VIRTUAL REALITY-BASED INTERVENTIONS FOR TREATING **DEPRESSION IN THE CONTEXT OF COVID-19 PANDEMIC: INDUCING THE PROFICIT IN POSITIVE EMOTIONS AS A KEY CONCEPT OF RECOVERY AND A PATH BACK TO NORMALITY**

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SUMMARY

Background: During the COVID-19 pandemic as much as 40% of the global population reported deterioration in depressive mood, whereas 26% experienced increased need for emotional support. At the same time, the availability of on-site psychiatric care declined drastically because of the COVID-19 preventive social restriction measures. To address this shortfall, telepsychiatry assumes a greater role in mental health care services. Among various on-line treatment modalities, immersive virtual reality (VR) environments provide an important resource for adjusting the emotional state in people living with depression. Therefore, we reviewed the literature on VR-based interventions for depression treatment during the COVID-19 pandemic.

Subjects and methods: We searched the PubMed and Scopus databases, as well as the Internet, for full-length articles published during the period of 2020-2022 citing a set of following key words: "virtual reality", "depression", "COVID-19", as well as their terminological synonyms and word combinations. The inclusion criteria were: 1) the primary or secondary study objectives included the treatment of depressive states or symptoms; 2) the immersive VR intervention used a head-mounted display (HMD); 3) the article presented clinical study results and/or case reports 4) the study was urged by or took place during the COVID-19-associated lockdown period.

Results: Overall, 904 records were retrieved using the search strategy. Remarkably, only three studies and one case report satisfied all the inclusion criteria elaborated for the review. These studies included 155 participants: representatives of healthy population (n=40), a case report of a patient with major depressive disorder (n=1), patients with cognitive impairments (n=25), and COVID-19 patients who had survived from ICU treatment (n=89). The described interventions used immersive VR scenarios, in combination with other treatment techniques, and targeted depression. The most robust effect, which the VR-based approach had demonstrated, was an immediate post-intervention improvement in mood and the reduction of depressive symptoms in healthy population. However, studies showed no significant findings in relation to both short-term effectiveness in treatment of depression and primary prevention of depressive symptoms. Also, safety issues were identified, such as: three participants developed mild adverse events (e.g., headache, "giddiness", and VR misuse behavior), and three cases of discomfort related to wearing a VR device were registered.

Conclusions: There has been a lack of appropriately designed clinical trials of the VR-based interventions for depression since the onset of the COVID-19 pandemic. Moreover, all these studies had substantial limitations due to the imprecise study design, small sample size, and minor safety issues, that did not allow us making meaningful judgments and conclude regarding the efficacy of VR in the treatment of depression, taking into account those investigations we have retrieved upon the inclusion criteria of our particularistic review design. This may call for randomized, prospective studies of the short-term and long-lasting effect of VR modalities in managing negative affectivity (sadness, anxiety, anhedonia, self-guilt, ignorance) and inducing positive affectivity (feeling of happiness, joy, motivation, self-confidence, viability) in patients suffering from clinical depression.

Key words: COVID-19 - depression - digital psychiatry - immersive virtual reality - lockdown - mHealth - negative affectivity pandemic - positive emotions - social restrictions - virtual reality

Abbreviations: AR - augmented reality; DASS-21 - Depression Anxiety Stress Scale; DSM-IV - Diagnostic and Statistical Manual of Mental Disorders, 4th revision; HMD - head-mounted display; ICU - intensive care unit; LCD - liquid crystal display; PICO-SD - P: participants, I: intervention, C: comparison, O: outcome, and SD: study design; PRISMA - Preferred Reporting Items for Systematic Review and Meta-Analysis; RDoC - Research Domain Criteria; SCID-I - Structured Clinical Interview for DSM-IV axis I disorders; SD - standard deviation; VR - virtual reality

