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INVITED REVIEWS

Using virtual reality to investigate psychological processes and mechanisms associated with the onset and maintenance of psychosis: a systematic review

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Abstract
Purpose In the last decade researchers have embraced virtual reality to explore the psychological processes and mechanisms that are involved in the onset and maintenance of psychosis. A systematic review was conducted to synthesise the evidence of using virtual reality to investigate these mechanisms.
Methods Web of Science, PsycINFO, Embase, and Medline were searched. Reference lists of collected papers were also visually inspected to locate any relevant cited journal articles. In total 6001 articles were potentially eligible for inclusion; of these, 16 studies were included in the review.
Results The review identified studies investigating the effect of interpersonal sensitivity, childhood bullying victimisation, physical assault, perceived ethnic discrimination, social defeat, population density and ethnic density on the real-time appraisal of VR social situations. Further studies demonstrated the potential of VR to investigate paranoid ideation, anomalous experiences, self-confidence, self-comparison, physiological activation and behavioural response.
Conclusions The reviewed studies suggest that VR can be used to investigate psychological processes and mechanisms associated with psychosis. Implications for further experimental research, as well as for assessment and clinical practise are discussed. The present review has been registered in the PROSPERO register: CRD42016038085.

Keywords Virtual reality · Adverse life events · Daily stressors · Stress sensitivity, psychosis

Introduction

Cognitive models of psychosis have investigated the psychological processes and mechanisms that play a role in psychosis and suggest that stressful life events can influence the way we perceive ourselves, others, and the world around us and can contribute to the onset and maintenance of psychosis [1–5]. These models have been supported by research which suggest that stress is a key feature in the onset and maintenance of mental health symptoms and disorders [6, 7]. Stress can be defined as a physiological reaction to a threat that involves the activation of the hypothalamic–pituitary–adrenal (HPA) axis [8–10]. This reaction is similar across all mammalian species. In humans the psychological conceptualisation of stress proposes that the emotional response and physiological activation that occur in a situation are dependent on the interpretation of a threat and on whether we think we will be able to cope with the event or not [11]. Stress is a dominant feature of many aetiological models of psychosis [9, 12, 13], however, stress is an elusive concept that is defined differently in different contexts. Reported stressful events can range from mild feelings of everyday stress and minor hassles (for example, living in a densely populated city; travelling in crowded public transport), through significant adverse life events (for example, bully victimisation; ethnic discrimination), to traumatic events (for example, physical assault; sexual abuse).

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A number of social factors that can be viewed as stressors have themselves been linked to an increased risk of psychosis. Urbanicity has been associated with higher levels of stress [14] and higher rates of psychosis [15, 16]. Higher psychosis rates have been found among migrants [17, 18] and have been linked to the perception of ethnic density [19, 20]. Furthermore, associations between perceived ethnic discrimination and psychosis in ethnic minority and immigrant groups have been reported in previous research [21–23]. Childhood bully victimisation has also been associated with an increase in psychosis and other mental health problems in adulthood [24, 25].

Also worth considering in this context is the evidence showing that individuals with schizophrenia have an increased sensitivity to daily hassles and report greater subjective stress [12, 26, 27]. These findings have stimulated interest in stress reactivity as an element of vulnerability [28] and an interest in how individuals with different levels of vulnerability for psychosis respond to daily stressors [29–31]. Interpersonal sensitivity is described as "an undue and excessive awareness of, and sensitivity to, the behaviour and feelings of others… particularly to perceived or actual situations of criticism or rejection…" (p. 342 [32]). Higher interpersonal sensitivity is linked to problems in interpersonal relationships, low self-esteem, as well as negative self-concepts, and it has been found to be higher in individuals at ultra high risk for psychosis [31, 33]. Previous studies have also found that a negative self-concept [34, 35]) and low or unstable self-esteem [34] are linked to higher levels of paranoia in clinical and non-clinical samples.

When thinking about possible underlying mechanisms in the onset of psychosis is important to consider that prolonged exposure to social adversity and social exclusion have been linked to high prevalence rates of anomalous experiences (such as a propensity to hallucinations, high endorsement of psychic items or higher trait paranoia) in the general population and have been found to be associated with the same risk factors present in people with psychosis [36–40]. Stressful life events have also been linked to paranoid ideation [41]. Paranoid ideation has been defined as "the unfounded fear that others intend to cause you harm" [42, 43] and is the most common type of delusional belief recorded by individuals with psychosis [44] and it is a common delusional belief in the general population [45].

