Social environments and mental health

Geraets, Chris Neeltje Wil

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CHAPTER 7

General discussion

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Over the past two decades, research on virtual reality (VR) and mental health has been rapidly expanding. Many studies have shown the potential of VR, though further development is strongly needed. With this thesis, we aimed to increase knowledge on the use of VR for mental healthcare. This was done by performing experimental research as well as investigating the effects of a novel VR-based cognitive behavioral therapy (VR-CBT) in patients with a psychotic disorder and generalized social anxiety disorder (SAD). In this final chapter, an overview and discussion of the main findings will be provided.

Main findings

In **Chapter 2** we used a new VR paradigm to examine whether people with higher psychosis liability keep larger interpersonal distances to others when moving through a virtual café and whether social stressors - in terms of crowdedness, hostility and being of an ethnic minority – influences this distance. Results showed that interpersonal distance regulation in response to social stressors is unaltered in people with psychosis or at ultra-high risk for psychosis. Environmental social stress, social anxiety and distress triggered both people with high and low psychosis liability to maintain larger interpersonal distances.

Chapter 3 investigated the validity of facial emotions of avatars in 100 healthy individuals. The VR emotion recognition task was compared with two conventional tasks using black and white photos and videos. Results showed that performance was very similar between the three tasks. Furthermore, eye-tracking revealed differences in watching behavior across emotions, similar to findings in literature using real faces. These findings support the utility of VR emotional stimuli for assessment and training of emotion recognition.

In **Chapter 4** we examined the effectiveness of a 16-session VR-CBT intervention in 116 paranoid patients with a diagnosis of a psychotic disorder in a multicentre randomized controlled trial (RCT). The intervention was particularly effective in decreasing paranoia and safety behavior, both at post-treatment and at 6-month follow-up as compared to the waiting list. However, no increase in social activity was found during the study period.

In **Chapter 5** we zoomed in on the effects of VR-CBT on positive and negative mental states in daily life, as assessed with the experience sampling method (ESM). VR-CBT significantly decreased negative affective mental states over time but did not increase positive affect. Furthermore, we explored whether VR-CBT may alter the temporal dynamics between negative mental states and paranoia using a network perspective. Interestingly, limited connections were present between paranoia and negative mental states, even at baseline. Thus, no cascade of mental states reinforcing each other was observed. However, mental states mainly reinforced themselves over time. We found preliminary indications that VR-CBT might impact this self-reinforcing mechanism for paranoia.

Chapter 6 examined the feasibility and preliminary effectiveness of VR-CBT in fifteen patients with generalized SAD. We used the same treatment protocol as the RCT for patients with a psychotic disorder. The results of this uncontrolled pilot study showed that VR-CBT is feasible. Findings suggest that VR-CBT can be effective in reducing anxiety (measured both with questionnaires and ESM) as well as depression, and can increase quality of life.

Integration of findings

VR for assessment and understanding of social behavior in psychiatric disorders

It has long been hard to experimentally take into account social environmental factors in research and assessment due to methodological issues. With VR technology we can recreate (social) events in controlled laboratory settings. Herewith VR broadens possibilities in two ways: by providing more ecologically valid tasks to measure (social) behavior and by enabling studying of person-environment interactions.

A need for assessing social processes with more ecologically valid measures has been expressed [1]. Questionnaires and conventional tasks often cannot take into account the multimodal, contextual, and dynamic aspects of social behavior, and may not sufficiently resemble the complex real-world experiences they aim to measure [1]. This may also be reflected in the lack of generalizability of several social cognition and social functioning measures to real-life behavior and functioning [2].

Increasingly more studies use VR to study person-environment interactions. Standardized presentation of VR environments enables differentiating between objective characteristics of the context and an individual's interpretation of that context [1]. Research has shown that VR surroundings can elicit thoughts, feelings and provoke psychiatric symptoms such as paranoid ideations [3–5]. Consistent with these studies, we demonstrated that social environmental stressors (i.e., crowded environment, being of ethnic minority and hostility) can trigger anxiety and distress, and that such stressors influence the distances people keep to others (Chapter 2). Similarly, Dotsch and Wigboldus showed with a VR ethnic minority paradigm that Caucasian people maintained more distance when approaching North-African avatars as opposed to Caucasian avatars [6]. These studies are examples of social stress paradigms, though more variation in stress paradigms is needed. For example, paradigms using both social and non-social stressors, such as noise in the environment or a chaotic environment, can help distinguish between different types of stressors and their impact on thoughts, feelings and behavior in relation to psychiatric disorders.

Our study also demonstrates that the methods we use influence and arguably limit results. Contrary to previous findings, we did not find people with psychosis to keep larger interpersonal distances to others. A difference with previous research is that we could measure interpersonal distance implicitly in VR, or in other words, without people knowing that the behavior is being measured or of interest. Previous research used retrospective or explicit measures, such as questionnaires or tasks (e.g., drawing this preferred distance to others). This suggests that how we think we act, is not always translatable one-to-one to how we behave. Therefore, for studying – and ultimately influencing - social behavior VR technology seems of major importance. These findings also advocate for validation research in the field of social behavior, as we demonstrated that VR experimental paradigms can yield different results than conventional paradigms.

