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Application of 360° virtual reality videos in the assessment of paranoia in schizophrenia patients: a pilot study

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Summary

Aim. Virtual Reality (VR) has been widely used in psychiatry, including psychotic disorders. The main advantage of VR is its high ecological validity and controllability of the virtual environment. Our main goal was to test whether, similarly to computer-generated VR, 360-degree videos are able to elicit a state of social paranoia in prone individuals.

Method. Sixteen schizophrenia patients and twenty-three healthy individuals were assessed using Leibowitz Social Anxiety Scale and additionally, in the patient group, the Positive and Negative Syndrome Scale (PANSS–6) and Peters Delusional Inventory (PDI) were used. The participants viewed four 360-degree videos with and without social content on a VR headset. Meanwhile, subjects' heart rate was measured continuously. After the exposure, both groups were assessed with Social State Paranoia Scale (SSPS) and asked about momentary anxiety and sense of presence.

Results. The schizophrenia patients reported higher momentary anxiety, although the results of SSPS did not differ significantly between groups. In the control group the heart rate decreased between first non-social and social video, whereas in the patient group it did not differ significantly. There was a significant correlation of paranoid ideation experienced on daily basis (PDI) and elicited in VR (SSPS) in the patient group.

Conclusions. In conclusion, paranoid responses can be triggered in patients with schizophrenia by 360-degree videos.

Key words: virtual reality, schizophrenia, paranoia

Introduction

Virtual reality (VR) is a technology that has begun to be used intensively in the field of psychiatry for at least two decades. Unlike classical media, in VR the gap between the real experience and the simulation of that experience becomes much smaller. This is expressed by a strong sense of presence, which is the feeling of "being inside" the virtual environment. This makes the sensations experienced in VR authentic and real enough to trigger lasting changes in people, much like real world experiences [1].

Virtual reality is being increasingly applied in the field of mental health. So far, there have already been several hundred publications on the use of this technology in the development of theoretical concepts, diagnosis, and treatment of mental illness. Current attempts are also being made to use VR when working with patients suffering from psychotic disorders. So far, dozens of studies [2] have been conducted where the participants were people with psychosis, usually with a diagnosis of schizophrenia. Most publications have focused on exploring the mechanisms involved in psychosis, particularly paranoia, with fewer focused on diagnosis and treatment. Despite concerns that people with psychosis may be reluctant to use virtual reality, as a large proportion of them may hold delusional beliefs towards new, unfamiliar technologies, mainly for fear of being spied on, the findings to date do not support this notion. The vast majority of patients perceive VR positively, and after exposure to the virtual environment (VE) they do not experience undue distress [3–5]. Based on the results of one systematic review [6], psychotic patients did not exhibit distress related to VR-based research procedures and did not experience an increase in psychotic symptoms after VR exposure. Only in one study [7] did a participant drop out due to an increase in psychotic symptoms during the exposure, which may have been related to the relatively stressful procedure – the impact of social stress in VR was investigated.

Numerous publications on the topic of mechanisms of paranoia [8, 9] highlight two advantages associated with the use of virtual reality. One is full control over the presented environment, the other is the ability to elicit realistic responses, including physiological reactions of the body to stimuli in the virtual world. Until recently, one of the obstacles to the proliferation of VR in psychiatry was the costs associated with it. For several years now, due to the booming market of commercial goggles, hardware costs have ceased to be an obstacle, but the software costs associated with developing the corresponding applications are still relatively high. Therefore, alternatives to the computer-generated environments are being sought. One of such methods is to use pre-recorded 360-degree videos. Unlike computer-generated environments, specialized technological skills are not required in this case to create and operate such an environment [10]. When playing such a video on goggles, the viewer is able to look around in all directions and is completely surrounded by the video. Compared to computer-generated environments, 360-degree films have one significant disadvantage – they are completely non-interactive, meaning that the user's behavior does not affect the VE content in any way. It has been repeatedly demonstrated that even non-interactive

VEs can have a similar impact on the viewer as the real world. For example, 360° videos depicting natural scenery, such as a forest or a beach, have a positive effect on viewers' affect and reduce stress levels, which is sometimes also reflected in objective indicators of physiological state, such as galvanic skin response [11, 12].

