slope for time. The estimation method was set to restricted maximum likelihood and the covariance structure to unstructured. Treatment effects were established by the time X group interaction for posttreatment and follow-up separately by comparing each to baseline.

2.5.2. Network analyses

Temporal associations were estimated using multilevel vector autoregressive (VAR) modelling (Bringmann et al., 2013) and were depicted as networks. Networks were constructed for baseline and posttreatment. Networks depict if mental states predict one another at the next time point. Nodes represent mental states, edges represent regression coefficients.

2.5.2.1. Item selection. To reduce the chance of overfitting, five ESM items were included in network analyses. Mental states representing different underlying constructs related to paranoia and negative affect were selected, as these have been found to be strongly related. Candidate items were: "dislike", "hurt", "suspicious", "anxious", "insecure", "down", "lonely", and "unsafe". Items were excluded if the person-period-centered item was correlated too strongly with other items (r > 0.5), had a skewed distribution (skewness >0.8), showed to little within-person variation over time (mean squared successive difference (MSSD) <0.90), and when the MSSD and percentages mode scored differed between groups at baseline (tested with *t*-tests). "Hurt" and "dislike" showed too little variation (MSSD <0.82) and were eliminated. The final selected items were: "suspicious", "unsafe", "anxious", "down", and "lonely".

Regression coefficients were estimated with multilevel vector autoregressive (VAR) models (Bringmann et al., 2013). For each network, five multilevel VAR models were fitted to obtain the regression coefficients of the network connections strengths (edges) between the nodes (mental states). The five models included either "suspicious", "unsafe", "anxious", "down", or "lonely" as the dependent variable. Independent variables, for all models, were the lag_{t-1} of the same five variables, which were included as fixed effects. Variables were person-period-mean centered prior to the analyses, to separate within- and between-person effects (Curran and Bauer, 2011). To model possible trends in variables, the observation number was included as a predictor in all models. Models included random intercepts for the participant level and random slopes for the observation number (which were allowed to be correlated). Only within-day associations were modelled, overnight lags were excluded. Significance of regression coefficients was tested with permutation tests (100,000 permutations, fixed effects tested two-sided) (Klippel et al., 2017; Snippe et al., 2017). Networks were visualized using the *R*-package *qgraph* (Epskamp et al., 2012).

Differences in network edges (regression coefficients) were tested with permutation testing. We tested whether edge weights differed between groups at baseline. Next, we tested whether edge weights changed over time within groups. Finally, we tested whether change over time differed between groups.

Average intranode (autocorrelations) and internode connectivity was calculated per network by averaging the absolute edge weights of a network. Change in network connectivity was tested from baseline to posttreatment, and whether change differed between the groups. Significance was tested with permutation tests.

2.5.3. Contemporaneous associations

As mental states might influence one another faster than the timeframe between signals in this study, post hoc multilevel analysis were performed to assess contemporaneous relations for suspicious (Epskamp et al., 2018). Suspicious was chosen as this was the main focus of VR-CBT. We examined whether "suspicious" was predicted by "unsafe", "anxious", "down", and "lonely" at the same measurement occasion. Further, the model included the observation number as a predictor, a random intercept for participant and a random slope for observation number. Regression coefficients, within group differences, and differences in change over time were tested with permutation tests (100,000 permutations, fixed effects tested two-sided).

3. Results

In total, 91 patients were included. Groups did not differ in baseline characteristics (Table 1) nor in the main outcome feeling suspicious. Four participants did not fully finish VR-CBT, they completed respectively 3, 4, 5 and 9 sessions. ESM response rates were high; at baseline on average 47.5 (SD = 13.2) out of 70 ESM assessments were completed. On average 43.0 posttreatment (SD = 10.2) and 43.1 follow-up assessments (SD = 10.7) were completed.

3.1. Mental state levels

In general - over both groups - there was a significant decrease from pre to posttreatment (main effect of time) in feeling hurt, insecure,

Table 1
Demographic and clinical characteristics.

	VR-CBT	TAU
	N = 43	N = 48
Age, years	38.1 (10.0)	40.9 (10.0)
Male	29 (67.4%)	34 (70.8%)
Dutch origin	32 (74.4%)	29 (60.4%)
DSM-IV psychoses spectrum diagnosis		
Schizophrenia	37 (86.0%)	42 (87.5%)
Schizoaffective disorder	1 (2.3%)	4 (9.5%)
Not-otherwise specified psychotic disorder	5 (11.6%)	2 (4.1%)
Duration of illness, years	15.4 (11.3)	15.9 (9.4)
Medication use		
Antipsychotics	41 (95.3%)	47 (97.9%)
Antidepressants	14 (32.6%)	14 (29.2%)

Note: Data are n (%) or mean (standard deviation). VR-CBT, virtual reality cognitive behavioral therapy; TAU, treatment as usual.

Table 2
Weighted means, standard deviations and test results of mental states over time.