Though the type of paradigm can influence results, traditional and VR paradigms can also yield similar results. We showed that emotions in virtual faces are recognized similarly to

real faces (Chapter 3). This is of importance for future interventions and research using "emotional" avatars, as it indicates that emotions of virtual faces can be used as stimuli. Currently, several research groups are using these stimuli amongst others for VR-CBT in the Netherlands, Belgium, Sweden and the USA [7,8].

Interestingly, for emotion recognition, we also found preliminary indications that the environment might influence this process. In a healthy population sample, more attention was directed to the eyes when recognizing emotions in a crowded shopping street. This could indicate that when the environment gets more demanding of cognitive load, attention gets directed more to the area – the eye region – which is overall most informative for emotion recognition [9,10]. For patients with a neurologic or psychiatric condition, the environment is expected to be more demanding, due to impairments in cognition and attention. Therefore we would expect adverse effects of environmental factors on emotion recognition to be more pronounced in these populations, but further research is needed to test this. Such information is of relevance for how we train emotion recognition skills, as current interventions often use isolated faces as stimuli, even though in real life recognition takes place in highly complex and demanding situations.

Effectiveness of VR-CBT in psychosis and social anxiety

After VR-CBT patients experienced less anxiety, paranoid ideation, and a decrease in the use of safety behavior in social situations (Chapter 4 and 6). These findings are consistent with the research of Freeman and colleagues which is the only other study investigating VR-CBT in patients with a psychotic disorder [11]. They found in a randomized pilot (n = 30) that 6-session VR-CBT was effective in treating persecutory delusions. Patients with a psychotic disorder were immersed in a VR train and lift environment where they tested threat beliefs while dropping safety behavior. In comparison to VR exposure therapy, VR-CBT led to large reductions in paranoia and distress in the real world as assessed with real wold tasks patients found difficult (e.g., going into a shop). Thus both Freeman's and our trial showed large improvements in paranoia and a transfer of benefits to real life. Recently, Pot-Kolder et al. investigated the short-term cost-effectiveness of VR-CBT in the psychosis sample of our RCT. VR-CBT was found to be an economically valid and cost-effective approach for improving patients' health [12].

Regarding (generalized) social anxiety two RCTs tested immersive VR interventions using exercises with semi-structured scenarios [13,14]. Kampmann and colleagues showed that VR exposure therapy (using solely behavioral techniques) was effective in reducing social anxiety and stress in patients with generalized SAD (n = 60) [14]. However, *in vivo* exposure therapy was superior to VR exposure therapy in improving social anxiety, general anxiety, depression and quality of life. Bouchard et al. found VR-CBT to be more effective compared to CBT with *in vivo* exposure (n = 59) [13]. Further, therapists found VR-CBT more practical, and therapeutic alliance, an aspect related to treatment outcome, was similar for both interventions.

In general, meta-analysis and reviews on SAD show that VR therapies result in large effect sizes when compared to a passive control condition or waiting list. However, compared to active control conditions, such as in vivo exposure, similar effectiveness is mostly found [15–17].

This actually tends to be the same for all kinds of anxiety disorders. Carl and Stein conclude in their meta-analysis that when VR therapy is more accessible or preferred, VR therapy can be considered an acceptable and effective alternative [16].

Another important factor to take into account when looking at treatment efficacy is time. A meta-analysis investigated the relationship between time and CBT treatment effect size from 1998 until 2018 [18]. A positive relation between the calendar year and CBT effectiveness for delusions was found, indicating that the effect increased over time. For VR mediated therapies with continuously on-going developments, a similar trend may occur as technical possibilities are increasing rapidly. Developments permit application of new intervention techniques and improvements in software and hardware will result in higher realism and immersion. Such technological improvements are likely to increase treatment efficacy over time.

VR-CBT and social functioning

We expected that if people experience less anxiety during social encounters and avoid less social situations – as practiced in VR – social functioning would also improve. However, VR-CBT did not impact social activity or loneliness in patients with a psychotic disorder or generalized SAD. These two facets of social functioning are important, as limited social contacts and loneliness can form a large burden [19].

Possibly more time is needed than the 6-month duration of the studies in this thesis before treatment effects translate into having more social encounters. Alternatively, we operationalized social activity as the proportion of occasions participants were in the company of others when the ESM app signaled. In hindsight, this was not optimal as in practice, we only knew if people were in company during those ±25 minutes a day that people were completing the diary.

Loneliness did not improve either. Loneliness is more strongly related to subjective aspects of social isolation than objective indicators of solitude [20]. Ludwig et al (2019) examined the relationship between loneliness and symptoms, social cognition and functional outcomes [21]. They found that self-reported loneliness in psychosis was most strongly related to guilt and self-esteem, and was also associated with depression and paranoia. Therefore they suggest that interventions for loneliness should incorporate techniques to improve several of these factors [21]. With VR-CBT we solely targeted paranoia, which may explain the lack of effect.

In short, VR-CBT was insufficient for improving social functioning. As causes of problems in social functioning are often multiple, interventions probably need to be multifaceted as well. Lincoln et al report in their systematic review on CBT for paranoia and hallucinations that targeted CBT focusing on specific symptoms (such as our VR-CBT studies) have higher effect sizes compared to generic CBT that is not symptom focused [22]. Therefore they suggest that evidence-based targeted CBT interventions should be seen as modules that can be combined into more comprehensive therapies. Using a modular approach the content can be adapted according to the individual's needs [23].