In recent years, there has been an emergence of first publications from studies using VR in the form of 360-degree videos – used to assess cognitive function, especially memory [13, 14], as well as to assess the severity of social anxiety [15, 16]. On the other hand, it is relatively common to use VR in the form of 360° videos in relaxation training, including, among others, mindfulness [17–19]. Just before our paper was completed, the first study using 360° immersive videos to assess paranoia in a non-clinical population was published [20]. The study used 3 social VEs, that is, an elevator, a library, and a bar. One hundred and fifty subjects were screened for trait paranoia, immersed into one of the three VEs, and then assessed with state paranoia, sense of presence and cybersickness scales. Overall, there are relatively few studies in the field of psychiatry using this VR technology. The current pilot study focuses on the effects of different environments presented in 360° technology on subjective anxiety and paranoid thinking in schizophrenia patients and healthy individuals. The study is exploratory in nature, with the additional goal of verifying previous results of individuals exhibiting paranoid thinking to neutral virtual social environments. If similar results are obtained as in the studies using computer-generated environments, it would be possible in the long term to use this technology to assess and treat persecutory delusions in psychotic patients at an expense many times lower than that of computer-generated environments.

Materials

Thirty-nine subjects, including 16 schizophrenia patients with a diagnosis confirmed by an experienced clinician, based on ICD-10 criteria, and 23 healthy subjects participated in this study. Patients were recruited from inpatient day centers managed by the Association for the Development of Community Psychiatry and Care in Krakow, i.e., Community Self-Help House and Occupational Therapy Workshops, or from the Medilinorm outpatient clinic in Krakow. The control group was recruited from the Telemedicine and Medical Informatics Student Research Group of the Jagiellonian University. The exclusion criteria for participation in the study were: diagnosed epilepsy, active addiction, personality disorders and CNS damage. Subjects using vision correction tools were eligible for the study – the necessary visual acuity correction was entered on the device for each individual.

Methods

The study was conducted after approval of the Bioethics Committee of the Jagiellonian University (no. 1072.6120.269.2019). The study used standard Samsung Gear

VR virtual reality goggles, paired with a Samsung Galaxy S7 smartphone. Along with the goggles, the subjects wore a Jazz-novo oculometer (Ober Consulting Poland). In our study, the oculometer was used to measure heart rate (HR). 360-degree videos were recorded by the research team in the city of Krakow in several locations – a city park, the Main Square, and in the elevator of a residential building. Each film lasted between 1.5–3 minutes. A Samsung Gear 360 camera was used to record the videos in 4K 30 fps.

The Positive and Negative Syndrome Scale (PANSS-6), a shortened 6-item version, was used to assess the severity of positive and negative symptoms of schizophrenia [21]. The Leibowitz Social Anxiety Scale (LSAS) was used to assess the severity of social anxiety [22]. The Peters et al. Delusions Inventory (PDI) was used to measure the severity of psychotic-like experiences [23]. A persecutory subscale consisting of items 11-15 was extracted in the study. Social paranoia status was measured using the State Social Paranoia Scale (SSPS) [24]. Ten of the 20 items of this scale assess paranoid thinking in social situations, and the sum of their scores forms the persecutory subscale. In our study, we used only the results of the persecutory subscale. Due to the lack of a Polish language version, the scale was translated by the authors into Polish. Momentary sense of presence and momentary anxiety were measured using 1-item scales developed by the researchers. After exposure to VR, participants answered several questions about mood and their own feelings.

At baseline, subjects completed clinical questionnaires and scales. Additionally, in the patient group, every participant was examined by a psychiatrist with the PANSS-6 scale. The participant then put on a Jazz-novo oculometer, followed by Samsung Gear VR goggles and watched the first series of 360° videos, consisting of a non-social film 1 (urban green area) and a social film 1 (Krakow market square), both lasting about 5 minutes. After the exposure, the subject completed the momentary anxiety and sense of presence scales, and the SSPS scale. Subsequently, the subject put on the goggles again and watched the second series of videos, consisting of non-social film 2 (empty elevator) and social film 2 (elevator with passengers), each about 3 minutes, after which the subject once again completed the aforementioned questionnaires and surveys. During presentation of the film packages, the subjects were in a standing position.

For quantitative variables, normal distribution was tested using the Shapiro-Wilk test. For variables meeting the normal distribution criterion, intergroup comparisons were performed with use of the Student's T-test for independent groups, and for variables not meeting this criterion, with the Mann-Whitney U test. Intergroup comparisons of nominal variables were performed using the chi-square test. Because of small group sizes, occasional outliers and, in the case of single-item tools, many variables having the same value (tied ranks), the non-parametric Kendall rank test was used in the correlation analysis. Analyses of heart rate between and within both groups were performed using a mixed 2-factor ANOVA. The homogeneity of variances and covariances was assessed by Levene's and Box's M test, respectively. A significance level of alpha=0.05 was assumed in all analyses. Calculations were performed using IBM SPSS 26 software.

