

Environmental Social Stress, Paranoia and Psychosis Liability: A Virtual Reality Study

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The impact of social environments on mental states is difficult to assess, limiting the understanding of which aspects of the social environment contribute to the onset of psychotic symptoms and how individual characteristics moderate this outcome. This study aimed to test sensitivity to environmental social stress as a mechanism of psychosis using Virtual Reality (VR) experiments. Fifty-five patients with recent onset psychotic disorder, 20 patients at ultra high risk for psychosis, 42 siblings of patients with psychosis, and 53 controls walked 5 times in a virtual bar with different levels of environmental social stress. Virtual social stressors were population density, ethnic density and hostility. Paranoia about virtual humans and subjective distress in response to virtual social stress exposures were measured with State Social Paranoia Scale (SSPS) and self-rated momentary subjective distress (SUD), respectively. Pre-existing (subclinical) symptoms were assessed with the Community Assessment of Psychic Experiences (CAPE), Green Paranoid Thoughts Scale (GPTS) and the Social Interaction Anxiety Scale (SIAS). Paranoia and subjective distress increased with degree of social stress in the environment. Psychosis liability and pre-existing symptoms, in particular negative affect, positively impacted the level of paranoia and distress in response to social stress. These results provide experimental evidence that heightened sensitivity to environmental social stress may play an important role in the onset and course of psychosis.

Key words: psychosis/ultra high risk/stress/sensitization/virtual reality

Introduction

The social environment influences the risk of onset, as well as the course of psychotic disorders.¹ Urban birth,

childhood social adversity, neighborhood ethnic density, and social disorganization are risk factors for onset of psychosis.²⁻⁵ Social stress may mediate these associations, given that psychosocial stress is associated with both risk of onset and relapse of psychosis.^{6,7} Current theories of psychosis suggest that psychosis liability impacts individual sensitivity to experiences of social stress,⁸ in particular when the level of perceptual stimuli in the environment is high⁹ and when the stress involves negative judgment of others.¹⁰ Pre-existing (subclinical) paranoia, social anxiety, and negative affect may fuel this sensitivity, culminating in increasingly strong, sensitized psychotic responses to social stress exposure.^{8,11}

Experimental studies of patients with persecutory delusions found that paranoia increased when they entered a busy shopping street and that this effect was partly mediated by anxiety and depression.^{12,13} Experience sampling studies showed associations between the occurrence of minor stressors in daily life and intensity of psychotic experiences in patients and, to a lesser extent, their first-degree relatives and the general population.^{11,14,15} However, these approaches are not sufficient to investigate which aspects of the social environment contribute to the onset of psychotic symptoms and which individual characteristics moderate this outcome, as daily social environments are complex, never exactly the same, strongly influenced by the individual's behavior or presence of an observer, and cannot be controlled. Arguably the only way to test the mechanism of sensitized psychotic responses to the social environment, and the moderators thereof, would be to randomize individuals to controlled experimental environments with varying degree of social stress, quantifying environmental effect sizes as a function of liability to psychosis and prior level of (minor) symptoms. Virtual Reality (VR)

technology, ie, substituting sense data from the natural world with sense data about a virtual world that change in response to the user's actions, resulting in a "sense of presence" in an interactive 3-dimensional virtual world, offers the possibility to do so.^{13,16} VR is relatively new in psychosis research, but several studies have shown that VR is feasible, safe and valid for psychotic disorders.^{17,18} Recent studies found that paranoid response to a neutral virtual environment was higher in people at ultra high risk for psychosis (UHR) than in healthy controls, and that paranoid ideations were associated with social defeat¹⁹ and a history of bullying victimization.²⁰

In this study, we aimed to test social stress sensitivity as a mechanism of psychosis, by exposing individuals with different levels of liability to psychosis to 5 social stress environments in VR. We hypothesized that:

1. Paranoia and subjective distress increase with degree of environmental social stress;
2. Liability to psychosis, and (subclinical) psychotic and affective symptoms are associated with more paranoia and subjective distress in social environments; and
3. Degree of environmental social stress interacts with psychosis liability and pre-existing symptoms on paranoia and subjective distress.