VR-CBT working mechanisms in psychosis

In this thesis, we used two different perspectives to investigate the potential working mechanisms of VR-CBT. We investigated mechanisms with mediation analysis (Chapter 4) and temporal mental state networks (Chapter 5). In accordance with literature, dropping of safety behavior was found to be a crucial factor for reducing paranoid ideation (explaining 34% of the change in paranoid ideation) [11,24]. Freeman et al. investigated whether testing threat predictions of persecutory delusions and dropping safety-seeking behavior in VR would lead to a greater reduction in paranoid ideation than VR exposure alone [11]. Indeed, dropping of safety behavior, rather than solely exposure to the feared environment, led to large reductions in paranoid ideations and distress.

Breaking down safety behavior contributes to recovery, as this behavior prevents the development of new experiences and associations. VR is especially suitable for breaking down such behaviors because within the first therapy session most patients are exposed to (VR) environments they usually avoid. Thus in this first session, people start working already on breaking down safety behavior such as avoidance. Further, self-reported social cognition mediated the effect of VR-CBT on paranoid ideation. This improvement in social cognition may be caused by actively challenging cognitions during sessions, or as a secondary effect of safety behavior breaking down, causing people to process social information more adequately.

Zooming in at momentary mental states, no strong temporal associations (within a ±90-minute timeframe) were found between feeling paranoia, lonely, down, anxious and safe. Further, relations between mental states did not change after VR-CBT. Mental states mainly maintained themselves, but there were indications that VR-CBT may intervene in this process, bringing flexibility into mental states. No similar studies in patients with a psychotic disorder are available for comparison as this is a relatively new field. Although the association between negative affect and paranoia is well documented [4,25–29], our findings suggest that moment-to-moment changes in affect do not play a major role in the persistence of paranoia. In contrast, safety behavior and a better understanding of social interactions are of importance for reducing paranoia.

Investigating working mechanisms also brings statistical challenges. We used mediation analysis to investigate the potential working mechanisms of VR-CBT. However, the temporal order of the mediation analysis was based on the assumed mechanisms of VR-CBT but reversed direction of causality cannot be ruled out. Further, in statistical analysis we cannot enter an endless number of variables. Therefore a priori choices had to be made, and we could only investigate a limited number of factors when investigating working mechanisms.

Beyond diagnosis: transdiagnostic approaches

VR-CBT was effective in both patients with a psychotic disorder and SAD, and results were remarkably similar. Further, in both disorders anxiety and paranoia are common, which advocates for transdiagnostic approaches. Transdiagnostic use of VR interventions seems appropriate as VR surroundings and the content of interventions can be personalized to great extent. Especially for symptom-oriented interventions, we could move beyond diagnoses

and future symptom-oriented trials could broaden inclusion criteria, or have no inclusion criteria regarding specific disorders at all [22]. Similar approaches have already been adapted for hallucinations [22].

Next-generation VR

Whereas in this thesis VR therapy was provided by a trained psychologist, recently two trials started investigating automated VR interventions for paranoia [30–32]. For public speaking anxiety, self-led VR interventions have already been tested. Lindner and colleagues showed that a single session of self-led VR exposure therapy was equally effective as a therapist-led intervention, with sustained effects at 6-month follow-up [33].

Although the presence of a therapist is of importance to provide therapy for complex problems, standalone interventions using scripted dialogues and virtual coaches will be needed to scale-up the delivery of psychological therapy [22]. In the Netherlands, less than 5% of patients with a psychotic disorder receive CBT, even though Dutch psychosis care guidelines state CBT as standard care that should be available for everyone [34]. Reasons for this are the limited number of CBT-trained psychologists, and most psychologists who are trained spent only a small proportion of their time on CBT [35]. Many studies for anxiety used VR as a tool for exposure, especially in the first generation interventions VR was used to mimic real-world situations. However, the potential of VR goes far beyond the augmentation of VR as an exposure tool as has been shown e.g., by VR-CBT trials. With VR activities can be carried out that are impossible or infeasible. For example, the latest advancements enable patients to roleplay with avatars and afterward replay the conversation from the perspective of each interlocutor or as an outsider. This can be helpful, as it can provide insights into interactions and can also show e.g., whether you make eye contact. Also, this provides new opportunities for providing feedback.

Another development that can facilitate learning by looking directly from someone else's perspective is referred to as embodiment or body ownership [36–38]. Slater explains embodiment as follows: "embodiment can occur when someone sees a life-sized virtual body substituting her or his own, from a first-person perspective. This virtual body can be programmed to move synchronously with the participant's real body movements, thus leading to the perceptual illusion that the virtual body is her or his actual body" [38]. Often a mirror in the virtual surrounding is used so that someone can observe his/her virtual body. In his review, Slater explains that embodiment can result in changes in attitudes, perception and cognition and behavior through implicit learning [38].

For example, Osimo et al. induced cognitive changes by letting people explain personal problems to a therapist avatar resembling themselves or Sigmund Freud [39]. People alternately switched between themselves receiving therapy, and the therapist avatar thus offering themselves therapy. When the therapist resembled Freud, the mood of participants improved more as compared to the self-resembling therapist avatar. Therefore, Osimo et al. suggest that embodied perspective-taking can cause detachment from habitual ways of thinking and can lead to cognitive changes.