Results

The study groups differed significantly in sex and age – the patient group as opposed to the control group had a higher percentage of males (62.5% vs. 26.09%, p=0.023) and a higher mean age of the subjects (36.00 vs. 19.22, p<0.001) (Table 1). The groups differed in Leibowitz Social Anxiety Scale and momentary anxiety at measurement 1 and measurement 2 – higher values of both scales were observed in the patient group. Additionally, the percentage of participants manifesting symptoms of social phobia (LSAS>55) was significantly higher in the patient group. In terms of other tools, the groups did not differ significantly (Table 2). The patient group had similar levels of positive and negative symptoms, with both domains of mild severity (<9 points on each subscale). An attempt was made to determine the possible influence sex and age on the results. Because the assumptions of the test were not met, it was not possible to perform an analysis of covariance. To determine the effect of differences in the sex ratio between the two groups, a comparison of the variables from Table 2 was performed between the males and females separately for patients and for controls. The only significant difference was the SSPS score in the second series of videos in the control group – in males the SSPS2 value was significantly higher than in females (p=0.030). For age, correlations were made with the variables from Table 2 in the patient and control groups. In the patient group, none of the variables correlated with age, while in the control group we detected a positive correlation of age with SSPS1 (tau-b=0.400, p=0.041) and a negative correlation of age with momentary anxiety 1 and 2 (tau-b=-0,442, p=0.022; tau-b=-0.429, p=0.021).

Table 1. **Comparison of characteristics in both groups**

	Patient group (n = 16) Mean (SD)	Control group (n = 23) Mean (SD)	p-level
Sex	Females: 6 (37.50%) Males: 10 (62.50%)	Females: 17 (73.91%) Males: 6 (26.09%)	p=0.023[b]
Age	36.00 (9.06)	19.22 (0.736)	p<0.001 [a]
Illness duration (years)	11.50 (7.51)	-	
Number of hospitalizations	4.94 (4.45)	-	
Discomfort symptoms in closed spaces	Absent: 9 (56.25%) Present: 7 (43.75%)	Absent: 15 (65.22%) Present: 8 (34.78%)	p=0.571[b]

a – Mann-Whitney U test, b – Chi-square test

Table 2. **Comparison of results in both groups**

	Patient group (n = 16) Mean (SD)	Control group (n = 23) Mean (SD)	p-level
LSAS	69.81 (28.05)	40.61 (18.43)	p<0.001 [c]
Social phobia (LSAS>55)	13 (81.25%)	6 (26.09%)	p=0.002 [b]
Momentary anxiety 1	3.06 (3.07)	0.70 (1.06)	p=0.003 [a]
Momentary anxiety 2	3.56 (3.29)	1.30 (1.82)	p=0.024 [a]
Sense of presence 1	6.13 (2.80)	5.87 (2.30)	p=0.682 [a]
Sense of presence 2	5.65 (2.76)	5.65 (2.76)	p=0.254 [c]
SSPS1 (persecutory)	14.63 (7.51)	10.91 (2.17)	p=0.107 [a]
SSPS2 (persecutory)	14.81 (10.06)	10.83 (1.70)	p=0.187 [a]
PDI	134.60 (120.94)	-	-
PDI (paranoid)	16.13 (16.24)	-	-
PANSS-6	13.15 (4.85)	-	-
PANSS–6 (positive)	6.31 (2.72)	-	-
PANSS-6 (negative)	6.85 (4.53)	-	-

a – Mann-Whitney U test, b – Chi-square test, c – Student's T-test

LSAS – Leibowitz Social Anxiety Scale; PANSS-6 – 6-item Positive and Negative Syndrome Scale; PDI – Peters et al. Delusions Inventory; SSPS – Social State Paranoia Scale