While there is a long tradition of research in these processes and mechanisms they are usually assessed with retrospective self-report questionnaires or interviews. Limited evidence is available researching underlying psychological processes and mechanisms in real-life or in ecologically valid environments [46, 47]. In the last decade, researchers in the field of psychosis have embraced Immersive Virtual Reality (hereafter shortened to VR) as a method to explore the psychological mechanisms associates with the onset and maintenance of psychosis. VR environments are displayed in colour and in 3D using a head-mounted-display. The user is fully immersed in the environment and can interact with the environment either by head movements, full body turning or with a joystick. The sounds of the environment are heard through headphones [48] (please see https://www.youtube.com/watch?v=svG6kXC2PQA for an example). VR environments elicit sense of presence [49] and trigger real time cognitive, emotional, behavioural, and physiological responses to real time situations [50]. This sense of 'being there' as if it were a real life situation has lead researcher to describe VR environments as ecologically valid [50, 51]. Aside from allowing to simulate "real life" social situation and bring them into a laboratory setting, the added value of VR is that it allows the researcher to measure real time responses, and at the same time it enables to control and manipulate each aspect of an environment [52]. VR enables thus researchers to expose participants to exactly the same social environment and to measure the individual cognitive, emotional, behavioural and physiological response to the environment. It also enables to investigate the association between an individual prior exposure to social and environmental factors (e.g., history of migration, or bully victimisation) and their real-time response to a social environment. The VR environment itself can also be manipulated, for example, the number of virtual characters in an environment can be changed, as can be their ethnicity, their facial expression, their behaviour or what they say. Sounds, like for example indistinct background conversations, crowd murmuring or laughter or other noises like background music or sound of traffic can also be manipulated.

The aim of this manuscript was to review experimental studies that used VR to investigate the underlying psychological processes and mechanisms associated with the onset and maintenance of psychosis.

Method

Design

We conducted a systematic review of the literature and described the results in a qualitative synthesis. The review was registered on the PROSPERO register CRD42016038085.

Selection procedure

The databases used to conduct the search were Web of Science, PsycINFO, Embase, and Medline. Reference lists

of collected papers were also visually inspected to locate any relevant cited journal articles. Studies were included in the review if they were: written in English; contained original empirical findings, and published in a peer-reviewed journal. Studies were excluded from the review if they were treatment studies; case studies; reviews; not available in English; theses; or book chapters. Only studies of immersive VR were included.

Search criteria

Studies for review were identified following a keyword search for the terms 'virtual reality' OR 'VR' in conjunction with 'social stress' OR 'adverse life events' OR 'urban', OR 'migration', OR 'bullying', OR 'discrimination', OR 'social defeat', OR 'social entrapment', OR 'stress', AND 'psychological processes', OR 'mechanisms', OR 'mental health', OR 'paranoia', OR 'anxiety', OR 'depression', OR 'trauma', OR 'psychosis' OR 'schizophrenia'. Appropriate truncations and wild cards were used to identify permutation of the terms searched, e.g., stress* to search for: stress, stressors, stressful; paranoi* to search for: paranoia, paranoid.

Quality assessment

Quality of the reviewed studies was assessed independently by LV and MRC using the Evaluation of Public Health Practise Project (EPHPP) Quality Assessment Tool for Quantitative Studies [53]. A global rating for the paper is described as follows: Strong = no weak ratings; Moderate = one weak rating; Weak = two or more weak ratings on the subscales (selection bias; study design; confounders; blinding; data collection methods; withdrawals and dropouts) The EPHPP is available online (http://ephpp.ca/tools.html). Rating disagreements were resolved by consensus.

Results

Information extraction

The search resulted in 5999 articles (final search conducted 4 March, 2016); two more manuscripts were identified by publication alerts email from journals. From these 6001 studies we identified 16 experimental studies which used full immersive VR to research adverse life events, daily stressors and psychological processes associated with psychosis (see Fig. 1).

Qualitative synthesis

The reviewed studies were organised in two categories. The first category describes studies which used VR to investigate the association between baseline characteristics and the real-time response to a neutral social VR environment. The second category includes studies that manipulated one or more aspects of the environment to measure how the manipulation would influence the real-time response to VR environment. Finally, we reviewed overarching findings from both categories regarding whether VR can be used to investigate real-time response to social situations.

Studies exploring the association between baseline characteristics and the real-time response to a neutral social VR environment

The ten studies summarised in Table 1 used VR to explore the association between existing characteristics of participants and their response to a VR social situation. In two studies the environment was a library, the remaining studies used an underground train environment. Both the library environment and the underground were designed to be perceived as neutral social environments. Virtual characters or avatars showed neutral behaviours typical of such social situations, but that could be interpreted as ambiguous like for example, looking at the participant, smiling, or avatars talking to each other. This was done on purpose as the main aim of the studies was to explore 'unfounded' real-time paranoid ideation in VR rather than a response to a genuinely hostile environment [54].

Childhood bullying victimisation, physical assault, perceived ethnic discrimination, and social defeat

Five studies investigated whether having experienced adverse life events was associated with higher levels of paranoid ideations in the neutral social VR environments. All five studies used the VR underground train environment. Childhood bullying victimisation [55]; being the victim of a physical assault [56, 57]; perceived ethnic discrimination [58] and social defeat [59] were found to be associated with real-time paranoid ideation in the VR social environment.