	VR-CBT			TAU			Time[a]				Time x treatment[b]			
	Pre	Post	Follow-up	Pre	Post	Follow-up								
	N = 43	N = 43	N = 39	N = 48	N = 48	N = 44	Pre-Post		Pre-Follow-up		Pre-Post		Pre-Follow-up	
	M (SD)	M (SD)	M (SD)	M (SD)	M (SD)	M (SD)	b (95% CI)	p	b (95% CI)	p	b (95% CI)	p	b (95% CI)	p
Paranoia														
Suspicious	2.97 (1.41)	2.69 (1.38)	2.72 (1.44)	3.22 (1.58)	3.25 (1.66)	3.22 (1.60)	0.03 (−0.28:0.25)	0.11	−0.04 (−0.27:0.19)	0.09	−0.32 (−0.64:−0.01)	**0.04**	−0.21 (−0.54:0.12)	0.22
Dislike	3.22 (1.53)	2.83 (1.47)	2.78 (1.42)	3.31 (1.49)	3.41 (1.63)	3.45 (1.63)	0.10 (−0.12:0.32)	0.08	0.11 (−0.12:0.34)	0.09	−0.49 (−0.81:-0.16)	<**0.01**	−0.51 (−0.85:−0.18)	<**0.01**
Hurt	3.09 (1.67)	2.75 (1.52)	2.67 (1.47)	3.10 (1.63)	3.27 (1.73)	3.36 (1.80)	0.17 (−0.08:0.43)	**0.02**	0.18 (−0.07:0.44)	**0.01**	−0.51 (−0.88:−0.14)	<**0.01**	−0.56 (−0.93:−0.19)	<**0.01**
Negative affect														
Down	2.92 (1.14)	2.69 (1.10)	2.55 (1.10)	3.32 (1.49)	3.27 (1.46)	3.30 (1.43)	−0.05 (−0.25:0.15)	0.59	−0.05 (−0.27:0.17)	0.27	−0.17 (−0.47:0.11)	0.24	−0.33 (−0.65:-0.01)	**0.04**
Anxious	2.98 (1.13)	2.58 (1.14)	2.65 (1.19)	3.26 (1.55)	3.23 (1.57)	3.21 (1.52)	−0.04 (−0.24:0.16)	0.15	−0.11 (−0.34:0.13)	0.65	−0.37 (−0.66:-0.08)	0.**01**	−0.23 (−0.57:0.11)	0.19
Insecure	3.11 (1.06)	2.79 (1.10)	2.65 (1.17)	3.39 (1.35)	3.32 (1.38)	3.32 (1.36)	−0.08 (−0.25:0.10)	<**0.01**	−0.12 (−0.32:0.09)	<0.**001**	−0.25 (−0.51: 0.01)	0.06	−0.17 (−0.64:-0.03)	0.**03**
Disappointed	2.99 (1.36)	2.85 (1.44)	2.67 (1.38)	3.11 (1.52)	3.02 (1.65)	3.07 (1.71)	−0.10 (−0.31:0.11)	0.10	−0.11 (−0.35:0.13)	**0.02**	−0.05 (−0.35:0.25)	0.74	−0.21 (−0.57:0.14)	0.23
Lonely	2.86 (1.06)	2.64 (1.08)	2.60 (1.12)	3.21 (1.47)	3.13 (1.39)	3.09 (1.43)	−0.09 (−0.27:0.10)	**0.02**	−0.13 (−0.32:0.05)	<**0.01**	−0.14 (−0.42:0.13)	0.30	−0.11 (−0.39:0.16)	0.41
Guilty	2.85 (1.50)	2.66 (1.44)	2.63 (1.43)	2.81 (1.45)	2.83 (1.58)	2.82 (1.54)	0.02 (−0.18:0.21)	0.22	−0.01 (−0.26:0.23)	0.21	−0.20 (−0.48:0.08)	0.15	−0.20 (−0.56:0.16)	0.27
Unsafe	3.44 (1.17)	3.19 (1.16)	3.15 (1.23)	3.46 (1.34)	3.43 (1.36)	3.34 (1.46)	−0.02 (−0.20:0.16)	**0.04**	−0.11 (−0.32:0.09)	**0.02**	−0.23 (−0.49:0.03)	0.08	−0.12 (−0.42:0.17)	0.41
Annoyed	2.88 (1.26)	2.77 (1.25)	2.71 (1.23)	2.96 (1.21)	3.04 (1.30)	2.96 (1.22)	0.08 (−0.13:0.28)	0.78	−0.03 (−0.27:0.20)	0.29	−0.19 (−0.49:0.11)	0.20	−0.12 (−0.46:0.23)	0.50
Positive affect														
Cheerful	4.24 (1.10)	4.33 (1.29)	4.41 (1.27)	4.01 (1.32)	4.10 (1.30)	4.11 (1.40)	0.05 (−0.15:0.26)	0.30	0.06 (−0.24:0.41)	0.19	0.04 (−0.25:0.33)	0.77	0.09 (−0.24:0.40)	0.60
Enthusiastic	3.89 (1.24)	4.02 (1.43)	4.18 (1.28)	3.65 (1.15)	3.63 (1.19)	3.73 (1.24)	0.03 (−0.18:0.24)	0.30	0.12 (−0.08:0.32)	**0.01**	0.10 (−0.21:0.41)	0.52	0.14 (−0.16:0.43)	0.36
Content	4.37 (1.06)	4.48 (1.20)	4.62 (1.17)	4.06 (1.19)	4.11 (1.17)	4.08 (1.34)	0.03 (−0.16:0.21)	0.30	−0.02 (−0.22:0.18)	0.19	0.09 (−0.18:0.35)	0.51	0.23 (−0.06:0.53)	0.12
Relaxed	4.34 (1.03)	4.47 (1.14)	4.59 (1.10)	4.20 (1.17)	4.25 (1.15)	4.24 (1.35)	0.08 (−0.09:0.26)	0.09	0.08 (−0.13:0.29)	0.09	0.05 (−0.20:0.31)	0.67	0.11 (−0.20:0.41)	0.49
I like myself	4.64 (1.23)	4.75 (1.29)	4.90 (1.27)	4.44 (1.27)	4.53 (1.32)	4.64 (1.41)	0.06 (−0.12:0.23)	0.17	0.16 (−0.05:0.37)	**0.01**	0.06 (−0.20:0.31)	0.66	0.09 (−0.22:0.40)	0.57

Note: M, mean; SD, standard deviation; b, parameter estimate (regression coefficient); CI, confidence interval; VR-CBT, virtual reality cognitive behavioral therapy; TAU, treatment as usual; pre, baseline; post, posttreatment; follow-up, 6-month follow-up assessment.