Methods

Participants

Individuals aged 18–35 years with different levels of liability to psychosis were included. We defined a high-liability group based on phenotype, ie, the experience of (subclinical) psychotic symptoms. This group had 2 categories: (1) Patients with psychotic disorder, whose first diagnosis of psychotic disorder was established within the last 5 years. DSM-IV diagnosis was established with a semi-structured interview (SCAN; Schedules for Clinical Assessment in Neuropsychiatry²¹ or CASH; Comprehensive Assessment of Symptoms and History²²). All psychotic disorders

were included, except for substance-induced psychotic disorder and psychotic disorder due to a medical condition; and (2) Patients at UHR for psychosis, according to the Comprehensive Assessment of At-Risk Mental States (CAARMS) criteria.²³ The low psychosis liability group consisted of: (3) Siblings of patients with a psychotic disorder, who never had a psychotic episode themselves; and (4) Controls with a negative (first-degree family) history of any psychotic disorder. Exclusion criteria were a history of epilepsy, IQ lower than 75 and poor command of the Dutch language. Psychosis, UHR and sibling groups were recruited from 5 psychiatric institutes in the Netherlands. Controls were recruited with flyers at schools for vocational or higher education and in dentist offices in The Hague, and among the staff of a psychiatric institute in The Hague. Written informed consent was obtained from all participants. The study was approved by the medical ethical committee of Leiden University Medical Center.

VR Set-up

The virtual environment was a bar with an indoor and an outdoor part (figure 1), built by CleVR with Vizard software.²⁴ Participants were standing during experiments and could turn around 360 degrees. In order to walk around in the virtual environment, they used a Logitech F310 Gamepad. They wore a Sony HMZ-T1 Head Mounted Display with a HD resolution of 1280 × 720 per eye, with 51.6 diagonal field of view, a 3DOF tracker for head rotation, and built in headphones. Virtual humans (avatars) were sitting or standing at a table, chatted and had drinks. Bar background noises were played during the experiments.

Virtual Social Stressors

We created 3 sources of social stress in the virtual environment.



Fig. 1. Screenshot of the virtual bar environment. Source: CleVR.

1. Population density: the number of avatars in the bar was variable, by which we could simulate population density and could manipulate level of perceptual stimuli. In the quiet, low stress condition, the number of avatars in the bar was 6. In the stressful, crowded situation, the number was 40.
2. Ethnic density: ethnic appearance of an avatar was Dutch or North African. In the low ethnic density condition, more than 80% of the avatars was Dutch for non-Dutch participants and North African for Dutch participants. In the high ethnic density condition, the ethnic distribution was the opposite.
3. Hostility: in the low-stress condition, avatars had a neutral facial expression. When participants approached, avatars looked only briefly at them, after which they resumed their activities. In the stressful condition, avatars looked in an angry, hostile fashion at participants for 5 seconds, as participants approached, and also at other, random, moments.

Experiments

All participants underwent 5 experiments of 4 minutes each, in a single session. In all experiments, they were instructed to explore the bar. Five avatars had a number (0–99) on their clothing. In order to engage participants in the experiment and to make them look at all avatars, they had to find these avatars, and to report the highest number and gender of the avatar with the highest number.

Virtual social stress was introduced at 4 levels:

1. No stress—quiet, high ethnic density and neutral avatars;
2. One stressor—crowded;
3. Two stressors—(1) crowded and low ethnic density, (2) crowded and hostile avatars;
4. Three stressors—crowded, low ethnic density and hostile avatars.

High population density was part of all stress conditions, because ethnic density and hostility could only be simulated effectively with a high number of avatars. The order of the experiments was random, except that the fifth experiment always had at least 2 stressors.

Measures

Baseline. Sociodemographic characteristics included age and sex. Ethnicity was defined as Dutch if the subject and both parents were born in the Netherlands, and as non-Dutch in all other cases. Level of education was classified as no/ primary education, vocational education ((V)MBO), higher secondary education (HAVO/VWO), higher tertiary education (HBO/University). Paranoia was assessed with the Green Paranoid Thoughts Scale (GPTS),²⁵ social anxiety with the Social Interaction Anxiety Scale (SIAS)²⁶ and minor positive, negative and

depressive symptoms with the Community Assessment of Psychic Experiences (CAPE).²⁷

During and After Experiments. In order to assess how actively participants explored the virtual bar during the experiments, their position in the bar was recorded every second, and the distance between current and all other recorded positions was calculated. The average of these distance scores is an indication of distance covered during the experiments; the SD reflects the degree to which participants were at different positions in the bar.