Interpersonal sensitivity

The correlation between interpersonal sensitivity and real-time paranoid ideation during VR was investigated in five studies [60–64]. All studies found that heightened interpersonal sensitivity was associated with higher levels of paranoia in the VR library or in the underground train.

Studies investigating the effect of a manipulation on the response to a VR environment

The six studies listed in Table 2 have used a manipulation to investigate the real-time response to the VR environment.

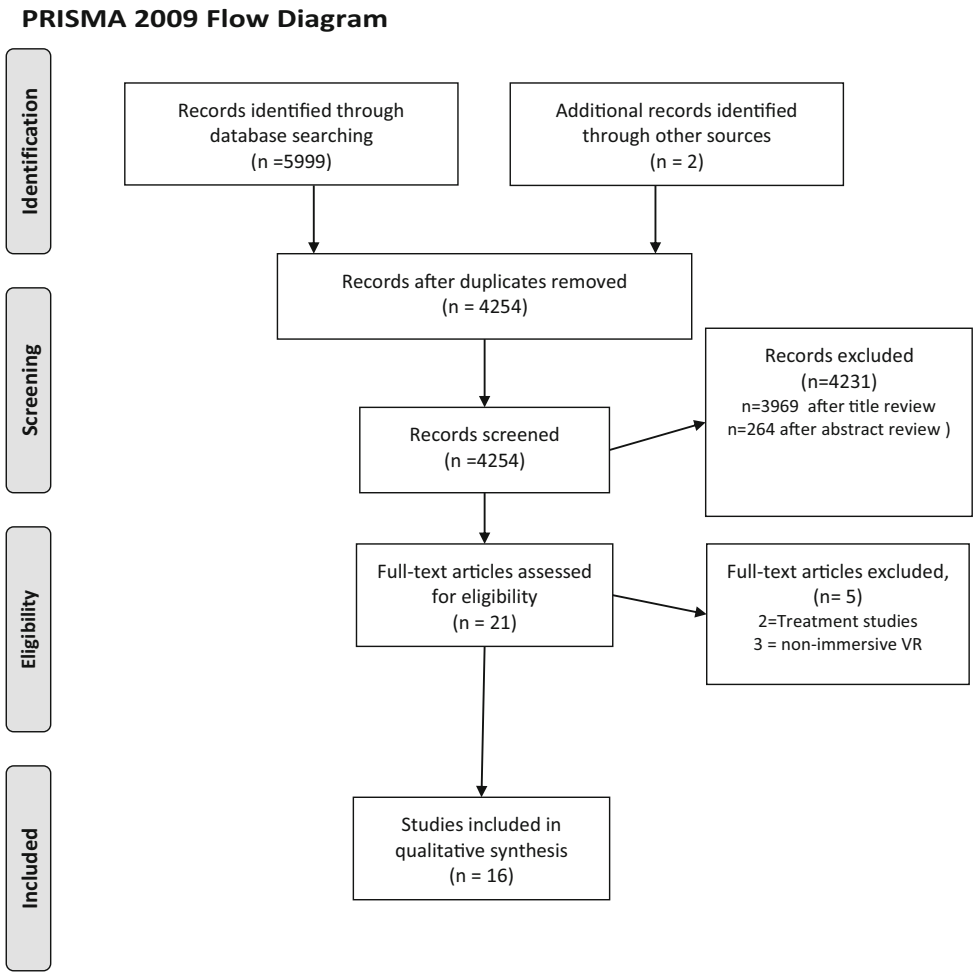

Fig. 1 PRISMA 2009 flow diagram

The studies have used different environments: a bar, a student flat, and the underground train described earlier.

Population density and ethnic density

Two studies investigated how manipulating population density and ethnic density effected paranoid ideation in a VR bar environment [65, 66]. The findings suggested that increased population density, hostility of the avatars, and a different ethnicity were associated with higher levels of paranoia in the VR bar.

Self-confidence and social comparison

Two experiments indicated that VR can be useful to measure self-confidence and social comparison. In the first study, participants underwent a manipulation aimed to induce low or high self-confidence. In the high self confidence induction they were instructed to think about a time in their life when they felt self-confident and they were provided with a list of confidence statements. In the low-confidence induction, participants underwent a similar procedure but regarding their least self-confident experience. Low self-confidence was associated with higher paranoid ideation in VR underground train [67].

The second experiment manipulated the height of participants in the VR environment and found that a lowered height was associated with negative social-comparison [68].