[a] Values indicate the p-values of the type III fixed main effect F-tests of time of the multilevel models. sp-values < .05 are presented in bold.

[b] Values indicate the p-values of the type III fixed interaction effect F-tests of time and treatment of the multilevel models, thus the treatment effect. p-values < .05 are presented in bold.

lonely and unsafe (see Table 2). These time effects remained significant at follow-up. By 6-month follow-up, feeling disappointed, enthusiastic, as well as “I like myself” had changed in general compared to baseline.

Significant treatment effects (interaction of time X treatment) were found at posttreatment for feeling suspicious, disliked, hurt, and anxious; these mental states decreased significantly more after VR-CBT than TAU. At posttreatment trend effects of treatment were found for feeling insecure ($p = .06$) and unsafe ($p = .08$). At follow-up, significant treatment effects of VR-CBT were observed for feeling disliked, hurt, down, and insecure in comparison with TAU.

3.2. Temporal networks

The temporal associations between mental states are shown in Table 3 and Fig. 1. At baseline the TAU and VR-CBT group differed significantly in the relation between feeling anxious$_{t-1}$ and lonely$_t$ ($b = 0.11$, $p = .04$); a negative relation was found in the VR-CBT group, and no significant relation for TAU. Both baseline networks had in common that strong significant associations were present for the autocorrelations (i.e., the time-lagged effect of a mental state on itself), and the time-lagged association between feeling down$_{t-1}$ and lonely$_t$. Post hoc checks for coefficients stability were performed by ommiting one of five predictors. Results showed similar and thus table coefficients.

Within the VR-CBT group, only the anxious$_{t-1}$-lonely$_t$ association in the network decreased significantly from pre to posttreatment ($b_{pre} = -0.08$; $b_{post} = 0.05$, $p < .01$). Within the TAU group networks, the down$_{t-1}$-suspicous$_t$ relation decreased significantly from pre to posttreatment ($b_{pre} = 0.07$; $b_{post} = -0.02$, $p = .02$). However, when testing the difference in change from pre to posttreatment between the groups, no significant differences were found.

Internode connectivity (i.e., average of the absolute regression coefficients of lagged associations between mental states) did not change over time for both the VR-CBT ($b_{inter} = 0.00$, $p = .77$) and TAU group ($b_{inter} = 0.00$, $p = .87$), and change did not differ between groups.

Intranode connectivity (autocorrelations) showed a trend reduction in the VR-CBT group; the connectivity decreased from pre to posttreatment ($b_{intra} = -0.07$, $p = .08$). Intranode connectivity did not change over time for TAU ($b_{intra} = -0.01$ $p = .82$). Change in connectivity did not differ significantly between groups ($b = 0.06$, $p = .25$).

3.3. Contemporaneous associations

Post hoc multilevel analysis showed that suspicious was significantly associated at the same time point with lonely, anxious, and unsafe at baseline in both groups (Table 3). At baseline, the down-suspicious relation differed significantly between the VR-CBT and TAU network; a positive association was found in the TAU group, and no significant relation in the VR-CBT group ($b_{vr\text{-}cbt} = 0.04$; $b_{tau} = 0.16$, $p < .01$).

The association between feeling suspicious and feeling lonely, anxious, and unsafe did not change over time for VR-CBT or TAU. There was a significant difference in change over time between groups in the down-suspicious relation. Whereas for the VR-CBT group there

Table 3
Associations between mental states and change in associations over time.