Limitations

The research of this thesis should be interpreted in light of several limitations. As for each chapter limitations have been discussed already, only general limitations will be described here.

First, participants included in the studies may not be fully representative. Concerning the VR-CBT intervention (Chapter 4-6), the most severe and avoidant patients probably did not participate as these patients tend to avoid treatment. This limits the generalizability of our findings. More mobile VR systems that can be used at home could provide a solution for these most avoidant patients to lower thresholds to engage in therapy.

Second, we did not compare VR-CBT to an active control group in neither the RCT nor the pilot study. This limits the claims we can make about the effectiveness of the intervention. Positive effects may have partly derived from the increased amount of contact with therapists.

Third, the follow-up period for VR-CBT was restricted to six months. Longer follow-ups are needed to provide more information on the enduring effects of the intervention, as well as secondary effects. Secondary effects, such as increased social networks or improvements in social and occupational functioning, may take place even after the six-month follow-up period.

Fourth, we mainly used self-report measures to establish the efficacy of VR-CBT. Although ESM is a special form of self-report that does not suffer from recall bias, more objective measures would be recommended for future research [1]. For example, (social) activity levels could be measured with smartwatches or smartphone applications such as Behapp [40–42]. Behapp passively monitors social behavior in terms of social interactions performed with a smartphone (amongst others the number and duration of calls and WhatsApp use) and keeps track of locations through Bluetooth and GPS. Furthermore, reports from family, friends and staff could contribute to measuring social functioning.

Fifth, the VR paradigms had limitations. VR is not 'real', and VR environments still cannot completely resemble real-world situations, especially regarding social behavior. For example, social interactions were limited in VR-CBT as sentences had to be pre-recorded. Therefore, interactive conversations or roleplaying was not possible. Both participants and therapists experienced this as a strong limitation. Furthermore, although the emotion recognition task was performed in a VR shopping street with avatars, next to gaze and turning towards the participant there was no (verbal) interaction with the avatars (Chapter 3). This contrasts with real situations where emotional states are often estimated during conversations.

Finally, the paradigm for measuring interpersonal distance was rather complex (Chapter 2). Choices had to be made on how to define interpersonal distance, as it was measured continuously. Thus the complexity of VR environments also brings new measurement challenges. On the one hand, we need complexity, as it resembles real-world situations better, on the other hand, gathered data must remain meaningful. Finally, in this interpersonal distance paradigm only social stressors were included and no non-social stressors such as noise. This would have improved the research paradigm and enable differentiating effects between types of stressors.

Future research directions

VR as a tool for clinical assessment

An underdeveloped field is the use of VR as a clinical assessment tool [43–45]. VR assessment has been described as very promising as it enables assessment within a context as opposed to self-report and behavioral tasks in laboratory settings. [44,46]. Despite these prospects, most VR symptom studies for psychotic and anxiety disorders have been conducted to validate VR environments or to gain knowledge, but not for diagnostic purposes. There is a promising strand of VR research assessing paranoia, cognitive and social functioning in psychotic disorders [44,47]. However, this research mainly shows that psychiatric symptoms can be assessed in VR. Development of diagnostic tasks and studies on the reliability and validity are needed [44,47].

Concerning our research, the VR emotion recognition task (Chapter 6) needs to be tested in patient samples in which emotion recognition problems are common, such as patients with psychosis, autism and neurological damage, to assess the reliability and validity. Also, research on the cognitive and neural mechanisms underlying the processing of virtual and real emotional faces is needed. Herewith it can be established whether the processing of virtual and real emotional faces is similar, which will be relevant for future assessments and interventions targeting emotion processing.

Integration of VR with other technologies

The integration of VR with other technologies could enormously advance the field. For example, the use of tactile feedback or VR gloves will allow people to see their hands in VR and interact with virtual objects. This can enable more gamified applications as well as embodied interventions. Gamified VR can enhance therapy engagement and potentially the efficacy of interventions.

Furthermore, incorporating physiological measures could provide researchers and therapists with objective measures during VR sessions. Measuring physiological distress through hearth-rate variability (HRV) could form a valuable addition to psychiatry. Targeting stress-regulation with HRV has been piloted in several biofeedback interventions and was found to be promising for paranoia and stress adaptation in psychosis patients [48–50]. Next to ECG, recent studies showed that HRV stress levels can also be derived from the pupil diameter [51,52]. A benefit of pupil measures is that eye-tracking can be integrated into head-mounted displays and no extra wearables are needed.

VR-CBT: the next steps

Although the effects of VR-CBT were positive, it also revealed improvements for the intervention. First, future research needs to incorporate options for flexible dialogues with avatars which will enhance personalization [15]. This is a crucial improvement as treatment goals in patients with social anxiety and psychosis often concern situations in which interaction takes place. Furthermore, incorporating avatars that show more mood states than neutral and hostile, as well as gestures, will improve possibilities for therapists to create real-like social situations. Future research should also (unlike the studies in this thesis) incorporate

homework since a meta-analysis on attrition of VR exposure therapy for anxiety found that homework was the best predictor for non-attrition [53]. Thus, homework may improve efficacy by reducing drop-out and by stimulating practicing new behavior in the real world. Which also has an additional advantage as real-world practicing also promotes generalization.