Physiological activation and behavioural response

Manipulation of the VR environment triggered not only the cognitive and emotional response to a social situation, but also the physiological changes and behavioural response. Galvanic skin response, heart rate and behavioural response (distance kept from the avatars) was found to be triggered by changes in population density and ethnic density in a VR bar environment [69]. The same environment was used to investigate galvanic skin response in a sample of individuals with psychosis [65]. Distance kept from the avatar was also measured in a study which

Table 1 Studies exploring the association between baseline characteristics of participants and the cognitive, emotional, behavioural, and physiological response to an immersive VR social environment to ($n = 10$)

Study (country)	Area studied	Design	Participants	Mean age (SD)	VR equipment	VR task	Measures	Main findings	EPHPP global rating
Freeman et al. [61] (United Kingdom)	Persecutory ideation	Within subjects design	24 healthy participants (12 male and 12 females)	26 (6)	CAVE Immersive projection system and Crystal Eyes shutter-glasses	Library with 5 avatars who occasionally showed potentially ambiguous behaviour (e.g., looking, smiling, talking)	BSI; SSPS; STAI; VR paranoia questionnaire; Semi structured interview and observer ration of persecutory ideation; SUS	Individuals attributed mental states to avatars, including paranoid intentions. Persecutory ideation was associated with interpersonal sensitivity	Moderate
Freeman et al. [62] (United Kingdom)	Persecutory ideation	Within subjects design	30 healthy participants (15 males and 15 females; 70 % White ethnicity)	22 (5)	CAVE Immersive projection system and Crystal Eyes shutter-glasses	Library with 5 avatars who occasionally showed potentially ambiguous behaviour (e.g., looking, smiling, talking)	SSPS; LSHS; Structured Interview for assessing perceptual abnormalities; Need for closure: DASS-21; IPSM; PSCS; Probabilistic reasoning task; SADS; VR paranoia questionnaire; VR-Social avoidance and distress scale; SUS	Individuals attributed mental states to avatars, including paranoid intentions. Persecutory ideation was predicted by baseline anxiety, timidity and hallucination predisposition. No association was found with probabilistic reasoning or need for closure	Moderate
Freeman et al. [70] (United Kingdom)	Paranoid ideation and social anxiety	Within subjects design	200 participants from general population (100 males and 100 females; 63 % White ethnicity; 47 % graduate degree or higher; 17 % unemployed)	37.5 (13.3)	HMD: VR1280	Participants experienced a underground train ride with avatars who occasionally showed potentially ambiguous behaviour (e.g., looking, smiling, talking)	WAIS; DASS-21; PSWQ; Worry domains questionnaire; Cathastrophizing interview; BCSS; IPMS; Cognitive flexibility; Probabilistic reasoning; CAPS; MAP; Life stressors checklist; SSQ; SELSA; SSPS; SADS	Higher baseline perceptual abnormalities was a predictor of paranoid ideation but not of social anxiety.	Strong

Table 1 continued

Study (country)	Area studied	Design	Participants	Mean age (SD)	VR equipment	VR task	Measures	Main findings	EPHPP global rating
Freeman et al. [64] (United Kingdom)	Persecutory ideation and associated factors	Within subjects design	Group 1 ($n = 30$): low non-clinical paranoia (83 % White ethnicity) Group 2 ($n = 30$): high non-clinical paranoia (77 % White ethnicity) Group 3 ($n = 30$): Clinical Persecutory delusions (53 % White ethnicity) Each group had 18 males and 12 females	Group 1: 44.2 (11.2) Group 2: 36 (11.7) Group 3: 44.2 (11.7)	HMD: VR1280	Participants experienced a underground train ride with avatars who occasionally showed potentially ambiguous behaviour (e.g., looking, smiling, talking)	GPTS; SSPS; VAS hostility; DASS-21; PSWQ; IPSM; Beads task; CAPS; Life stressors checklist; WAIS; SSQ Simulation sickness questionnaire	There was an increase in levels of anxiety, worry, interpersonal sensitivity, depression, anomalous experiences and trauma history across the three groups of paranoia. Jumping to conclusion was only present in the persecutory delusions group	Strong
Freeman et al. [57] (United Kingdom)	Paranoia and PTSD following an assault	Within subject comparison	106 participants recruited in an A&E department after having experienced a distressing physical assault (79 males and 27 females; 52 % White ethnicity; 31 % unemployed)	34.4 (11.6)	HMD: NVIS SX111	Participants experienced a underground train ride with avatar avatars who occasionally showed potentially ambiguous behaviour (e.g., looking, smiling, talking)	Posttraumatic diagnostic scale; Structural Clinical Interview for DSM-IV; GPTS; PANSS; SSPS; Thoughts and feelings during the assault scale; CPQ; MDS;TMQ; IQQ; RIQ; SBQ; PCI; Perceived negative response of others; CSS; PSWQ; ISM; Catastrophizing Interview; BCSS; Cognitive flexibility scale; CAPS; MAP; VAS: PTSD; Paranoia	PTSD and Paranoia were correlated but distinct experiences	Strong
Freeman et al. [56] (United Kingdom)	Paranoia in VR as predictor of paranoia and PTSD 6 months after experiencing an assault	Within subject comparison	As above	As above	As above	Participants experienced a underground train ride with avatars who occasionally showed potentially ambiguous behaviour (e.g., looking, smiling, talking)	PANSS; GPTS; VAS: PTSD; Paranoia; PSRS; Posttraumatic diagnostic scale; SSPS	Response to the VR environment predicted the severity of PTSD and paranoia symptoms at 6 months	Strong