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INTRODUCTION

Since the emergence of the COVID-19 pandemic, studies around the world have reported an increased incidence of signs and symptoms of depression in the general population, and also in vulnerable groups such as females, students and youth, the elderly, and people with a history of bipolar depression or other mental disorders (Fountoulakis et al. 2021, 2022a,b, Nadareishvili et al. 2022, Panfil et al. 2022, Smirnova et al. 2021, Vrublevska et al. 2021, 2022, Zhang et al. 2022). Despite this increasing need, attendance at medical facilities drastically declined in the early months of the pandemic (Brandizzi et al. 2022, Carrasco et al. 2021, Di Lorenzo et al. 2022), mostly because of the social isolation measures and precautions. On the other hand, the large COMET-G study based on the joint analysis of the data (n=55, 589) from 40 countries, indicated a global 40.3% incidence of depressive mood, and 26.2% reported a need for emotional support during the pandemic (Fountoulakis et al. 2022a). Thus, since the pandemic began, a gap has emerged between the increasing numbers of individuals over the world with depressive symptoms and the declining availability of healthcare in the face of the pandemic (Anderson et al. 2021).

Responses to this challenge include various attempts to substitute in-person visits with telepsychiatry (Sasangohar et al. 2020, Stewart & Appelbaum 2020, Wasserman et al. 2020). However, forms of medical assistance based on mobile communication technologies have been characterized by the low level of patients' adherence to therapy (Aboujaoude et al. 2021), and their efficacy in relation to clinical states of depression was found to be controversial (Astafeva et al. 2022). Moreover, telemedicine approaches have a disadvantage due to the specific nature of psychiatric assessments and the particular care needs of patients with depression. Such approaches are inherently limited within their ability to create a comfortable and safe environment, and in their fitness to provide thorough clinical observation and deliver supportive, thoughtful, and in-depth verbal communication, in particular, in mild depression where language and appropriate conversation with patient especially matter (Smirnova et al. 2018, Wasserman et al. 2020).

VR-based interventions using virtual (VR) or augmented (AR) reality devices present an emerging approach to telepsychiatry for patients with depression (Baghaei et al. 2021, Imperatori et al. 2020). An immersive VR-environment can create favorable conditions both for clinical examination and for delivery of therapeutic interventions. According to the recent scoping reviews, a technique of creating virtual rooms with immersive environments, which also fit the needs of psychiatric assessment, represents the most relevant applications of VR technology in the treatment of depression. Other viable approaches include the use of VR-gaming technologies for diagnosis, cognitive behavioral therapy (CBT) and cognitive training, and distraction of patients from stressful events via a safe environment which offers the engaging virtual content (Baghaei et al. 2021, Chitale et al. 2022). Following this background, our review addressed a narrative synthesis of reports on the use of immersive VR for depression treatment in the setting of the COVID-19 pandemic.

SUBJECTS AND METHODS

Methods

The review sequentially addresses the following topics: (i) the number of the studies performed during the COVID-19 pandemic and using VR scenarios for managing the symptoms of depression; (ii) the studies that included VR interventions and have been focused on the treatment of depressive episodes; (iii) the particular treatment methods based on VR use; (iv) any differences between the pre-pandemic VR-based studies and those trials initiated during the COVID-19associated lockdown; (v) the perspectives of the VR modality in depression treatment; (vi) disputable and challenging issues related to the VR-based approaches in the treatment of depression.

Subjects and search strategy

The PubMed and Scopus databases were searched for the paper types "article", "review", "conference paper", "note", "short survey", "case report" using a set of key words consisting of the terms "virtual reality", "depression", "COVID-19", as well as their terminological synonyms and word combinations, without any language criteria restrictions. The chosen time period from 2020 to 2022 was in line with the start of the COVID-19 pandemic. Additionally, we performed a manual search on the Internet using the keywords "virtual reality" and "depression", and "COVID-19".

Selection criteria. We reviewed the studies that examined the treatment of depression using VR technologies during the period of the COVID-19 pandemic, focusing on the following inclusion criteria: 1) the primary or secondary study objectives included the treatment of depressive states or symptoms; 2) the intervention entailed immersive VR using a headmounted display (HMD); 3) the article presented clinical study results and/or case report; 4) the study was urged by or took place during the COVID-19associated lockdown period.