The next step will be to compare VR-CBT to conventional CBT. This is needed to replicate our findings and to investigate whether VR-CBT is more effective, efficient (i.e., are fewer sessions needed for a similar effect) and/or cost-effective in comparison with conventional CBT. Recently, a multicentre RCT has started to investigate this in patients with a psychotic disorder (TOPIC; Dutch Trial Register: NL7758). Furthermore, studies with follow-ups longer than 12 months are extremely rare for VR interventions. Follow-ups focussing on the stability of results in the long term are strongly needed [43].

Network perspective of mental states in psychosis

A relatively recent perspective on psychiatric disorders is the network perspective. In short, it entails that mental states or symptoms can activate each other, like nodes in a network [54]. Concerning mental states in psychiatric disorders, a dysfunctional cascade may exist of mental states triggering each other [54–56]. We did not find evidence to confirm this on a group level for paranoia in psychosis patients who participated in the VR-CBT trial. This may be caused by the large heterogeneity between patients in terms of symptoms and functioning, which questions the usefulness of network analyses on a group level for psychosis patients.

Alternatively, different mechanisms may be involved. We found indications that mental states may be mainly self-maintaining. Therefore, based on our findings we formulated two hypotheses on the maintenance of mental states in psychosis, in particular paranoia. The first hypothesis states that mental states such as paranoia are mainly self-maintaining in individuals with a psychotic disorder as indicated by high autocorrelations of mental states over time. The second hypothesis states that mental states in daily life, once activated, may recover more quickly after treatment and regain flexibility as a consequence of the therapy. Future research is needed to investigate these hypotheses.

Clinical Implications

VR-CBT intervention

This thesis shows that paranoia and social anxiety can be effectively treated with VR-CBT and that VR-CBT can induce changes in daily life. Even though practicing in daily life was not a part of the intervention, therapeutic effects did generalize to everyday life. The results of this thesis also emphasize the importance of intervening on safety behavior in patients with a psychotic disorder and thus intervening on a behavioral level.

To improve social functioning, targeted CBT for several domains seems to be needed. A modular approach would be suited for this. Using an individually tailored case formulation-driven approach and combining evidence-based interventions e.g., for social cognition, paranoia, hallucinations and insomnia may together result in improvements in social functioning, one of the most important fields of recovery for patients [22,57].

Our findings also had practical implications. First, in response to the experiences of patients and therapists the VR-CBT software has been improved. VR environments and avatars have gained in realism and dynamic conservations with an avatar or even a group of avatars are now possible by using a microphone and a speech scrambler [8]. Improvements have been made in (mixed) emotions and gestures of avatars, the usability of the software and the quality of graphics. See Fig 1 for screenshots of the 2014 VR environment (used in Chapters 4 and 6) and of the VR-CBT software released in 2019. Interestingly, although high realism of VR seems of importance, the 2014 software already produced good results. This indicates that high-end VR graphics are not per se necessary for therapeutic effects.

Fig 1. 2D screenshots of a 2014 VR bus environment and a 2019 VR café environment. (Source: CleVR).

Dissemination of VR technology

Dissemination of VR mediated interventions and eHealth innovations in general for mental healthcare has proven to be tough. Several obstacles have been identified such as high costs, technical obstacles, reservations against technology, limited treatment indications and therapists found VR difficult to apply due to a lack of training [43,58,59].

Because VR-CBT was found to be effective, several steps were undertaken for dissemination. GGZ Delfland (participating center of the VR-CBT trial), health insurer DSW and VR company CleVR submitted an innovative care performance application for VR-CBT at the Dutch Healthcare Authority (Nederlandse Zorgautoriteit; BR/REG-17163). This application was approved for a pilot period of two years. In practice, this entails that VR-CBT can be reimbursed by health insurance companies in the Netherlands and that the hourly compensation is higher for VR-CBT than regular CBT to compensate for VR equipment costs.

Education for mental health care professionals is also needed for implementation. Options for this can be VR-specific training for licensed psychologists, but also including this subject in postmaster education. Furthermore, participating in scientific trials as a mental health care institution can be a good way for knowledge dissemination. This stimulates personnel to become familiar with the technology in a more structured fashion. Currently, in the Netherlands, training for VR-CBT and other VR mediated interventions are provided by our research group (www.vrmentalhealth.nl).

The above-mentioned steps were important for implementation. An improved version of the VR-CBT intervention used in this thesis is commercially available. This was another implementation factor: working together with a commercial partner (CleVR) for the development and implementation, who are also able to provide technical support. Currently, 25 different mental health care institutions in the Netherlands are using VR-CBT software.

Concluding Remarks

The research in this thesis shows that VR is an extremely helpful tool that has added value in the field of mental health in multiple ways. VR provides new options to perform research, assessments and interventions in ecologically valid environments. The results of our VR-CBT studies are promising, though further research is needed to confirm the efficacy and cost-effectiveness. VR is a continuously progressing field that has not reached its full potential yet. More research, as well as education of healthcare professionals, is needed and innovations such as stand-alone VR sets which people can use at home, will be essential for the future.