Table 1 continued

Study (country)	Area studied	Design	Participants	Mean age (SD)	VR equipment	VR task	Measures	Main findings	EPHPP global rating
Shaikh et al. [58] (United Kingdom)	Perceived ethnic discrimination and paranoid ideation	Cross sectional between participants independent design	64 Ultra High Risk individuals (UHR) (38 males 26 females; 36 % White British; 56 % Unemployed; 13 % Higher education) 43 Healthy Controls (20 males, 23 females; 37 % White British; 7 % Unemployed; 33 % Higher education)	UHR 22.5 (4.0) HC 24 (4.0)	HMD: VR1280	Participants experienced a underground train ride with avatars who occasionally showed potentially ambiguous behaviour (e.g., looking, smiling, talking)	Prodromal questionnaire; SSPS; PEDQ-Community version	UHR reported higher levels of perceived ethnic discrimination. Higher levels of perceived ethnic discrimination were associated with greater paranoia in VR in the entire sample	Strong
Valmaggia et al. [63] (United Kingdom)	Paranoid ideation	Within subject comparison	21 Ultra High Risk individuals (UHR) (13 males and 8 females; 57 % White ethnicity; 33 % unemployed)	25 (4.7)	CAVE Immersive projection system and Crystal Eyes shutter-glasses	Participants experienced a underground train ride with avatars who occasionally showed potentially ambiguous behaviour (e.g., looking, smiling, talking)	GPTS; PS; ISM; DASS; LSHS; Paranoia Scale; Beads Task; Wisconsin Card Sorting Task; National Reading Test; Pre and Post VR VAS: anxiety; VR Questionnaire; Semi structured interview and observer ration of persecutory ideation. Follow-up assessment after one week to monitor intrusions and adverse effects in the week following the experiment	Paranoid ideation in VR were predicted by baseline paranoia; anxiety; stress, perseveration and interpersonal sensitivity VR did not increase anxiety or cause negative experiences in the week following the experiment	Strong

Table 1 continued

Study (country)	Area studied	Design	Participants	Mean age (SD)	VR equipment	VR task	Measures	Main findings	EPHPP global rating
Valmaggia et al. [55] (United Kingdom)	Childhood bullying victimisation and paranoid ideation	Cross sectional between participants independent design	64 Ultra High Risk individuals (UHR) (38 males 26 females; 36 % White British; 56 % Unemployed; 13 % Higher education 43 Healthy Controls (20 males, 23 females; 37 % White British; 7 % Unemployed; 33 % Higher education)	UHR 22.5 (4.0) HC 24 (4.0)	HMD: VR1280	Participants experienced a underground train ride with avatars who occasionally showed potentially ambiguous behaviour (e.g., looking, smiling, talking)	Retrospective bullying questionnaire; SSPS	UHR were more likely to have experienced childhood bullying. Childhood bullying victimisation was associated with paranoid ideation in the VR independent of clinical status	Strong
Valmaggia et al. [59] (United Kingdom)	Social defeat and paranoid ideation	Cross sectional between participants independent design	As above	As above	HMD: VR1280	Participants experienced a underground train ride with avatars who occasionally showed potentially ambiguous behaviour (e.g., looking, smiling, talking)	Comprehensive Assessment of the at risk mental state; Prodromal questionnaire; SCS; Defeat Scale; Entrapment Scale; DASS; SSPS	UHR subjects reported significantly higher levels of social defeat than controls and their paranoid appraisals were predicted by level of social defeat at baseline	Strong

HMD Head Mounted Display, *GPTS-B* Green Paranoia Thoughts Scale-B, *VAS* Visual Analogical Scale, *SCS* Social comparison scale, *SSPS* Social State Paranoia Scale, *GSR* Galvanic skin response, *HR* Heart rate, *STAI* Spielberg Trait Anxiety Inventory, *SUS* Slater, Usoh, Steed Sense of Presence Scale, *BSI* Brief Symptom Inventory, *LSHS* Launay Slade Hallucination Scale, *DASS* Depression Anxiety Stress Scale, *IPSM* Interpersonal sensitivity Measure, *PSCS* Private Self-Consciousness Scale, *SADS* Social Avoidance and distress scale, *WAIS* Wechsler Abbreviated scale for intelligence, *PSWQ* Penn State Worry questionnaire, *BCSS* Brief core schema scale, *CAPS* Cardiff Anomalous perceptions scale, *MAP* Maudsley Addiction Profile, *SSQ* Social support questionnaire, *SELSA* Social and emotional loneliness scale for adults, *SCS* Social Comparison Scale, *PANSS* Positive and Negative Symptom Scale, *CPQ* Cognitive processing questionnaire, *MDS* Mental defeat Scale, *TMQ* Trauma Memory questionnaire, *IQQ* Intrusions Qualities questionnaire, *RIQ* Response to intrusion questionnaire, *SBQ* Safety behaviour questionnaire, *PCI* Posttraumatic cognition inventory, *CSS* Crisis support scale, *PSRS* Psychotic Symptoms rating Scale, *PEDQ* Perceived Ethnic Discrimination Questionnaire- Community version, *SIAS* Social Interaction Anxiety Scale, *DACOBS* Davos Assessment of Cognitive Biases Scale, *RSES* Rosenberg Self-esteem rating scale