After each experiment, participants were asked to rate their maximum momentary subjective distress during the experiment (SUD) in units on an analogue scale, with range 0 (no distress at all) to 100 (worst possible distress). Paranoid thoughts about avatars were measured after each experiment with the State Social Paranoia Scale (SSPS).²⁸

Statistical Analyses

All analyses were conducted with Stata version 11. Differences in sociodemographic characteristics and exploration behavior in the virtual bar between psychosis liability groups were tested with Chi square tests (categorical variables) and ANOVA (continuous variables). For the analyses of the effects of virtual social stressors on paranoia and subjective distress, multilevel random intercept regression models were used, taking into account the repeated measure structure of the data. The *B* is the fixed regression coefficient of the predictor in the multilevel model. We analyzed the data using the multilevel random intercept XTREG procedure in Stata. First, effects of social stressors were investigated. For each subject, SSPS and SUD scores of experiments 3a and 3b (see *Experiments*) were summed together and divided by 2, in order to create average paranoia and distress scores for experiments with 2 stressors. Regression models were fitted with paranoia and peak subjective distress during experiments as dependent variables, number of stressors as independent variable and age, sex, level of education and psychosis liability as covariates. To estimate effect sizes of the separate stressors, Stata LINCOM procedure was used. Thus, the effect of population density was calculated by comparing stress level 2 with level 1, the ethnic density effect by comparing level 3a with level 2, and the effect of hostility by comparing level 3b with level 2. Second, differences in paranoia and subjective distress in VR between psychosis liability groups were examined. Third, associations between baseline symptoms and paranoia and distress in VR were explored, irrespective of psychosis liability group. Symptom domains were analyzed separately, but also entered simultaneously in a regression model, to test which baseline symptoms contributed most to paranoia and distress in VR. Fourth, interaction terms between social stress on the one hand, and psychosis liability and baseline symptoms on the

other were added to the models. *B* coefficients of the main effects and the interaction terms were compared using the MARGINS dydx procedure, estimating linear marginal effects at the different virtual social stress levels.

Results

Fifty-three healthy controls, 42 siblings, 20 patients at UHR for psychosis, and 55 patients with psychotic disorder were included. Sociodemographic characteristics, baseline level of symptoms and use of psychotropic medication are shown in table 1. The UHR and psychosis groups had significantly higher levels of all symptoms than controls, and psychosis patients had a lower level of education. The proportion of males was much higher in the psychosis group than in the other groups.

ANOVA showed a difference between the psychosis liability groups in distance covered by participants during the experiments ($F = 2.864, df = 3, P = .039$). No statistically significant differences remained in post hoc Bonferroni corrected group comparisons (supplementary table 1). There was only a trend level significance of lower distance covered by the psychosis group compared to controls (mean difference 0.28, 95% CI, $-0.01-0.57, P = .063$). SD scores, indicating variation in positions, did not differ between groups.

Virtual social stress elicited paranoid thoughts and subjective distress in participants. Table 2 shows that both

measures increased with increasing numbers of virtual stressors. The *B* of the linear effect of number of social stressors on paranoia, adjusted for age, sex, level of education and psychosis liability, was 2.74 (95% CI: 2.31–3.17, $P < .0005$). The adjusted *B* of the linear effect of social stressors on subjective distress was 2.26 (95% CI, 1.52–3.00, $P < .0005$). Of the specific virtual stressors, population density (linear combination of experiment 2 compared to 1) had a strong positive effect on both paranoia and distress (table 3). Hostility (linear combination of experiment 3b compared to 2) was significantly and positively associated with paranoia, but not with subjective distress. Ethnic density (linear combination of experiment 3a compared to 2) was associated with neither paranoia nor distress.

Compared to subjects with low psychosis liability, those with high liability reported more paranoia and subjective distress in VR (table 3), *B* 3.62 (95% CI, 1.39–5.84) and 17.94 (10.99–24.90), respectively. Of the separate liability groups, only UHR patients had significantly higher paranoia than healthy controls; the UHR and psychosis groups had higher levels of distress (figure 2).