References

1. Hermans K, Achterhof R, Myin-Germeys I, Kasanova Z, Kirtley O, Schneider M. Improving ecological validity in research on social cognition. In: Lewandowski KE, Moustafa AA, eds. *Social Cognition in Psychosis*. London: Elsevier Academic Press; 2019:249-268. doi:10.1016/B978-0-12-815315-4.00010-0

2. Horan WP, Kern RS, Shokat-Fadai K, Sergi MJ, Wynn JK, Green MF. Social cognitive skills training in schizophrenia: An initial efficacy study of stabilized outpatients. *Schizophr Res*. 2009;107(1):47-54. doi:10.1016/j.schres.2008.09.006

3. van Bennekom MJ, de Koning PP, Denys D. Virtual Reality Objectifies the Diagnosis of Psychiatric Disorders: A Literature Review. *Front Psychiatry*. 2017;8(163):1-7. doi:10.3389/fpsyt.2017.00163

4. Veling W, Pot-Kolder R, Counotte J, van Os J, van der Gaag M. Environmental Social Stress, Paranoia and Psychosis Liability: A Virtual Reality Study. *Schizophr Bull*. 2016;42(6):1363-1371. doi:10.1093/schbul/sbw031

5. Freeman D. Studying and Treating Schizophrenia Using Virtual Reality: A New Paradigm. *Schizophr Bull*. 2008;34(4):605-610. doi:10.1093/schbul/sbn020

6. Dotsch R, Wigboldus DHJ. Virtual prejudice. *J Exp Soc Psychol*. 2008;44(4):1194-1198. doi:10.1016/j.jesp.2008.03.003

7. Klein Tuente S, Bogaerts S, van IJzendoorn S, Veling W. Effect of virtual reality aggression prevention training for forensic psychiatric patients (VRAPT): study protocol of a multi-center RCT. *BMC Psychiatry*. 2018;18(251):1-9. doi:10.1186/s12888-018-1830-8

8. Nijman SA, Veling W, Greaves-Lord K, et al. Dynamic Interactive Social Cognition Training in Virtual Reality (DiSCoVR) for social cognition and social functioning in people with a psychotic disorder: study protocol for a multicenter randomized controlled trial. *BMC Psychiatry*. 2019;19(272):1-11. doi:10.1186/s12888-019-2250-0

9. Calvo MG, Nummenmaa L. Perceptual and affective mechanisms in facial expression recognition: An integrative review. *Cogn Emot*. 2016;30(6):1081-1106. doi:10.1080/02699931.2015.1049124

10. Wells LJ, Gillespie SM, Rotshtein P. Identification of Emotional Facial Expressions: Effects of Expression, Intensity, and Sex on Eye Gaze. Key A, ed. *PLoS One*. 2016;11(12):1-20. doi:10.1371/journal.pone.0168307

11. Freeman D, Bradley J, Antley A, et al. Virtual reality in the treatment of persecutory delusions: Randomised controlled experimental study testing how to reduce delusional conviction. *Br J Psychiatry*. 2016;209(1):62-67. doi:10.1192/bjp.bp.115.176438

12. Pot-Kolder R, Veling W, Geraets C, et al. Cost-Effectiveness of Virtual Reality Cognitive Behavioral Therapy for Psychosis: Health-Economic Evaluation Within a Randomized Controlled Trial. *J Med Internet Res*. 2020;22(5):1-13. doi:10.2196/17098

13. Bouchard S, Dumoulin S, Robillard G, et al. Virtual reality compared with in vivo exposure in the treatment of social anxiety disorder: A three-arm randomised controlled trial. *Br J Psychiatry*. 2017;210(4):276-283. doi:10.1192/bjp.bp.116.184234

14. Kampmann IL, Emmelkamp PMG, Hartanto D, Brinkman W-P, Zijlstra BJH, Morina N. Exposure to virtual social interactions in the treatment of social anxiety disorder: a randomized controlled trial. *Behav Res Ther*. 2016;77:147-156. doi:10.1016/j.brat.2015.12.016

15. Emmelkamp PMG, Meyerbröker K, Morina N. Virtual Reality Therapy in Social Anxiety Disorder. *Curr Psychiatry Rep*. 2020;22(32). doi:10.1007/s11920-020-01156-1

16. Carl E, Stein AT, Levihn-Coon A, et al. Virtual reality exposure therapy for anxiety and related disorders: A meta-analysis of randomized controlled trials. *J Anxiety Disord*. 2019;61:27-36. doi:10.1016/j.janxdis.2018.08.003

17. Chesham RK, Malouff JM, Schutte NS. Meta-Analysis of the Efficacy of Virtual Reality Exposure Therapy for Social Anxiety. *Behav Chang*. 2018;35(3):152-166. doi:10.1017/bec.2018.15

18. Sitko K, Varese F, Sellwood W, Hammond A, Bentall R. The dynamics of attachment insecurity and paranoid thoughts: An experience sampling study. *Psychiatry Res*. 2016;246:32-38. doi:10.1016/j.psychres.2016.08.057

19. Michalska da Rocha B, Rhodes S, Vasilopoulou E, Hutton P. Loneliness in Psychosis: A Meta-analytical Review. *Schizophr Bull*. 2018;44(1):114-125. doi:10.1093/schbul/sbx036