Table 2 Studies exploring the cognitive, emotional, behavioural, and physiological response to a manipulation in the VR social environment to ($n = 6$)

Study (country)	Area studied	Design	Participants	Mean age (SD)	VR equipment	VR task	Measures	Main findings	EPHPP global rating
Atherton et al. [67] (United Kingdom)	Self-confidence and paranoid ideation	Within subjects design	26 males (from a general population sample who scored >17 on GPTS-Paranoia)	43.4 (16.3)	HMDs: NVIS SX111 or VR1280	Before VR participants received a low or a high self-confidence manipulation. Participants experienced an underground train ride with avatars who occasionally showed potentially ambiguous behaviour (e.g., looking, smiling, talking)	GPTS-B; VAS social confidence; SCS; SSPS	Induced low self confidence led to higher levels of paranoia and more negative views of the self in the VR environment	Strong
Brinkman et al. [69] (The Netherlands)	Physiological response to changes in population density and ethnic density	Two by two within-subject design	2 Males (1 with schizoaffective disorder) 24 Healthy Controls (20 male and 4 female; all White Dutch)	29 (9.2)	HMD: Emagin Z800 3DVisor	Participants moved freely in a bar with different population density and avatar ethnic density	GSR, HR, Subjective discomfort; Distance from avatar	Increased population density and ethnic density are associated with more fluctuation in physiological arousal in the VR environment	Weak
Freeman et al. [68] (United Kingdom)	Persecutory ideation and social comparison after height was altered	Two condition, two period crossover trail	60 females from the general population (with paranoid thinking in the last month; 78 % White ethnicity; 55 % graduate degree or higher)	31.5 (13)	HMD: NVIS SX111	Participants experienced a underground train ride with avatars who occasionally showed potentially ambiguous behaviour (e.g., looking, smiling, talking) The height of the participant was lowered during the experimental condition	GPTS-B; SSPS; SCS	A lowered height was associated with higher levels of paranoid ideation and in more negative views about the self compared to others	Strong
Fornells-Ambrojo et al. [60] (United Kingdom)	Perception of trustworthiness and interpersonal distance	Between group comparison	61 healthy male (77 %: White ethnicity; 90 % students)	25.3 (7.3)	CAVE Immersive projection system and Crystal Eyes shutter-glasses	Participants moved in a student flat and interacted with a virtual flatmate. The contingency behaviour of the flatmate was manipulated to be high in one condition and low in the other	SSPS; STAI; Relationship Questionnaire; Distance kept from avatar; Trustworthiness of the avatar; SUS	High subjective trust was not associated with less distance from the avatar. Higher trait paranoia was associated with heightened sensitivity to contingency behaviour	Moderate
Veling et al. [65] (The Netherlands)	Paranoid thoughts and associated social anxiety, cognitive bias, self esteem	Cross sectional between participants independent design	17 patients with a first episode of psychosis (FEP) (14 males, 3 females; 35 % White Dutch ethnicity) 24 healthy controls (20 males, 4 females; 100 % White Dutch ethnicity)	FEP 27.3 (5.5) HC 29 (9.2)	Emagin Z800 3D Visor	Participants moved freely in a bar with different population density and avatar ethnic density	GPTS; SIAS; DACOBS; RSES; Simulation sickness questionnaire; SSPS; Galvanic skin response	Patients reported more paranoid thoughts, showed more proximity to the avatars and higher galvanic skin response to avatars of a different ethnicity from their own	Strong

Table 2 continued

Study (country)	Area studied	Design	Participants	Mean age (SD)	VR equipment	VR task	Measures	Main findings	EPHPP global rating
Veling et al. [66] (The Netherlands)	Paranoid thoughts and stress sensitivity	Cross sectional between participants independent design	Group 1: 20 UHR (7 males, 13 females 75 % White Dutch ethnicity) Group 2: 55 Individuals with psychosis (42 males, 13 females; 53 % White Dutch ethnicity Group 3: 42 siblings of people with psychosis (23 males, 19 females; 75 % White Dutch ethnicity) Group 4: 53 controls with negative first degree family history of psychosis (25 males, 28 females; 70 % White Dutch ethnicity)	UHR 24 (4.5) Psychosis 26 (4.7) Siblings 26.4 (4.8) Controls 24.6 (4.4)	Sony HMZ-T1	Participants moved freely in a bar with different population density, avatar ethnic density and hostility of facial expression of the avatars	GPTS; SIAS; Community Assessment of psychic experiences; VAS: subjective distress; SSPS	Increase social stress was associated with increase in paranoia and subjective distress in VR. Negative affect and psychosis liability were associated with higher levels of paranoia in VR	Strong