			VR-CBT		TAU		VR-CBT	TAU	Δ VR-CBT - TAU
			Pre b	Post b	Pre b	Post b	Δ Pre-post	Δ Pre-post	Δ Change
Temporal associations									
Suspicious$_{t-1}$	→	Suspicious$_t$	**0.19****	0.03	**0.17****	**0.21****	−0.16	0.05	−0.20
Anxious$_{t-1}$	→	Anxious$_t$	**0.08***	0.08	**0.11****	**0.11****	0.00	0.00	0.00
Down$_{t-1}$	→	Down$_t$	**0.15****	**0.10***	**0.24****	**0.19****	−0.05	−0.05	−0.01
Unsafe$_{t-1}$	→	Unsafe$_t$	**0.17****	**0.13****	**0.13****	**0.14****	−0.04	0.01	−0.05
Lonely $_{t-1}$	→	Lonely$_t$	**0.27****	**0.19****	**0.17****	**0.13****	−0.08	−0.05	−0.03
Mean intranode connectivity[a]			0.17	0.11	0.16	0.16	−0.07	−0.01	0.06
Down$_{t-1}$	→	Suspicious$_t$	0.03	**0.07***	0.07	−0.02	0.05	**−0.09***	0.14
Lonely $_{t-1}$	→	Suspicious$_t$	0.04	0.02	0.01	0.03	−0.02	0.02	−0.04
Anxious$_{t-1}$	→	Suspicious$_t$	0.02	**0.08***	0.02	0.03	0.07	0.01	0.05
Unsafe$_{t-1}$	→	Suspicious$_t$	0.00	0.03	0.05	0.04	0.03	−0.01	0.04
Down$_{t-1}$	→	Anxious$_t$	**0.09***	0.07	0.06	0.01	−0.02	−0.05	0.04
Suspicious$_{t-1}$	→	Anxious$_t$	0.05	0.07	0.06	0.05	0.03	−0.01	0.03
Lonely $_{t-1}$	→	Anxious$_t$	0.04	−0.01	0.01	**0.06***	−0.05	0.05	−0.10
Unsafe$_{t-1}$	→	Anxious$_t$	0.00	−0.01	0.07	**0.08***	−0.01	0.01	−0.02
Suspicious$_{t-1}$	→	Down$_t$	0.07	0.02	0.02	−0.01	−0.04	−0.03	−0.02
Lonely $_{t-1}$	→	Down$_t$	**0.05***	0.03	0.06	0.05	−0.03	−0.01	−0.02
Anxious$_{t-1}$	→	Down$_t$	0.04	**0.09***	−0.01	0.02	0.04	0.04	0.01
Unsafe$_{t-1}$	→	Down$_t$	0.00	0.02	0.06	**0.10****	0.03	0.04	−0.02
Down$_{t-1}$	→	Unsafe$_t$	0.05	0.05	−0.01	−0.02	0.00	−0.01	0.01
Suspicious$_{t-1}$	→	Unsafe$_t$	0.01	0.03	0.05	0.06	0.01	0.01	0.00
Lonely $_{t-1}$	→	Unsafe$_t$	0.00	0.01	0.03	0.02	0.01	−0.01	0.02
Anxious$_{t-1}$	→	Unsafe$_t$	−0.03	0.03	0.01	0.03	0.06	0.02	0.04
Down$_{t-1}$	→	Lonely$_t$	**0.12****	0.07	**0.13****	0.03	−0.05	−0.11	0.05
Suspicious$_{t-1}$	→	Lonely$_t$	0.03	−0.05	−0.01	0.08	−0.08	0.08	−0.16
Anxious$_{t-1}$	→	Lonely$_t$	**−0.08***	0.05	0.03	0.03	**0.13****	0.00	0.13
Unsafe$_{t-1}$	→	Lonely$_t$	0.01	0.01	0.05	0.08	0.00	0.02	−0.02
Mean internode connectivity [a]			0.04	0.04	0.04	0.04	0.00	0.00	0.00
Contemporaneous associations									
Down	Suspicious		0.04	**0.11****	**0.16****	0.04	**0.08***	**−0.12****	**0.20****
Lonely	Suspicious		**0.07****	0.03	**0.10****	**0.11****	−0.04	0.02	−0.05
Anxious	Suspicious		**0.25****	**0.25****	**0.25****	**0.18****	0.01	−0.08	0.08
Unsafe	suspicious		**0.15****	**0.11****	**0.17****	**0.16****	−0.04	−0.01	−0.03

Note: VR-CBT, virtual reality cognitive behavioral therapy; TAU, treatment as usual; pre, baseline; post, posttreatment; Δ, difference in b coefficients. b, are b coefficients of multilevel models, the multilevel models included the lag (t-1) of the five mental state variables and observation number as fixed effects, a random intercept for the participant level and random slopes for the time variable (observation number).

* p-value <.05.

** p-value <.01.

Please cite this article as: C.N.W. Geraets, E. Snippe, M. van Beilen, et al., Virtual reality based cognitive behavioral therapy for paranoia: Effects on mental states and the dy..., Schizophrenia Research, https://doi.org/10.1016/j.schres.2020.05.047