Baseline levels of paranoid thoughts, social anxiety, (minor) positive, negative and depressive symptoms were all strongly associated with both paranoia and subjective distress in VR, with *B*'s ranging from 0.13 to 2.68 (supplementary table 2). When all baseline symptom domains were entered simultaneously in the regression

Table 1. Characteristics of Study Sample

	Controls (<i>N</i> = 53)	Siblings (<i>N</i> = 42)	UHR (<i>N</i> = 20)	Psychosis (<i>N</i> = 55)
Sociodemographic				
Age	24.6 (4.4)	26.4 (4.8)	24.0 (4.5)	26.0 (4.7)
Male sex, <i>N</i> (%)	25 (47.2)	23 (54.8)	7 (35.0)	42 (76.4) ^a
Non-Dutch origin, <i>N</i> (%)	16 (30.2)	11 (26.2)	5 (25.0)	26 (47.3)
Level of education, <i>N</i> (%)				
No/primary	0 (0.0)	0 (0.0)	0 (0.0)	3 (5.5) ^a
Vocational ((V)MBO)	13 (24.5)	11 (26.2)	8 (40.0)	25 (45.5) ^a
Higher secondary (HAVO/VWO)	10 (18.9)	4 (9.5)	5 (25.0)	10 (18.2) ^a
Higher tertiary (HBO/University)	30 (56.6)	26 (61.9)	7 (35.0)	17 (30.9) ^a
Symptoms^b				
Paranoid thoughts	37.5 (9.1)	36.1 (6.1)	69.0 (26.6) ^a	56.2 (30.6) ^a
Social anxiety	16.8 (11.6)	15.6 (10.4)	38.6 (19.7) ^a	28.3 (16.1) ^a
Depressive symptoms	12.5 (2.8)	12.3 (2.2)	20.4 (4.7) ^a	14.8 (3.4) ^a
Positive symptoms	24.3 (4.6)	23.6 (3.1)	31.7 (7.5) ^a	31.2 (8.8) ^a
Negative symptoms	21.5 (4.6)	21.2 (3.7)	32.4 (7.9) ^a	27.1 (6.3) ^a
Use of psychotropic medication, <i>N</i> (%)^c				
None	49 (94.2)	39 (92.9)	6 (30.0)	18 (32.7)
Antipsychotic	0 (0.0)	0 (0.0)	0 (0.0)	35 (63.6)
Antidepressant	1 (1.9)	1 (2.4)	12 (60.0)	5 (9.1)
Benzodiazepine	0 (0.0)	0 (0.0)	4 (20.0)	6 (10.9)
Other	2 (3.8)	2 (4.8)	5 (25.0)	2 (3.6)

Note: UHR, Ultra High Risk.

^a $P < .05$, ANOVA or Chi-square test with post hoc comparisons, controls as comparison group.

^bParanoid thoughts assessed with Green Paranoid Thoughts Scale, Social Anxiety with Social Interaction Anxiety Scale, other symptoms with Community Assessment of Psychic Experiences.

^cSelf-report.

Table 2. Paranoid Thoughts and Subjective Distress in Virtual Reality, by Degree and Type of Virtual Social Stress

Virtual Social Stress Condition	Mean (SD)	<i>B</i> ^a	95% CI	<i>P</i> -value
Paranoia				
Number of stressors				
No stress	13.60 (6.2)	—	—	—
1 stressor	16.25 (8.1)	2.66	1.35–3.96	<.0005
2 stressors	16.78 (9.3)	3.17	1.85–4.49	<.0005
3 stressors	22.51 (11.4)	9.14	7.82–10.45	<.0005
Population density	—	2.65	1.31–3.99	<.0005
Ethnic density	—	0.55	–0.81–1.91	.426
Hostility	—	6.01	4.66–7.36	<.0005
Subjective distress				
Number of stressors				
No stress	26.96 (24.4)	—	—	—
1 stressor	32.81 (26.3)	5.41	3.11–7.71	<.0005
2 stressors	31.68 (25.0)	5.13	2.84–7.42	<.0005
3 stressors	34.48 (27.6)	7.60	5.30–9.90	<.0005
Population density	—	5.38	3.01–7.74	<.0005
Ethnic density	—	–1.35	–3.75–1.04	.269
Hostility	—	0.50	–1.87–2.89	.678

Note: ^aMultilevel random regression analysis regression coefficient *B*, adjusted for age, sex, ethnicity, level of education and psychosis liability; compared to the no stress condition. *B* coefficients of separate stressors calculated by comparisons of the linear effects of 2 conditions (see text).