Heart rate (HR) analysis was performed in both groups. HR scores were calculated from a 20-second measurement during oculometer calibration before each series of films and at the middle of each film. There was one outlier in the patient group, so it was excluded from the analysis. HR in all time points was normally distributed. There was homogeneity of variances and covariances. For series one, a statistically significant interaction between group and time was observed in HR frequency, $F(1.475; 51.618) = 7.616$; $p=0.003$, partial $\eta 2 = 0.179$. HR frequency between the groups was not significantly different at any of the 3 measurement points (p1=0.179; p2=0.259; p3=0.139). For the patient group, a statistically significant effect of time on HR frequency was present $F(1.34; 18.47) = 12.72$; $p=0.001$, partial $\eta 2 = 0.494$. HR was significantly different between calibration 1 and non-social film 1 (M1=86.52(3.47); M2=93.45(2.68); p=0.016), calibration 1 and social film 1 (M1=86.52(3.47); M3=97.21(2.69); p=0.006), while it was near significance between non-social film 1 and social film 1 (M2=93.45(2.68), M3=97.21(2.69); p=0.057). For the control group, a statistically significant effect of time on HR frequency was present $F(2; 44) = 15.50$; $p<0.001$; partial $\eta 2=0.413$. HR was significantly different between calibration 1 and non-social film 1 (M1=89.97(2.22); M2=96.81(1.61); p<0.001), between non-social

film 1 and social film 1 (M2=96.81(1.61); M3=92.83(1.56); p=0.002), while it was not significantly different between calibration 1 and social film 1 (M1=89.97(2.22); M3=92.83(1.56); p=0.208). In the second series of films, there was no statistically significant interaction between group and time in HR frequency, F(1.69; 52.29) = 1.08; p=0.337, partial η2=0.34. The main time effect indicates a statistically significant difference in HR frequency across various time points, F(1.69; 52.29) = 14.46; p<0.001, partial η2=0.318. Main effect for HR showed that HR was significantly different between measurements during calibration 2 and non-social film 2 (M1=87.04(1.96); M2=92.89(1.39; p=0.006), during calibration 2 and social film 2 (M1=87.04(1.96); M3=94.91(1.36); p<0.001), while it was not significantly different between measurements during non-social film 2 and social film 2 (M2=92.89(1.39); M3=94.91(1.36); p=0.271). The main group effect indicates no statistically significant difference in HR frequency between groups, F(1; 31) = 0.153; p=0.699, partial η2=0.05.

Correlation analysis between selected variables was performed. The severity of delusional thoughts (PDI) in the patient group was positively correlated with SSPS in VR in the first social video (tau=0.440; p=0.033) and did not reach statistical significance in the second social video (tau=0.402, p=0.058). Measures of momentary anxiety and social paranoia during both series of films were not correlated with each other in either group. Sense of presence was negatively correlated with the intensity of momentary anxiety only in series one in the control group. All correlation results are presented in Table 3. For the second series, an additional analysis was performed by dividing the entire study population into a group of people without claustrophobic features and those declaring at least mild discomfort in enclosed spaces. Only in the case of the second group, a positive association between presence and momentary anxiety was observed in the second video series (elevator) (tau=0.481; p=0.023).

Table 3. **Correlations of the clinical tools in the group of patients and control group. The Kendall's Tau-b correlation coefficient was utilized**

Variable 1	Variable 2	Correlation (Tau-b) patient group	Correlation (Tau-b) control group
PDI persecutory	SSPS 1	0.440**	-
PDI persecutory	SSPS 2	0.402	-
LSAS	SSPS 1	-0.266	-0.198
LSAS	SSPS 2	0.453*	0.012
Momentary anxiety 1	Momentary anxiety 2	0.574**	0.554**
SSPS 1	SSPS 2	0.708**	-0.094
Momentary anxiety 1	SSPS 1	0.250	-0.165
Momentary anxiety 2	SSPS 2	0.323	0.110
Sense of presence 1	Sense of presence 2	0.702*	0.702*

table continued on the next page

Sense of presence 1	Momentary anxiety 1	0.335	-0.380*
Sense of presence 2	Momentary anxiety 2	0.134	0.126

** – Correlation significant p<0.01 (two-sided); * – Correlation significant p<0.05 (two-sided)
LSAS – Leibowitz Social Anxiety Scale; PDI – Peters et al. Delusions Inventory; SSPS – Social State Paranoia Scale

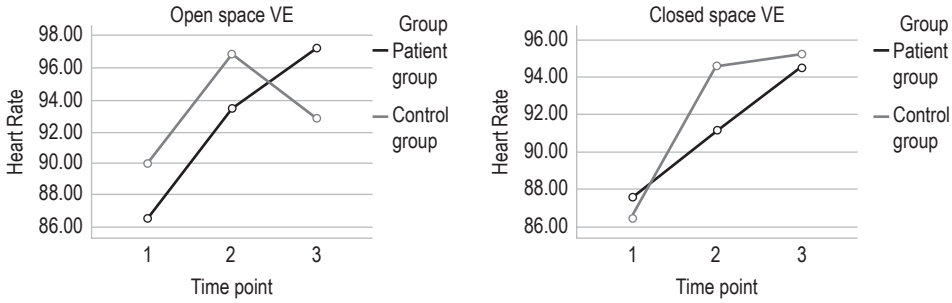

Figure 1. **Illustration of the heart rate change between different time points (1 – calibration, 2 – non-social 360° video, 3 – social 360° video) in both groups. First video series on the left, second on the right**