HMD Head Mounted Display, *GPTS-B* Green Paranoia Thoughts Scale-B, *VAS* Visual Analogical Scale, *SCS* Social comparison scale, *SSPS* Social State Paranoia Scale, *GSR* Galvanic skin response, *HR* Heart rate, *STAI* Spielberg Trait Anxiety Inventory, *SUS* Slater, Usoh, Steed Sense of Presence Scale, *BSI* Brief Symptom Inventory, *LSHS* Launay Slade Hallucination Scale, *DASS* Depression Anxiety Stress Scale, *IPSM* Interpersonal sensitivity Measure, *PSCS* Private Self-Consciousness Scale, *SADS* Social Avoidance and distress scale, *WAIS* Wechsler Abbreviated scale for intelligence, *PSWQ* Penn State Worry questionnaire, *BCSS* Brief core schema scale, *CAPS* Cardiff Anomalous perceptions scale, *MAP* Maudsley Addiction Profile, *SSQ* Social support questionnaire, *SELSA* Social and emotional loneliness scale for adults, *SCS* Social Comparison Scale, *PANSS* Positive and Negative Symptom Scale, *CPQ* Cognitive processing questionnaire, *MDS* Mental defeat Scale, *TMQ* Trauma Memory questionnaire, *IQQ* Intrusions Qualities questionnaire, *RIQ* Response to intrusion questionnaire, *SBQ* Safety behaviour questionnaire, *PCI* Posttraumatic cognition inventory, *CSS* Crisis support scale, *PSRS* Psychotic Symptoms rating Scale, *PEDQ* Perceived Ethnic Discrimination Questionnaire-Community version, *SIAS* Social Interaction Anxiety Scale, *DACOBS* Davos Assessment of Cognitive Biases Scale, *RSES* Rosenberg Self-esteem rating scale

Table 3 Immersive VR studies EPHPP quality assessment rating

Study	A Selection bias	B Study design	C Confounders	D Blinding	E Data collection method	F Withdrawals and drop out	Global rating
Atherton et al. [67]	Moderate	Moderate	Strong	Moderate	Strong	Strong	Strong
Brinkman et al. [69]	Weak	Moderate	Weak	Weak	Strong	Strong	Weak
Fornells-Ambrojo et al. [60]	Weak	Strong	Moderate	Moderate	Strong	Strong	Moderate
Freeman et al. [61]	Moderate	Moderate	Weak	Moderate	Moderate	Strong	Moderate
Freeman et al. [62]	Strong	Moderate	Weak	Moderate	Strong	Strong	Moderate
Freeman et al. [70]	Moderate	Moderate	Strong	Moderate	Strong	Strong	Strong
Freeman et al. [64]	Strong	Moderate	Strong	Moderate	Strong	Strong	Strong
Freeman et al. [68]	Strong	Moderate	Strong	Moderate	Strong	Strong	Strong
Freeman et al. [56]	Strong	Moderate	Strong	Moderate	Strong	Strong	Strong
Freeman et al. [57]	Moderate	Moderate	Strong	Moderate	Strong	Strong	Strong
Shaikh et al. [58]	Moderate	Moderate	Strong	Moderate	Strong	Moderate	Strong
Valmaggia et al. [63]	Moderate	Moderate	Moderate	Moderate	Strong	Moderate	Strong
Valmaggia et al. [55]	Moderate	Moderate	Moderate	Moderate	Strong	Moderate	Strong
Valmaggia et al. [59]	Moderate	Moderate	Strong	Moderate	Strong	Moderate	Strong
Veling et al. [65]	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate	Strong
Veling et al. [66]	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate	Strong

manipulated the contingency behaviour of avatars while participants were exploring a VR student flat [60].

VR to investigate real time responses to social situations

Paranoid ideations

As summarised in Tables 1 and 2, the large majority of studies investigated paranoid ideation and the associated correlates. VR was found to be a valid research method, not only to elicit and measure paranoid ideation in participants, but also to generate participant's attributions about positive, neutral and negative mental states to virtual characters as if they were real people [55, 58, 59, 61–63, 65, 66]. Furthermore, as illustrated in Tables 1 and 2 VR was found to be effective in generating paranoid ideation in people from general population samples [56, 57, 60–62, 68, 70] as well as from individuals with an ultra high risk for psychosis [55, 58, 59, 63, 66, 71] and those already experiencing a psychotic disorder [65, 66].

Anomalous experiences

Individuals experiencing anomalous experiences (such as a propensity to hallucinations, high endorsement of psychic items or higher trait paranoia) reported higher levels of paranoid ideation when exposed to a VR environment [60, 62–64, 66, 70]. These results confirm the validity of VR to assess real-time paranoia in response to a social situation, as it would be expected that an individual who reports trait paranoia would also experience paranoid ideation in an ecologically valid social VR environment.