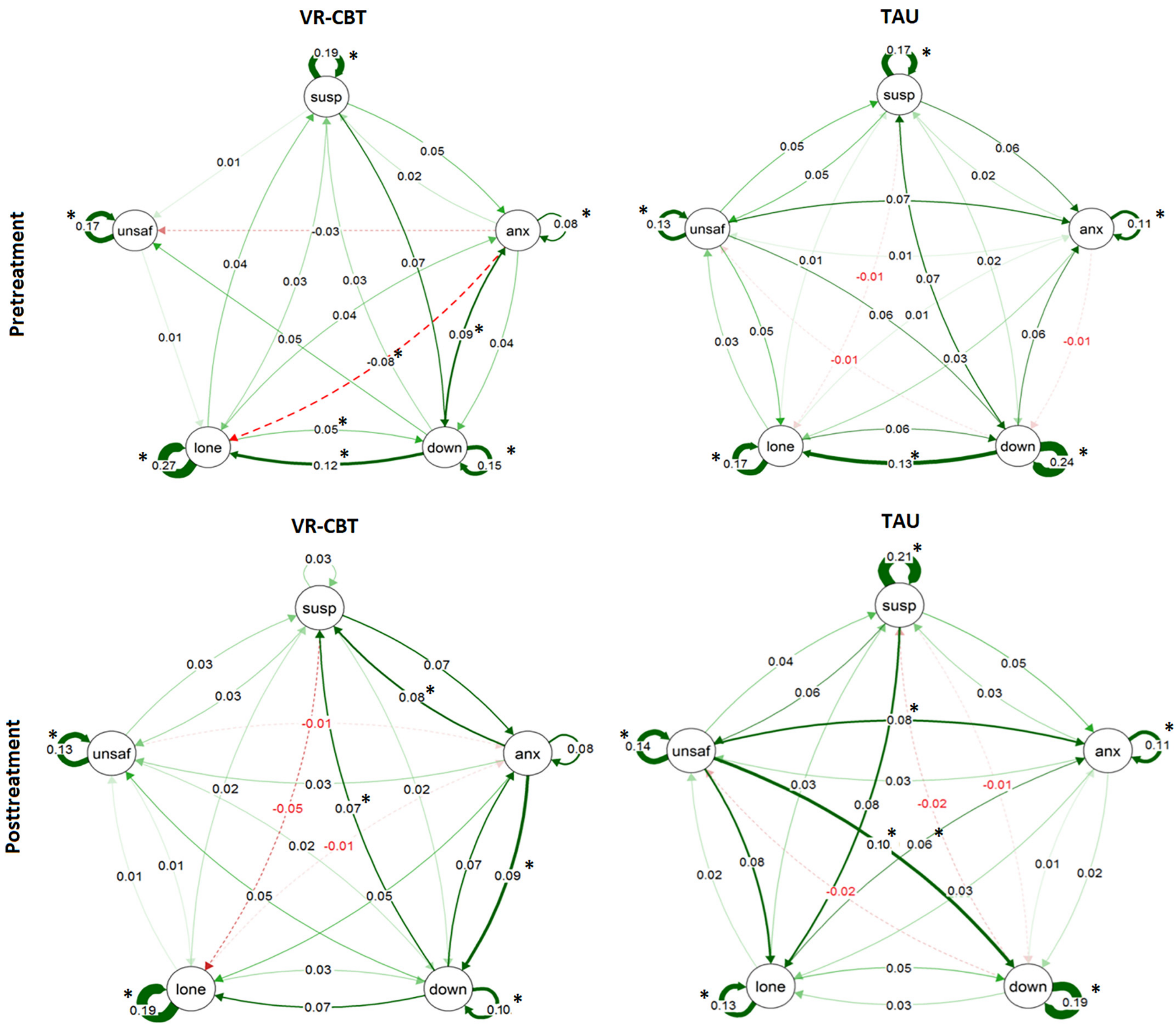

Fig. 1. Networks of mental states. *Note*: Anx = anxious, lone = lonely, susp = suspicious, unsaf = unsafe. Arrows represent lagged regression coefficients.

was no significant relation between down and suspicious at baseline, there was a significant positive association at posttreatment. For TAU only at baseline there was a significant association.

4. Discussion

This study examined the effects of VR-CBT on paranoia, positive and negative affect states in daily life and the dynamics among them. To our knowledge, this is the first study comparing pre and posttreatment networks in people with a psychotic disorder. We discuss three main findings: first, we found positive effects of VR-CBT on paranoia and negative affective states (i.e., feeling anxious, down, and insecure). Second, dynamic associations between paranoia and negative affective states from one moment to the next were not strong at baseline; states were best predicted by the same mental state at the previous moment. Third, dynamics between mental states were not affected by VR-CBT. There are indications that VR-CBT lowered autocorrelations, and that mental states, once activated, may recover quicker after therapy. Thus periods of heightened paranoia and negative affect seemed to last shorter.

4.1. Paranoia, positive and negative affect

After VR-CBT, patients reported feeling less suspicious, disliked and having lower levels of persecutory ideations (i.e., others want to hurt me) in comparison with TAU. Treatment effects on feeling disliked and persecutory ideations maintained at 6-month follow-up. By posttreatment, feeling anxious had decreased more after VR-CBT than TAU, and at follow-up, feelings of insecurity and down were also lower in the VR-CBT group. Further, improvements in negative affect seemed consistently larger in the VR-CBT group, though not significantly. VR-CBT did not influence positive affect.

This study extends our previous findings by showing that VR-CBT specifically effects three components of paranoia (dislike, hurt, and suspicious) (Pot-Kolder et al., 2018). In the long-term, VR-CBT seems to improve depressed mood (i.e., feeling down) and feeling insecure. As the proportion of clinical recovery for patients with psychotic disorders

Please cite this article as: C.N.W. Geraets, E. Snippe, M. van Beilen, et al., Virtual reality based cognitive behavioral therapy for paranoia: Effects on mental states and the dy..., Schizophrenia Research, https://doi.org/10.1016/j.schres.2020.05.047

tends to be relatively low, the finding that the therapy strongly influenced one of the core symptoms of psychosis – paranoia – as well as negative mental states in everyday life is of importance (Jääskeläinen et al., 2013).

An explanation for the lack of improvement in positive affect and several negative affect states could be the targeted approach of the intervention. Therapeutic effects of CBT have been reported to be specific. VR-CBT mainly focused on threat evoking situations, and not specifically on enhancing positive feelings. Patients e.g., learned throughout the therapy that (virtual) others did not hurt them, and that they can endure social embarrassment, without running away, screaming, or acting strangely. Negative beliefs were tested and falsified, thereby focusing on reducing paranoid and negative thoughts and feelings instead of increasing positive emotions. Possibly, secondary effects of reduced paranoia and negative affect will result in higher positive affect in the long-term, as a trend of increasing levels of positive affect was seen over time in all items, especially in the VR-CBT group. Another explanation could be that in patients with a long illness duration other factors have stronger impact on mood than paranoia, such as having limited social relations, unemployment, and past negative experiences.