Exclusion criteria were: (i) the article did not report the clinical study results and/or case report; (ii) the intervention used a non-immersive mode of VR; (iii) the study was designed and conducted before the COVID-19 pandemic; (iv) the immersive VR treatment did not target clinical depression or comorbid depressive state; (v) outcomes did not reflect symptoms of depression as assessed by the valid diagnostic instrument/standardized scale.

Data extraction

We analyzed the selected studies according to the PICO-SD algorithm (P: participants, I: intervention, C: comparison, O: outcome, and SD: study design) developed by the Cochrane Collaboration (Higgins et al. 2011). We extracted the key data on the characteristics of the studies including authorship, publication year, study design, number of participants, type of intervention and control, relevant outcome measure, main findings, and self-reported study limitations.

Quality assessment

Since only one of the selected studies had a randomized controlled trial design, we did not use a standard quality assessment scale to rank the studies, but accurately defined their limitations.

Qualitative analysis

The content analysis of the selected studies provided the basis for the data narrative synthesis and summarizing the obtained results. We followed our scientific hypothesis on the potentially efficient use of immersive VR for depression treatment in the setting of the COVID-19 pandemic and associated lockdown/ social restriction measures to systematize the findings for further precise planning of the evidence-based research in the field. The following parameters were in the focus of our professional attention: 1) depression was the main target for treatment, or was regarded as the mood disorder being concurrent with any other mental or somatic disease; 2) the participants were clinically diagnosed with depressive disorder or self-reported on a depressive state; 3) the intervention based on the immersive VR was prescribed/supervised by a health professional, or was used by the patient as a self-help technique; 4) the immersive VR treatment was combined with other treatment modalities or used separately as a basic therapy; 5) the level of immersion expansion provided by the VR equipment and the details of content/scenario of the VR session; 6) either the content of VR treatment was specially designed for the particular patient's condition, or the VR content was a standardized one for the general public use; 7) the duration and number of VR sessions; 8) the factor of a control group being included into the study design; 9) the depression severity as measured with valid scales; 10) the duration of the follow-up period; 11) the reported adverse events or issues of discomfort caused by the VR use/experience; 12) the restrictions or treatment limitations imposed by the COVID-19 pandemic. Dubious cases were discussed by the team under supervision of DS.

RESULTS

The PubMed and Scopus search results provided 902 headlines. The additional manual search in the Internet using the keywords "virtual reality" and "depression", and "COVID-19" resulted in 16 research papers. After removing the duplicates, within the 904 records, 807 papers were excluded from the review due to their irrelevance to the topic according to the inclusion criteria based on the detailed review of the titles and abstracts content. The full-text analysis of the remaining 97 articles revealed the three studies and one clinical case report that were eligible for inclusion; the other articles were excluded for the following reasons: (1) articles did not report clinical study results or clinical case (n=49); (2) studies were conducted before the COVID-19 pandemic (n=34); (3) studies did not include depression or depressive symptoms (n=6); (4) studies used non-immersive VR (n=3); (5) severity of depression was not measured (n=1), thus leaving only four studies meeting all the inclusion criteria. Figure 1 depicts a flow diagram detailing the review process and the results at each stage of the literature search.

Study characteristics are shown in Table 1. The studies included a combined sample of 155 participants with varying health status: representatives of healthy population (n=40), a person with the diagnosis of major depressive disorder (n=1), patients with cognitive impairments (n=25), and COVID-19 patients who had survived from the ICU treatment (n=89). The interventions used immersive VR scenarios in combination with other therapeutic techniques targeting depression or other major mental and behavioural disorder diagnosis. Studies were initiated and published during the period between 2020 and 2022 in the context of ongoing COVID-19 pandemic.