Table 3. Paranoid Thoughts and Subjective Distress in Virtual Reality, by Psychosis Liability Group

Psychosis Liability Group	Paranoia			Subjective Distress		
	<i>B</i> ^a	95% CI	<i>P</i> -value	<i>B</i> ^a	95% CI	<i>P</i> -value
Low ^b	—	—	—	—	—	—
High	3.62	1.39–5.84	.001	17.94	10.99–24.90	<.0005
Controls	—	—	—	—	—	—
Siblings	–1.86	–4.72–1.00	.203	–4.09	–13.02–4.83	.369
UHR	3.80	0.24–7.37	.037	17.90	6.68–29.13	.002
Psychosis	2.36	–0.43–5.16	.097	15.37	6.60–24.14	.001

Note: ^aMultilevel random regression analysis regression coefficient *B*, adjusted for age, sex, ethnicity, level of education and virtual experiment. Low liability and controls as reference groups.

^bHealthy controls and siblings classified as low psychosis liability, UHR and psychosis as high liability.

model, adjusted for age, sex, ethnicity, level of education and virtual experiment, paranoia in VR was predicted significantly only by depressive symptoms (*B* 0.60, 95% CI, 0.18–1.02, *P* = .005); subjective distress was associated only with social anxiety (*B* 0.39, 95% CI, 0.11–0.68, *P* = .007).

The effects of baseline symptoms on paranoia and subjective distress increased with level of virtual social stress. Adjusted interaction terms between social stress on the one hand and paranoid thoughts, social anxiety, positive, depressive and negative symptoms on the other, were all statistically significant, except for the interaction between social stress and paranoid thoughts on subjective distress (*P* = .057). Table 4 shows how *B* coefficients of the linear marginal effects of symptoms increased at the different levels of social stress exposure. Strongest interaction effects were found with depressive symptoms. There was

no significant interaction between social stress exposure and psychosis liability group, except for a stronger increase in paranoia with increasing social stress for the UHR group compared to controls (*B* interaction term 1.59, 95% CI 0.15–3.02, *P* = .03; *B*'s of marginal effects UHR group compared to controls 1.56 [–2.57–5.69], 3.14 [–0.49–6.77], 4.73 [1.07–8.39] and 6.32 [2.10–10.53] for 0–3 social stressors, respectively).

Discussion

This VR study provides experimental evidence of social stress sensitivity as a mechanism linking environment and psychosis. Paranoia and subjective distress increased with degree of social stress in the environment. High psychosis liability, pre-existing (minor) affective and, to a lesser degree, psychotic symptoms