4.2. Baseline interplay between emotions

In general, at baseline negative mental states were so persistently present that mental states mainly predicted themselves (high autoregression) in both groups. In a condition of persistent symptoms, the network may not be dynamic anymore. Based on network approaches of psychopathology, we hypothesized that patients with paranoia would show an inflexible vicious circle of mental states activating each other. In the study sample, we did not find strong evidence to support this at a group level, as at baseline no vicious circle of mental states were observed. Rather, affective states seemed to be mainly self-maintaining. This is called emotional inertia; this tendency of emotions to persist across time has been linked previously to psychopathology (Houben et al., 2015; Kuppens and Verduyn, 2017). Our findings therefore suggest that in psychosis, mental states seem to be self-maintaining, which advocates for symptom-oriented interventions.

Our findings are not completely in line with previous research. While strengths of associations in previous studies were of a similar order, previous research did show significant predictive values of negative affect for paranoia. An important difference with previous studies was the sample size; Wigman et al. (2015) ($n = 263$) and Klippel et al. (2017) ($n = 245$) used larger groups, and thus had more statistical power. Alternatively, there could still be vicious circles of mental states activating each other but these may vary between patients, due to individual differences.

4.3. VR-CBT and the interplay between emotions

We did not find evidence that VR-CBT influences the extent to which paranoia-related mental states reinforce one another. Overall connectivity between mental states (inter node connectivity), showed 0% change in both groups. For emotional inertia – autocorrelations of mental states – we found indications of a possible treatment effect (trend effect $p = .08$). Mental states in daily life, once activated, may resolve or recover faster after VR-CBT than after TAU. This break of perpetuating affective and paranoid states may be an alternative pathway by which mental states regain healthy flexibility. The largest decrease in inertia was found for suspiciousness, changing from 0.19 to 0.03 after VR-CBT ($p = .17$). For TAU the relation remained similar ($b_{pre} = 0.17$; $b_{post} = 0.21$). Thus, after therapy moments of suspiciousness seemed to recovered quicker. This indicates that VR-CBT may have influenced the persistence of feeling paranoid.

There are several explanations for the lack of findings regarding the interplay between mental states. First, VR-CBT may simply not have influenced emotion dynamics. This shows that even though average levels of paranoia improved and autocorrelations reduced, the relation with other mental states remained unaffected. Possibly the lack of change is caused by remaining underlying vulnerability or residual symptoms. People experienced lower paranoia levels after VR-CBT, but levels were still elevated compared to a healthy population (Collip et al., 2011). Similar results were found for both a mindfulness-based cognitive therapy and imipramine treatment in patients with depression; average levels improved but there was a lack of therapy effect on emotion dynamics (Snippe et al., 2017). Alternatively, changes may have occurred in the relation between paranoia and other mental states, though not with the four specific mental states that were researched in this study.

Further, although there were limited changes on a group level, individual dynamics may have changed. Patients with psychosis are quite heterogeneous. Therefore treatment goals and the specific content of VR-CBT sessions had a personalized character. This may have resulted in different dynamics being affected in different individuals. Further, cascades of mental states triggering other states may be caused mainly by secondary appraisals. Emotions are primarily generated by the appraisal of a situation, e.g., the thought “they want to hurt me” evokes suspiciousness. The behavior that follows, e.g., avoidance, may evoke new thoughts (secondary appraisal) like “I am a weak”, and cause someone to feel down. These secondary appraisals are likely to show more interpersonal variation, and may cause one person to become anxious and others to feel down. The heterogeneity in patients was also reflected in the random slope effects which improved all statistical models. This raises important questions regarding the usefulness of emotion dynamic networks on a group level.

4.4. Limitations

There were several limitations. First, items were rated on 7-point Likert scales, which limits the amount of variation compared to continuous ESM scales or questionnaires that generally have more items. Second, when examining associations at the same moment in time (contemporaneous), negative mental states were more interconnected with paranoia. Possibly mental states interact more than we found in our analyses, but these associations may be more volatile than the +-90 minute interval between diary measurements in this study. Third, conservative permutation tests were used for network analyses and group sizes were limited, which limits statistical power. Fourth, there was a baseline difference between groups on the $\text{Anxious}_{t\text{-}1}$ - Lonely_t association for which we do not have an adequate explanation as no other baseline difference (e.g., in characteristics) were observed. Fifth, data were analysed under the assumption that data was missing at random, which could be violated. Data were not imputed as this would impact auto-correlations artificially, and auto-correlations were specifically of interest in this study. Finally, due to the explorative nature of this study we did not correct the p-value for multiple testing, which could have resulted in accepting a hypothesis unjustifiably.

4.5. Conclusion

VR-CBT strongly reduced paranoia in daily life. At 6-month follow-up people who participated in VR-CBT also reported to be less down and insecure. Treatment effects did not transfer to positive mood states. We did not find robust evidence that negative mental states trigger paranoia in the next moment above and beyond the self-maintaining effects of paranoia. Treatment did not change the extent to which mental states reinforce each other. Our findings do suggest that mental states in daily life, once activated, may recover more quickly after VR-CBT and regained flexibility. Thus, this research further supports the usefulness of VR as a tool for therapy as VR-CBT improved paranoid and negative mental states. Further, if future research confirms our new hypothesis that VR-CBT may cause faster recovery of mental states, this could provide insights in the working-mechanisms of CBT.

Please cite this article as: C.N.W. Geraets, E. Snippe, M. van Beilen, et al., Virtual reality based cognitive behavioral therapy for paranoia: Effects on mental states and the dy..., Schizophrenia Research, https://doi.org/10.1016/j.schres.2020.05.047

Future research could investigate differences in mental states networks between between high and low paranoid patients or treatment responders and non-responders in a larger sample. Investigating changes when VR-CBT is successful in responders would help understanding how the therapy works. Further, this will provide insights in the utility of a network approach on a group level. Moreover, when measuring mental states continuously during an intervention, one could investigate if autocorrelations drop before mean levels do. Finally, investigating dynamics within individuals increases understanding in person-specific effects and therapy working mechanisms.