Discussion

The aim of the present study was to verify previous study results regarding the reactions of people with schizophrenia to social situations in virtual reality, this time in the form of 360° videos. The obtained results indicate that, in accordance with the assumptions, people with schizophrenia felt stronger anxiety in social situations and responded with greater emotional arousal, operationalized as an increase in HR frequency, in one of the two videos presenting social situations. Given the small size of both groups, the results should be interpreted with caution.

In the results of clinical scales used, both groups differed in the Leibowitz Social Anxiety Scale (LSAS) and in momentary anxiety in the first and second series of films – higher values of both scales were observed in the patient group. With regard to other tools, both groups did not differ significantly. It may seem surprising that there were no significant intergroup differences in the results of the State Social Paranoia Scale (SSPS). However, a similar result was obtained by other researchers [3] when comparing subjects in the persecutory delusions group and the non-clinical group [3]. The researchers explained this by the lack of emotional arousal in the subjects, for whom the virtual environment was safer than the cities in which they live, thus not increasing the anxiety experienced. In our study, the intensity of momentary anxiety in both groups remained relatively low and perhaps did not represent sufficient emotional arousal to lead to an increase in persecutory thoughts. This could be indicated by the

lack of significant correlation between SSPS scores and momentary anxiety in either group. This lack of correlation also implies that momentary anxiety was not due to a state of paranoia, and it is likely that the higher values in the patient group were related to free-floating type anxiety, possibly also present prior to VR exposure. However, this is only a speculation, as participants were not asked about momentary anxiety before exposure. In a different study [8], significant differences were observed in the severity of social paranoia state between groups of people experiencing and not experiencing paranoid thoughts on a daily basis. Nevertheless, given the p value, we suspect that by increasing the study sample, intergroup differences in social paranoia state would become statistically significant. It is worth mentioning the relatively high correlation between SSPS values in both series of films in the patient group, and the lack of any relationship between SSPS results in the control group. Although the presence in the control group of individuals displaying features of paranoid thinking is not excluded, it seems that the slightly higher SSPS scores in some individuals in the control group are a matter of chance rather than a deliberate response.

In the patient group, severity of paranoid thinking (persecutory PDI) was associated with greater severity of paranoia state in series 1 (SSPS 1). That is, patients with a greater tendency to think paranoid thoughts on a daily basis had a greater tendency to manifest persecutory delusions in virtual reality. This may support ecological validity of a non-interactive virtual social environment in the form of 360-degree videos. In none of the videos used did the recorded individuals show any hostile behavior; thus an experienced sense of threat in such an environment is known to be unfounded and it can be considered the result of paranoid thoughts. Such a conclusion is consistent with numerous studies of social paranoia in VR [4, 8, 25]. Thus, it appears that interaction with the environment is not necessary to elicit paranoid reactions in VR. The lack of significant association of the score on the PDI and SSPS scales after the second social movie may be due to the difference in the intensity of the stimuli eliciting paranoid reactions. In social video 1, numerous passersby frequently looked at the camera, which to the viewer may have given the impression of making eye contact with them. In social film 2, the elevator passengers made virtually no eye contact. The intensity of social anxiety was positively correlated with the severity of paranoia symptoms in VR only in the patient group during social video 2. Contrary to the first social video, in the second one the participants were in close proximity to the recorded people. As shown, people with social anxiety feel more comfortable being at a greater distance from unknown people, as well as misjudge the distance to other people as lesser than in reality [26]. We suspect that individuals with social anxiety traits, significantly more present in the patient group, due to the proximity of the recorded characters experienced greater negative emotional arousal and were more likely to paranoidly interpret the behaviors of those around them, which is consistent with the model of persecutory delusions formation [27]. In comparison, the only study on paranoia using 360° immersive videos [20] also observed a positive correlation between the tendency for paranoid thinking on a daily basis, as measured by the Green et al. Paranoid Thoughts Scale (GPTS),

and paranoia as a state, as measured by the SSPS scale. The researchers obtained correlation coefficients for the VE of an elevator, library, and bar of 0.51, 0.37, and 0.15, respectively, although the last one was not statistically significant. Importantly, the environments differed significantly in the intensity of social interactions (such as glances or smiles) – the elevator had the most (23) in the smallest area, while the bar had the least (13), dispersed in the largest area. This seems to confirm our results as well, with a significant association between paranoia as a trait (GPTS) and paranoia as a state (SSPS) observed in the environment with significantly more interactions, that is, the market square, as opposed to the elevator with very few interactions.