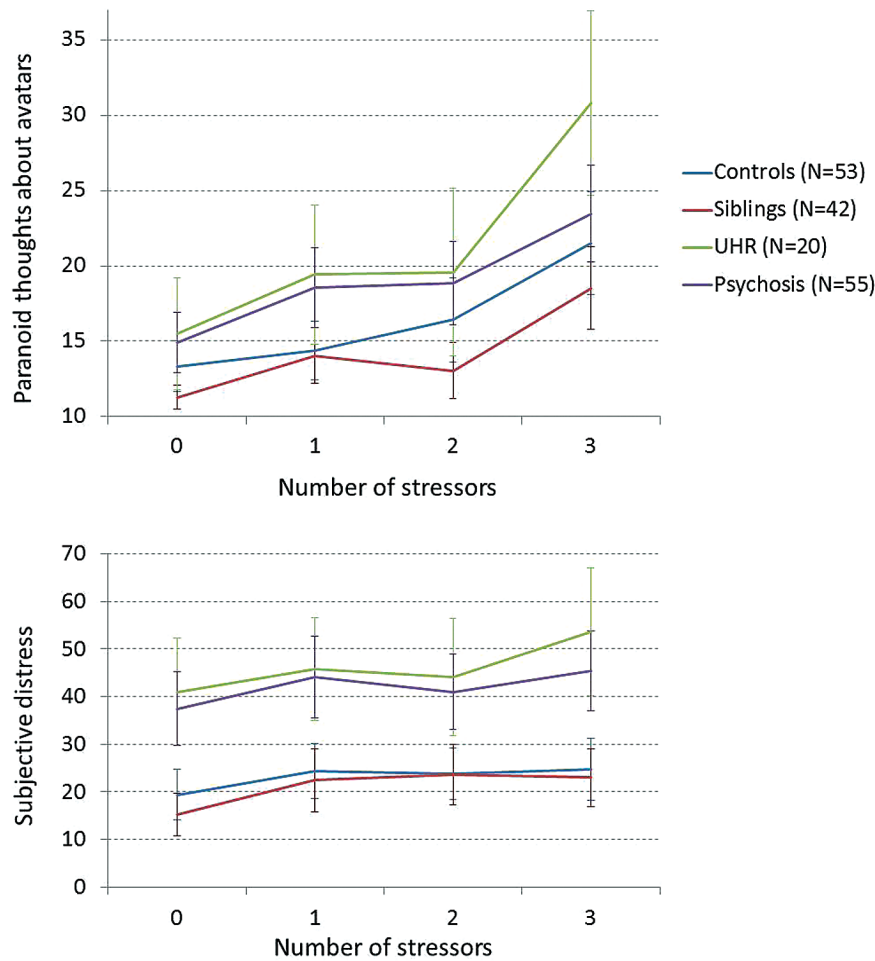


Fig. 2. Paranoia and subjective distress in Virtual Reality (VR), by degree of virtual social stress and psychosis liability.

Table 4. Effects of Baseline Symptoms on Paranoid and Stress Response, at Different Levels of Virtual Social Stress Exposure

	Paranoid Thoughts		Social Anxiety		Depressive Symptoms		Positive Symptoms		Negative Symptoms	
	<i>B</i> ^a	95% CI	<i>B</i>	95% CI	<i>B</i>	95% CI	<i>B</i>	95% CI	<i>B</i>	95% CI
Paranoia										
No stress	0.08	0.03–0.13	0.09	0.01–0.17	0.47	0.17–0.78	0.29	0.12–0.46	0.20	0.01–0.38
1 stressor	0.11	0.07–0.16	0.13	0.06–0.20	0.70	0.43–0.97	0.38	0.23–0.53	0.30	0.13–0.46
2 stressors	0.15	0.10–0.19	0.18	0.10–0.25	0.93	0.66–1.20	0.47	0.32–0.62	0.39	0.23–0.56
3 stressors	0.18	0.13–0.24	0.22	0.14–0.30	1.16	0.85–1.47	0.56	0.38–0.73	0.49	0.31–0.68
Subjective distress										
No stress	0.42	0.27–0.57	0.62	0.39–0.85	2.13	1.22–3.03	1.19	0.69–1.68	1.17	0.64–1.71
1 stressor	0.45	0.30–0.59	0.68	0.46–0.89	2.49	1.62–3.36	1.34	0.86–1.82	1.30	0.79–1.81
2 stressors	0.48	0.33–0.62	0.73	0.51–0.95	2.86	1.99–3.73	1.49	1.02–1.97	1.42	0.91–1.93
3 stressors	0.51	0.35–0.66	0.79	0.56–1.02	3.22	2.32–4.13	1.65	1.15–2.15	1.54	1.01–2.08

Note: ^aMultilevel random regression analysis, *B* coefficients, adjusted for age, sex, ethnicity and level of education, estimated using Stata margins dydx procedure, at the 4 levels of virtual social stress. All coefficients statistically significant (*P* < .05).

were associated with more paranoia and distress in social environments. Pre-existing symptoms had stronger impact on paranoia and distress when level of environmental social stress increased.

Strengths and Limitations

The main strength of this study is the experimental design, using VR as a tool to study interactions between the individual and complex social environments.

Environmental studies of psychosis are generally complicated by subjective retrospective information about social environment and events. Momentary assessment studies are closer to the action, but cannot control occurrence of events and remain dependent on subjective information about the environment. This study was the first to expose individuals experimentally to controlled complex social environments with different degrees of social stressors. Environmental social stress exposures were identical for all participants, except for the ethnic appearance of avatars, which depended on the ethnicity of the participant. Type and degree of environmental stress were controlled. It should be noted that participants could avoid exposure to a certain degree, as they navigated through the environments themselves and were free to choose where to look. To minimize variation in exposure, participants had a simple task that required extensive exploration of the VR environment and the avatars. Recording data of the position of participants in the virtual bar during experiments suggest that distance and area covered did not differ substantially between psychosis liability groups.