Role of the funding source

Funders had no involvement in the study design; in the collection, analysis and interpretation of data; in the writing of the report; nor in the decision to submit the article for publication.

Declaration of competing interest

All authors declare that they have no conflicts of interest.

Acknowledgement

We are grateful to Anya Kuranova for assisting with network analysis. This work was supported by Fonds NutsOhra; Stichting tot Steun VCVGZ; the European Research Council (ERC) under the European Union's Horizon 2020 research and innovative programme ERC-CoG-2015 - 681466).

References

Bak, M., Drukker, M., Hasmi, L., van Os, J., 2016. An n=1 clinical network analysis of symptoms and treatment in psychosis. PLoS One 11, e0162811. https://doi.org/10.1371/journal.pone.0162811.

Bentall, R.P., Corcoran, R., Howard, R., Blackwood, N., Kinderman, P., 2001. Persecutory delusions: a review and theoretical integration. Clin. Psychol. Rev. 21, 1143–1192. https://doi.org/10.1016/S0272-7358(01)00106-4.

Bringmann, L.F., Vissers, N., Wichers, M., Geschwind, N., Kuppens, P., Peeters, F., Borsboom, D., Tuerlinckx, F., 2013. A network approach to psychopathology: new insights into clinical longitudinal data. PLoS One 8. https://doi.org/10.1371/journal.pone.0060188.

Cho, H., Gonzalez, R., Lavaysse, L.M., Pence, S., Fulford, D., Gard, D.E., 2017. Do people with schizophrenia experience more negative emotion and less positive emotion in their daily lives? A meta-analysis of experience sampling studies. Schizophr. Res. 183, 49–55. https://doi.org/10.1016/j.schres.2016.11.016.

Collip, D., Oorschot, M., Thewissen, V., Van Os, J., Bentall, R.P., Myin-Germeys, I., 2011. Social world interactions: how company connects to paranoia. Psychol. Med. 41, 911–921. https://doi.org/10.1017/S0033291710001558.

Cramer, A.O.J., Waldorp, L.J., van der Maas, H.L.J., Borsboom, D., 2010. Comorbidity: a network perspective. Behav. Brain Sci. 33, 137–150. https://doi.org/10.1017/S0140525X09991567.

Curran, P.J., Bauer, D.J., 2011. The disaggregation of within-person and between-person effects in longitudinal models of change. Annu. Rev. Psychol. 62, 583–619. https://doi.org/10.1146/annurev.psych.093008.100356.

Delespaul, P.A., Devries, M.W., 1987. The daily life of ambulatory chronic mental patients. J. Nerv. Ment. Dis. https://doi.org/10.1097/00005053-198709000-00005.

Epskamp, S., Cramer, A.O.J.J., L., W., Schmittman, V.D., Borsboom, D., Waldorp, L.J., Schmittmann, V.D., Borsboom, D., 2012. Qgraph: network visualizations of relationships in psychometric data. J. Stat. Softw. 48, 1–18. doi:10.18637/jss.v048.i04.

Epskamp, S., van Borkulo, C.D., van der Veen, D.C., Servaas, M.N., Isvoranu, A.M., Riese, H., Cramer, A.O.J., 2018. Personalized network modeling in psychopathology: the importance of contemporaneous and temporal connections. Clin. Psychol. Sci. 6, 416–427. https://doi.org/10.1177/2167702617744325.

Fowler, D., Hodgekins, J., Garety, P., Freeman, D., Kuipers, E., Dunn, G., Smith, B., Bebbington, P.E., 2012. Negative cognition, depressed mood, and paranoia: a longitudinal pathway analysis using structural equation modeling. Schizophr. Bull. 38, 1063–1073 doi:10.1093/schbul/sbr019.

Freeman, D., 2007. Suspicious minds: the psychology of persecutory delusions. Clin. Psychol. Rev. 27, 425–457. https://doi.org/10.1016/j.cpr.2006.10.004.

Freeman, D., Garety, P.A., Kuipers, E., Fowler, D., Bebbington, P.E., 2002. A cognitive model of persecutory delusions. Br. J. Clin. Psychol. 41, 331–347. https://doi.org/10.1348/014466502760387461.

Freeman, D., Emsley, R., Dunn, G., Fowler, D., Bebbington, P., Kuipers, E., Jolley, S., Waller, H., Hardy, A., Garety, P., 2015. The stress of the street for patients with persecutory delusions: a test of the symptomatic and psychological effects of going outside into a busy urban area. Schizophr. Bull. 41, 971–979. https://doi.org/10.1093/schbul/sbu173.

Garety, P.A., Freeman, D., 1999. Cognitive approaches to delusions: a critical review of theories and evidence. Br. J. Clin. Psychol. 38, 113–154. https://doi.org/10.1348/014466599162700.

Garety, P.A., Freeman, D., 2013. The past and future of delusions research: from the inexplicable to the treatable. Br. J. Psychiatry 203, 327–333. https://doi.org/10.1192/bjp.bp.113.126953.

Garety, P.A., Kuipers, E., Fowler, D., Freeman, D., Bebbington, P.E., 2001. A cognitive model of the positive symptoms of psychosis. Psychol. Med. 31, 189–195. https://doi.org/10.1017/S0033291701003312.