A significant time and group interaction effect was observed in the results of the HR measures in the first series of videos. Initially, both groups experienced a similar increase in HR between calibrations in the non-social movie, which could be related to the novelty of the virtual environment and the slightly increased number of movements performed. Subsequently, HR frequency did not change significantly during the social movie in the patient group (although there was an increase in HR nearing statistical significance), whereas it began to decrease in the control group. In our opinion, there was an increase in anxiety and paranoid thoughts in the patient group in response to the social environment, which was associated with stimulation of the sympathetic nervous system leading to a further increase in HR. In the control group, the social environment was not a significant stressor, hence HR decreased to resting state. In the second series of videos, no effect of group and time interaction was observed. We believe that for the reasons described above, social movie 2 had less potential to elicit paranoid reactions and emotional arousal. Alternatively, the lack of difference may have been due to the fact that a significant proportion of subjects in both groups reported discomfort in confined spaces such as an elevator, hence the presence of social stimuli may have differentiated the two groups to a lesser extent. HR was measured after exposure to a virtual social environment by Veling et al. [4]. No significant differences were observed between the group with a first episode of psychosis and the healthy group in mean HR, and no significant differences in HR were observed between sessions in the virtual environment with different intensities of social stressors. According to the authors' hypothesis, this was due to the fact that mean HR was measured for each session, whereas most likely changes would be detectable when measuring HR shortly before and after a potential stressor [4].

Sense of presence remained constant throughout both series, similar in both groups, indicating that there were no differences in perceptions of the virtual environment between individuals with schizophrenia and healthy individuals. Contrary to expectations, no positive association was observed between sense of presence and momentary anxiety. Moreover, in the healthy group, in series 1, sense of presence increased as momentary anxiety decreased. We suspect that this is a random result, especially considering the fact that most of the control group had virtually no anxiety, as indicated by the very low mean score. Given that momentary anxiety may have been induced more by fear of enclosed spaces in the second series of videos, we made a comparison in subgroups

with present and absent features of claustrophobia. As suspected, in the group with features of claustrophobia we detected a positive relationship between momentary anxiety and sense of presence, which is consistent with the established association between emotions and sense of presence mentioned in the introduction [28].

From the feedback given by the subjects it can be concluded that the experience of being in VR was natural, most subjects did not feel the disparity between the individual real point of view and the camera perspective (120 cm above the ground). Respondents reported the experience of exposure to VR mostly as intriguing and declared willingness to repeat similar sessions.

One of the most important limitations of the study is the small size of both groups, especially the patient group. A second major limitation is the fact that the control group was different from the patient group in terms of sex and age distribution. However, this does not seem to have had a significant impact on the results, as previous studies on large groups of people have not observed any differences in the severity of perceived social paranoia between males and females, and the age of the subjects was not a significant predictor of the severity of paranoid thoughts in VR [8]. Another limitation is that heart rate measurements were performed using a Jazz-novo oculometer, which has a higher risk of measurement error than professional heart monitors. Furthermore, although only healthy individuals were recruited into the control group, according to the concept of the psychosis continuum, some individuals in the control group were also likely to exhibit paranoid thoughts. Hence, it would be reasonable to also assess this group using the PDI scale. A final limitation is the lack of validation of the translated SSPS scale.

Conclusions

In conclusion, similarly to the studies using a computer-generated environment, in the case of 360-degree video technology, the subjects displaying paranoid thinking traits presented persecutory beliefs towards human figures in a virtual neutral social environment, which was simultaneously associated with an increase in emotional arousal expressed by an increase in heart rate. Together with the reported relatively strong sense of presence, this result indicates a similar ecological validity of such an environment as compared to a computer-generated one, with the prospect of using this technology to design studies on the assessment and treatment of persecutory delusions in psychotic patients at a relatively low cost. It should be added, however, that the presented conclusions are only preliminary in nature and require confirmation in studies on much larger groups.

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