The study by Brimelow et al. (2022) included residents of an aged care facility (n=25), who have been diagnosed with a variety of mental disturbances from the complaints related to mild cognitive symptoms to the clinical states of progressive dementia, of whom eight (32%) had a diagnosis of depression (Brimelow et al. 2022). During six VR sessions the authors observed an immediate favorable effect of the VR intervention on mood and depression symptoms. Nevertheless, there was no prospective longitudinal data provided on this amelioration of mood, which hinders drawing any strong conclusions on the VR efficacy with respect to depression treatment. Moreover, the observed changes might well reflect the affective liability that is a symptom of neurocognitive disorders.

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	Study limitations	 Small sample size Adaptation to specific condition (dementia) No control group Observer bias 	 Small sample size No control group Self-reported evaluation No follow-up 	 No experimental control on immersive vs. non- immersive modality No active control group, controls were from waiting list and entered the study Small sample size Short follow-up period of 2 weeks 	 The presence of psychological distress at the follow-uptime point was not measured before randomization Language restrictions, for Dutch native speakers only Patients with primary neurological impairments or active psychiatric diseases were excluded 	in Dementia; lepressive disorder; 21 - Depression Anxiety e syndrome;
Table 1. Characteristics of included studies on the use of immersive virtual reality for depression treatment during the Covid-19 pandemic	Main findings	 Statistically significant reduction in depression scores (z= -2.60, P=0.009; r=0.69). The VR intervention elicited both immediate BPS outcomes (mood) and outcomes to more persistent BPS (depression, anxiety, agitation), where depression was reduced most significantly at follow-up. 2 participants had mild adverse effects, 3 participants reported discomfort using the HMD 	 PHQ-9 score reduced from initial 8 to 5 post-intervention SSQ score of 1.8 out of a potential 48 BAM score of 3 out of potential 21 The participant rated the use of the HMID as highly acceptable regardless the experienced mild simulator sickness symptoms 	 no significant effect of the modality (immersive vs. non- immersive) on the treatment results revealed a significant effect of time for depression, stress, general distress, perceived stress and hopelessness clinically significant improvements were registered for all outcomes 	 31% of COVID-19 ICU-survivors experienced psychological distress up to 6 months after discharge delayed ICU-VR intervention did not significantly improve psychological recovery or quality of life treatment of fully established psychiatric disorders may require more complex treatment strategies 	<i>Note:</i> HMD - head-mounted display; OERS - Observed Emotions Rating Scale; PEAR - Person-Environment Apathy Rating; CSDD - Cornell Scale for Depression in Dementia; GAD-7 - Generalized Anxiety Disorder 7-item scale; CMAI - Cohen Mansfield Agitation Inventory; BPS - behavioral and psychological symptom; MDD - major depressive disorder; BA - behavioral activation; PHQ-8, PHQ-9 - Patient Health Questionnaire-8, -9; SSQ - Simulator Sickness Questionnaire; BAM - Brief Agitation Measure; DASS-21 - Depression Anxiety Stress Scale; PSS - Perceived Stress Scale; BHS - Hospelessness Scale; RCT - randomized controlled trial; ICU - intensive care unit; PICS - postintensive care syndrome; IFS-R - Immact of Event Scale-Revised: HADS - Hospital Anxiety and Demession Scale: SF-36 - Short-Form 36: FO-5D - Furoean Onality of Life, 5 Dimensions
reality for depressic	Outcome, (measure)	Mood and apathy (OERS, PEAR), depression (CSDD), anxiety (GAD-7), agitation (CMAI)	Depression (PHQ-8, PHQ-9), physical tolerability (SSQ), emotional tolerability (BAM)	Depression, anxiety, stress (DASS-21), perceived stress levels (PSS), and hopelessness (BHS)	PICS-related psychological distress: PTSD (IES-R), anxiety and depression (HADS); and quality of life (SF-36, EQ-5D)	VR - Person-Environmation Inventory, BPS - tion Inventory, BPS - Q - Simulator Sickness andomized controlled ale: SF-36 - Short-Fc
e virtual	Control	оц	о	No treatment	Standard COVID- 19 post- ICU follow-up	zale; PE/ field Agita 8, -9; SS' ; RCT - 1 ression So
on the use of immersive	Intervention	6 sessions of immersive VR 360-degree videos on a wireless HMD (10 min VR experience)	4 weekly BA psycho- therapy online sessions using a VR HMD (2 -10 min VR experience) and home task of 12 VR sessions, supported by psychotherapy for MDD (1 hour per week), medication Fluoxetine and Mirtazapine.	VR-based self-help psychological protocol (1 week daily): immersive or non- immersive VR experience (10 min) and series of social exercises related to personal identity, relationships, and goals (done with a partner)	VR movie explaining the ICU treatment (14 min) once 3 months after discharge, during the visit to a COVID-19 post-ICU follow-up clinic along with standard follow-up	bserved Emotions Rating S ale; CMAI - Cohen Mansi tient Health Questionnaire-i - Beck Hopelessness Scale - Hosnital Anxiety and Den
fincluded studies	Type of study Participants, (n)	Residents of aged care facility with varying cognitive impairments, (25)	Patients with MDD, (1, male)	People in lockdown situation more than 2 months (40), control measure in waiting-list	COVID-19 patients survived ICU treatment, study group (45), control group (44)	display; OERS - Oi ty Disorder 7-item sc PHQ-8, PHQ-9 - Par 2d Stress Scale; BHS le-Revised; HADS -
aracteristics of	Type of study	Feasibility trial	Pilot study, case report	Effectiveness study	Multicenter RCT	 n - head-mounted eneralized Anxie ioral activation; PSS - Perceiv bact of Event Sca
Table 1. Ch	Study	Brimelow et al. (2021)	Paul et al. (2020)	Riva et al. (2021)	Vlake et al. (2022)	<i>Note:</i> HMD GAD-7 - G BA - behavi Stress Scale IES-R - Imp