20. Giacco D, Palumbo C, Strappelli N, Catapano F, Priebe S. Social contacts and loneliness in people with psychotic and mood disorders. *Compr Psychiatry*. 2016;66:59-66. doi:10.1016/j.comppsych.2015.12.008

21. Ludwig KA, Nye LN, Simmons GL, et al. Correlates of loneliness among persons with psychotic disorders. *Soc Psychiatry Psychiatr Epidemiol*. 2020;55:549-559. doi:10.1007/s00127-019-01789-5

22. Lincoln TM, Peters E. A systematic review and discussion of symptom specific cognitive behavioral approaches to delusions and hallucinations. *Schizophr Res*. 2019;203:66-79. doi:10.1016/j.schres.2017.12.014

23. Freeman D, Waite F, Emsley R, et al. The efficacy of a new translational treatment for persecutory delusions: study protocol for a randomised controlled trial (The Feeling Safe Study). *Trials*. 2016;17(134):1-8. doi:10.1186/s13063-016-1245-0

24. Freeman D, Garety PA, Kuipers E, Fowler D, Bebbington PE, Dunn G. Acting on persecutory delusions: The importance of safety seeking. *Behav Res Ther*. 2007;45(1):89-99. doi:10.1016/j.brat.2006.01.014

25. Fowler D, Hodgekins J, Garety P, et al. Negative Cognition, Depressed Mood, and Paranoia: A Longitudinal Pathway Analysis Using Structural Equation Modeling. *Schizophr Bull*. 2012;38(5):1063-1073. doi:10.1093/schbul/sbr019

26. Freeman D, Emsley R, Dunn G, et al. The Stress of the Street for Patients With Persecutory Delusions: A Test of the Symptomatic and Psychological Effects of Going Outside Into a Busy Urban Area. *Schizophr Bull*. 2015;41(4):971-979. doi:10.1093/schbul/sbu173

27. Myin-Germeys I, Kasanova Z, Vaessen T, et al. Experience sampling methodology in mental health research: new insights and technical developments. *World Psychiatry*. 2018;17(2):123-132. doi:10.1002/wps.20513

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

29. Oorschot M, Lataster T, Thewissen V, et al. Symptomatic remission in psychosis and real-life functioning. *Br J Psychiatry*. 2012;201(3):215-220. doi:10.1192/bjp.bp.111.104414

30. Freeman D, Yu L, Kabir T, et al. Automated virtual reality (VR) cognitive therapy for patients with psychosis: study protocol for a single-blind parallel group randomised controlled trial (gameChange). *BMJ Open*. 2019;9(8):1-8. doi:10.1136/bmjopen-2019-031606

31. Freeman D, Lister R, Waite F, et al. Automated psychological therapy using virtual reality (VR) for patients with persecutory delusions: study protocol for a single-blind parallel-group randomised controlled trial (THRIVE). *Trials*. 2019;20(87):1-8. doi:10.1186/s13063-019-3198-6

32. Lambe S, Knight I, Kabir T, et al. Developing an automated VR cognitive treatment for psychosis: gameChange VR therapy. *J Behav Cogn Ther*. 2020;30(1):33-40. doi:10.1016/j.jbct.2019.12.001

33. Lindner P, Miloff A, Fagernäs S, et al. Therapist-led and self-led one-session virtual reality exposure therapy for public speaking anxiety with consumer hardware and software: A randomized controlled trial. *J Anxiety Disord*. 2019;61:45-54. doi:10.1016/j.janxdis.2018.07.003

34. GGZ Standaarden. Zorgstandaard Psychose. *Kwaliteitsontwikkeling GGZ*. 2020:1-126. https://www.ggzstandaarden.nl/zorgstandaarden/psychose.

35. Staring T, van den Berg D, Schuurmans H, van der Vleugel B. *Praten Naast Pillen: Krijgt de Patient Met Psychose Dat Wel?*; 2019. https://www.vgct.nl/stream/19.05.vgctsurvey-praten-naast-pillen.pdf.

36. Slater M, Sanchez-Vives M V. Enhancing Our Lives with Immersive Virtual Reality. *Front Robot AI*. 2016;3. doi:10.3389/frobt.2016.00074

37. Bailey JO, Bailenson JN. When Does Virtual Embodiment Change Our Minds? *Presence Teleoperators Virtual Environ*. 2016;25(3):222-233. doi:10.1162/PRES

38. Slater M. Implicit Learning Through Embodiment in Immersive Virtual Reality. In: *Virtual, Realities and Mixed Augmented in Education*. Singapore: Springer; 2017:19-33. doi:10.1007/978-981-10-5490-7_2

39. Osimo SA, Pizarro R, Spanlang B, Slater M. Conversations between self and self as Sigmund Freud—A virtual body ownership paradigm for self counselling. *Sci Rep*. 2015;5(13899):1-14. doi:10.1038/srep13899

40. Wee ZY, Yong SWL, Chew QH, Guan C, Lee TS, Sim K. Actigraphy studies and clinical and biobehavioral correlates in schizophrenia: a systematic review. *J Neural Transm*. 2019;126:531-558. doi:10.1007/s00702-019-01993-2