Quality assessment

Several studies reached a strong rating on the EPHPP global rating (see Tables 1, 2, last column). No studies were excluded based on their quality. However, it is worth mentioning that a strong global rating on the EPHPP allows a moderate score on one of more subscales. Table 3 illustrates the subscale scores for each study: the majority of studies reached moderate scores on selection bias, indicating that the participants recruited for the study were not very likely to be representative of the target population. Indeed quite a few studies were conducted with healthy controls and student samples. The majority of studies had a within subject design, they did not always control for confounders, and often the outcome assessor was not blind to the experimental condition. Most studies had a sound data collection method and few reported withdrawals or drop-outs.

Discussion

We sought to review experimental studies that used VR to investigate the underlying psychological processes and mechanisms associated with the onset and maintenance of

psychosis. The term stress was consider to encompass a broad range of events and experiences encountered in the psychosocial domain that provoke feelings of distress, mental strain, or physiological symptoms of stress. These experiences included traumatic events, social adversity, stressful life events, and subjective feelings of stress and inability to cope.

Childhood bullying victimisation [55]; being the victim of a physical assault [56, 57]; perceived ethnic discrimination [58] and social defeat [59] were associated with paranoid ideation in a VR social environment. The ability to use VR to study the effect of adverse life events on real-time response to social situations in a controlled environment offers an exiting new way to research what contributes to stress sensitivity. Measuring the real-time physiological activation in social situations offers a number of possibilities not only for research purposes but also for assessment and treatment [10, 47]. Interestingly, VR has been shown to be an effective way to overcome excessive self-criticism in people with depression [72, 73], suggesting that VR can be not just a method to assess components of interpersonal sensitivity, but that it also has the potential to be used in the treatment of decrease interpersonal sensitivity.

It has generally been assumed that stress exposure leads to the development of psychosis and psychotic-like-experiences, however, reverse causality is also possible. Symptoms, personality traits and unusual behaviour may predispose individuals to stressful experiences [74]: for example, early symptoms may predispose an individual to bullying victimisation [25, 75, 76]. VR could be embedded in longitudinal research to allow the repeated measurements of current stress response alongside repeated measure of life stressors and symptoms. This type of research could also help in defining resilience factors in people who experience adverse life events, but do not go on to develop psychosis [77, 78]. Previous studies have recognised the similarity between anomalous experiences and intrusive symptoms of post-traumatic stress disorder (PTSD) [79] as well as co-morbid PTSD in people with psychosis (e.g., [80]). While not the topic of the current review, is also worth mentioning that the search revealed a rich body of literature demonstrating the use of VR-assisted therapy for mental health problems (for recent reviews see [71, 81, 82]), and the use of VR in the research, assessment and treatment of psychosis [83, 84] and PTSD [48, 85–87] has previously been the topic of extensive reviews. Lessons can, therefore, be learned from those studies to inform future experimental studies into the psychological mechanisms of psychosis.

Further evidence for the fact that VR is an ecologically valid method to assess real-time responses to social environments was found by studies looking at the effect of manipulating population density and the ethnic density of avatars on the levels of paranoid ideation and physiological activation [65, 66, 69]. Of interest in the context of urbanicity is the finding that changes in the architectural characteristics of a room in VR can be used to change the physiological reaction to closed spaces: compared to participants in a VR room without windows, participants in the room with windows and a nice calming view had lower cortisol reactivity to stress and a quicker recovery after a stress induction test [88].

Using VR to investigate anomalous experiences opens up engaging avenues for further research in the association between paranoid ideation and the mechanisms which underlie the propensity to experience hallucinations, such as self-monitoring, attributional biases, and mental imagery (e.g., [89, 90]). VR studies can also contribute to research the differences between clinical and non-clinical samples of people who report anomalous experiences [91, 92].

Limitations

There were limitations regarding the reviewed studies. The design of all studies was cross-sectional and life events were assessed retrospectively. A number of studies had small sample sizes and healthy control participants in some of the studies were exclusively from a student population, thus differences in social class, employment status, and level of education between people with psychosis and student samples may contribute to some of the differences found between groups. A final possible limitation is also the fact that the reviewed studies were conducted by a relatively small group of researchers who collaborate with each other and who have a strong research interest in paranoid ideation. The focus of research on paranoid ideation reflects on one hand, the long tradition and large body of research of the role of psychological mechanisms in the aetiology of paranoid symptoms [93–96]. On the other hand, this strong focus on paranoid ideation also reflects the interest of the clinical academics who conducted the studies, with the large majority of reviewed studies conducted by Freeman and colleagues, or by researchers who collaborated with him. Future VR research should ensure that other areas of stress research are not neglected.

Conclusion

The reviewed studies suggest that VR can be used to investigate psychological processes and mechanisms associated with psychosis. The ability to assess real-time, cognitive, emotional, behavioural and physiological

responses in a controlled but ecologically valid environment has enormous potential for future research in the mechanisms involved in the onset and maintenance of psychosis.

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