Green, C.E.L., Freeman, D., Kuipers, E., Bebbington, P.E., Fowler, D., Dunn, G., Garety, P.A., 2008. Measuring ideas of persecution and social reference: the Green et al. Paranoid Thought Scales (GPTS). Psychol. Med. 38, 101–111.

Houben, M., Van Den Noortgate, W., Kuppens, P., 2015. The relation between short-term emotion dynamics and psychological well-being: a meta-analysis. Psychol. Bull. 141, 901–930. https://doi.org/10.1037/a0038822.

Howes, O.D., Murray, R.M., 2014. Schizophrenia: an integrated sociodevelopmental-cognitive model. Lancet 383, 1677–1687. https://doi.org/10.1016/S0140-6736(13)62036-X.Schizophrenia.

Jääskeläinen, E., Juola, P., Hirvonen, N., McGrath, J.J., Saha, S., Isohanni, M., Veijola, J., Miettunen, J., 2013. A systematic review and meta-analysis of recovery in schizophrenia. Schizophr. Bull. 39, 1296–1306. https://doi.org/10.1093/schbul/sbs130.

Klippel, A., Viechtbauer, W., Reininghaus, U., Wigman, J., van Borkulo, C., Myin-Germeys, I., Wichers, M., 2017. The Cascade of stress: a network approach to explore differential dynamics in populations varying in risk for psychosis. Schizophr. Bull. 44, 328–337. https://doi.org/10.1093/schbul/sbx037.

Kuppens, P., Verduyn, P., 2017. Emotion dynamics. Curr. Opin. Psychol. 17, 22–26. https://doi.org/10.1016/j.copsyc.2017.06.004.

Myin-Germeys, I., Birchwood, M., Kwapil, T., 2011. From environment to therapy in psychosis: a real-world momentary assessment approach. Schizophr. Bull. 37, 244–247. https://doi.org/10.1093/schbul/sbq164.

Myin-Germeys, I., Kasanova, Z., Vaessen, T., Vachon, H., Kirtley, O., Viechtbauer, W., Reininghaus, U., 2018. Experience sampling methodology in mental health research: new insights and technical developments. World Psychiatry 17, 123–132. https://doi.org/10.1002/wps.20513.

Nelson, B., McGorry, P., Wichers, M., Wigman, J.T.W., Hartmann, J.A., 2017. Moving from static to dynamic models of the onset of mental disorder a review. JAMA Psychiatry 74, 528–534. https://doi.org/10.1001/jamapsychiatry.2017.0001.

Oorschot, M., Lataster, T., Thewissen, V., Lardinois, M., van Os, J., Delespaul, P.A., Myin-Germeys, I., 2012. Symptomatic remission in psychosis and real-life functioning. Br. J. Psychiatry 201, 215–220. https://doi.org/10.1192/bjp.bp.111.104414.

Pot-Kolder, R., Geraets, C.N.W., Veling, W., Staring, A.B.P., Gijsman, H.J., Delespaul, P.A., van der Gaag, M., 2018. Virtual-reality-based cognitive behavioural therapy versus waiting list control for paranoid ideation and social avoidance in patients with psychotic disorders: a single-blind randomised controlled trial. Lancet Psychiatry 5, 217–226. https://doi.org/10.1016/S2215-0366(18)30053-1.

Smith, B., Fowler, D.G., Freeman, D., Bebbington, P., Bashforth, H., Garety, P., Dunn, G., Kuipers, E., 2006. Emotion and psychosis: links between depression, self-esteem, negative schematic beliefs and delusions and hallucinations. Schizophr. Res. 86, 181–188. https://doi.org/10.1016/j.schres.2006.06.018.

Snippe, E., Viechtbauer, W., Geschwind, N., Klippel, A., de Jonge, P., Wichers, M., 2017. The impact of treatments for depression on the dynamic network structure of mental states: two randomized controlled trials. Sci. Rep. 7, 46523. https://doi.org/10.1038/srep46523.

Thewissen, V., Bentall, R.P., Oorschot, M., À Campo, J., Van Lierop, T., Van Os, J., Myin-Germeys, I., 2011. Emotions, self-esteem, and paranoid episodes: an experience sampling study. Br. J. Clin. Psychol. 50, 178–195. doi:https://doi.org/10.1348/014466510X508677.

Van Os, J., Lataster, T., Delespaul, P.A., Wichers, M., Myin-Germeys, I., 2014. Evidence that a psychopathology interactome has diagnostic value, predicting clinical needs: an experience sampling study. PLoS One 9. https://doi.org/10.1371/journal.pone.0086652.

Veling, W., Pot-Kolder, R., Counotte, J., van Os, J., van der Gaag, M., 2016. Environmental social stress, paranoia and psychosis liability: a virtual reality study. Schizophr. Bull. 1–9.

Wigman, J.T.W., Collip, D., Wichers, M., Delespaul, P., Derom, C., Thiery, E., Vollebergh, W.A.M., Lataster, T., Jacobs, N., Myin-Germeys, I., van Os, J., 2013. Altered transfer of momentary mental states (ATOMS) as the basic unit of psychosis liability in interaction with environment and emotions. PLoS One 8, e54653. https://doi.org/10.1371/journal.pone.0054653.

Wigman, J.T.W., van Os, J., Borsboom, D., Wardenaar, K.J., Epskamp, S., Klippel, A., Viechtbauer, W., Myin-Germeys, I., Wichers, M., 2015. Exploring the underlying structure of mental disorders: cross-diagnostic differences and similarities from a network perspective using both a top-down and a bottom-up approach. Psychol. Med. 45, 2375–2387. https://doi.org/10.1017/S0033291715000331.