41. Jongs N, Jagesar R, Koning I, et al. Passive behavioral monitoring in neuropsychiatric disorders using smartphone technology. *Eur Neuropsychopharmacol*. 2018;28(1):S87-S88. doi:10.1016/j.euroneuro.2017.12.126

42. Mulder T, Jagesar RR, Klingenberg AM, P. Mifsud Bonnici J, Kas MJ. New European privacy regulation: Assessing the impact for digital medicine innovations. *Eur Psychiatry*. 2018;54:57-58. doi:10.1016/j.eurpsy.2018.07.003

43. Fernández-Álvarez J, Di Lernia D, Riva G. Virtual Reality for Anxiety Disorders: Rethinking a Field in Expansion. In: Kim Y-K, ed. *Anxiety Diorders*. Singapore: Springer Nature; 2020:389-414. doi:10.1007/978-981-32-9705-0_21

44. Freeman D, Reeve S, Robinson A, et al. Virtual reality in the assessment, understanding, and treatment of mental health disorders. *Psychol Med*. 2017;47(14):2393-2400. doi:10.1017/S003329171700040X

45. Rus-Calafell M, Garety P, Sason E, Craig TJK, Valmaggia LR. Virtual reality in the assessment and treatment of psychosis: a systematic review of its utility, acceptability and effectiveness. *Psychol Med*. 2018;48(3):362-391. doi:10.1017/S0033291717001945

46. Riva G. Virtual reality as assessment tool in psychology. In: *Studies in Health Technology and Informatics*. ; 1997:71-79. doi:10.3233/978-1-60750-888-5-71

47. Macedo M, Marques A, Queirós C. Virtual reality in assessment and treatment of schizophrenia: a systematic review. *J Bras Psiquiatr*. 2015;64(1):70-81. doi:10.1590/0047-2085000000059

48. Clamor A, Koenig J, Thayer JF, Lincoln TM. A randomized-controlled trial of heart rate variability biofeedback for psychotic symptoms. *Behav Res Ther*. 2016;87:207-215. doi:10.1016/j.brat.2016.10.003

49. Breitborde NJK, Dawley D, Bell EK, Vanuk JR, Allen JJB, Lane RD. A personalized paced-breathing intervention to increase heart rate variability among individuals with first-episode psychosis following stress exposure. *Schizophr Res*. 2015;169(1-3):496-497. doi:10.1016/j.schres.2015.11.005

50. Maarsingh BM, Bos J, Van Tuijn CFJ, Renard SB. Changing Stress Mindset Through Stressjam: A Virtual Reality Game Using Biofeedback. *Games Health J*. 2019;8(5):326-331. doi:10.1089/g4h.2018.0145

51. Jerčić P. Arousal Measurement Reflected in the Pupil Diameter for a Decision-Making Performance in Serious Games. In: van der Spek E, Göbel S, Do E, Clua E, Baalsrud Hauge J, eds. *Entertainment Computing and Serious Games*. Springer; 2019:287-298. doi:10.1007/978-3-030-34644-7_23

52. Park S, Won MJ, Lee DW, Whang M. Non-contact measurement of heart response reflected in human eye. *Int J Psychophysiol*. 2018;123:179-198. doi:10.1016/j.ijpsycho.2017.07.014

53. Benbow AA, Anderson PL. A meta-analytic examination of attrition in virtual reality exposure therapy for anxiety disorders. *J Anxiety Disord*. 2019;61:18-26. doi:10.1016/j.janxdis.2018.06.006

54. Cramer AOJ, Waldorp LJ, van der Maas HLJ, Borsboom D. Comorbidity: A network perspective. *Behav Brain Sci*. 2010;33(2-3):137-150. doi:10.1017/S0140525X09991567

55. Nelson B, McGorry PD, Wichers M, Wigman JTW, Hartmann JA. Moving From Static to Dynamic Models of the Onset of Mental Disorder. *JAMA Psychiatry*. 2017;74(5):528-534. doi:10.1001/jamapsychiatry.2017.0001

56. Wigman JTW, Collip D, Wichers M, et al. Altered Transfer of Momentary Mental States (ATOMS) as the Basic Unit of Psychosis Liability in Interaction with Environment and Emotions. Scott JG, ed. *PLoS One*. 2013;8(2):1-11. doi:10.1371/journal.pone.0054653

57. Turner DT, Burger S, Smit F, Valmaggia LR, van der Gaag M. What Constitutes Sufficient Evidence for Case Formulation–Driven CBT for Psychosis? Cumulative Meta-analysis of the Effect on Hallucinations and Delusions. *Schizophr Bull*. 2020;(sbaa045). doi:10.1093/schbul/sbaa045

58. Eichenberg C, Wolters C. Virtual Realities in the Treatment of Mental Disorders: A Review of the Current State of Research. In: *Virtual Reality in Psychological, Medical and Pedagogical Applications*. InTech; 2012:35-64. doi:10.5772/50094

59. Botella C, Baños RM, García-Palacios A, Quero S. Virtual Reality and Other Realities. In: Hofmann SG, Asmundson G, eds. *The Science of Cognitive Behavioral Therapy*. San Diego, CA: Academic press; 2017:551-590. doi:10.1016/B978-0-12-803457-6.00022-2