The study had several limitations. The virtual environment was simulated, not photo-realistic and evidently still less complex than real life, which may reduce ecological validity. Previous studies, however, using similar VR software and environments, showed that experiences in these environments were correlated to real life experiences and symptoms, that participants reported all kinds of thoughts and feelings about avatars, and that virtual environments are sufficiently realistic to practice social behavior.^{18,29,30}

As there was no experiment with non-social stressors (eg, noise), it cannot be ruled out that the amount of stimuli in VR was more important than the social nature of the stressors. The additional effect of avatars' hostile looks compared to a similar environment with neutral avatars, however, suggests that the social aspect of stressors does matter.

While the psychosis group had significantly higher paranoid thoughts and other symptoms than controls and siblings, their level of symptoms was lower than that of the UHR group, suggesting that many had already partially recovered. The majority of the psychosis group and nobody in the UHR group reported using antipsychotic medication, which may have contributed to the higher symptom level in the UHR group, and may have led to underestimation of the psychosis liability effect on paranoia and distress in VR. Another limitation is that the number of participants in the separate groups was relatively small, in particular in the UHR group, implicating that the analyses of separate group should be interpreted with caution.

Environmental Social Stress and Psychosis

Current theories of psychosis state that environmental social stress contributes to the onset of psychosis by a process of sensitization, in interaction with liability to psychosis and subclinical symptoms.^{1,8,31} This liability can be caused by genetic factors, or by perinatal or childhood

environmental insults. Subsequent experiences of social stress may lead to an increasingly dysregulated dopamine system, as a result of which aberrant salience is assigned to environmental stimuli. Negative affect, dysfunctional cognitive schemas and more stress will build up.³² This vicious circle of sensitization and dopamine dysregulation eventually may lead to a psychotic state of delusions, hallucinations and negative symptoms.⁸ Our study supports these theories in several ways.

First, environmental social stress elicited paranoia and subjective distress in a dose-response fashion. More VR stressors resulted in greater levels of paranoia and distress. Not all separate stressors, however, had the same impact. Population density and hostility were significantly associated with paranoia, and only population density with subjective distress. Ethnic density was related to neither outcome measure, possibly because the majority of the participants was Dutch (66%) and ethnic density effects have primarily been described among ethnic minorities.³³ In addition, our non-Dutch avatars had a North African appearance, whereas most non-Dutch participants had an ethnic background other than North African.

Second, paranoia and distress in VR were stronger in those with higher psychometric psychosis liability, phenotypically defined as having (subclinical) psychotic symptoms. Genetic risk for psychosis was not associated with paranoia and stress, as siblings had similar responses as controls. UHR patients had the strongest response to social stress exposure. Use of antipsychotic medication might explain the dampening of psychotic symptoms and distress in the FEP patients compared to the UHR group.

Third, minor negative, psychotic and in particular depressive symptoms predicted paranoia and distress in VR. Negative affective state was an important driver of the psychotic and stress response to social stress exposure. This is consistent with cognitive models of paranoia³² in which negative affect is a core component in the development of paranoid delusions. An "affective route" to psychosis has been proposed, in which daily social stressors negatively influence affect, and disturbed affect in turn worsens biased appraisal of events and dysfunctional externalizing cognitions, eventually leading to paranoid delusions and other psychotic experiences.¹¹ Experience sampling studies also show that momentary negative affect predicts momentary paranoia in daily life.¹¹

Clinical Implications

We have demonstrated that it is possible to expose patients with psychosis and UHR patients to complex virtual social environments, and that exposure to these environments leads to meaningful responses, which are associated with clinical symptom profile. Exposure therapy for paranoia can be envisioned, with gradual, controlled exposure to increasingly stressful and paranoia-inducing social situations simulated in VR. Our group is currently

developing and testing such a VR exposure treatment. Several other pilot VR treatment studies have recently been published,¹⁷ it can be expected that more applications will be developed over the next few years.

The results of this study suggest that reactivity to daily social stress may be an important target for treatment in patients with high levels of psychosis liability. Reactivity may be modified by focusing on negative affect, biased appraisals and dysfunctional cognitive schemas in cognitive behavioral therapy, or by stress reduction techniques such as relaxation or meditation.^{34,35} Preliminary VR stress management studies were published recently, suggesting that this may represent a promising approach for reducing stress reactivity.^{36,37}

Supplementary Material

Supplementary material is available at <http://schizophreniabulletin.oxfordjournals.org>.

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