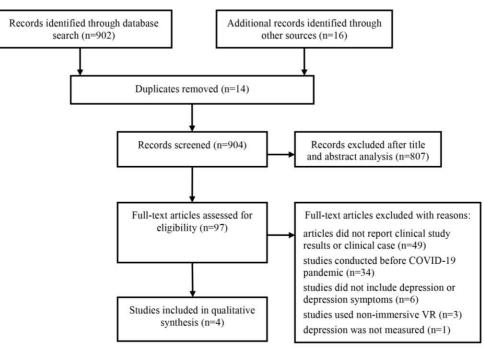


Figure 1. PRISMA flow diagram for the study selection on the use of immersive virtual reality for depression treatment during the COVID-19 pandemic

Another study (Riva et al. 2021) included 40 adult individuals who had experienced at least two months of strict social distancing measures in Italy. Eighteen subjects had an immersive VR experience, and 22 had a non-immersive VR experience lasting ten minutes every day, augmented by daily social communication exercises during one week period. Depression Anxiety Stress Scale (DASS-21) total score changes after the one week intervention and at the point of two-weeks follow-up represent the primary outcome measure in this study. Nonetheless, the authors did not report the proportion of the study population with the depression DASS-21 subscale score > 9 (the cut-off score between normal state of euthymia and mild depression (Lovibond & Lovibond 1995), although the pre-intervention mean (SD) score was only 8.9 (8.2). Nevertheless, the depression score significantly declined from the baseline to the endpoint, and remained low at the end of the follow-up period. However, no any significant effect of the VR immersion on the depression DASS-21 scores has been registered. There was no presentation of separate results for participants who did use or did not use the immersive VR as a matter of comparative analysis.

The group of Vlake et al. (2022) investigated the preventive antidepressive effect of a VR-based education in COVID-19 survivors after their discharge from an intensive care unit (ICU) (Vlake et al. 2022). Along with the standard COVID-19 post-ICU follow-up at the timepoint of three months after the discharge (baseline), the VR intervention in an intervention group consisted of an educational video on the activities performed in the ICU and important information about COVID-19, while the control group received only the standard treatment. The control-based study aimed to compare a long-term (3-, 4-, and 6-month follow-up) effect of VR-based education on the psychological outcomes in COVID-19 patients who have been discharged from ICU. The data analysis included the depression subscale score on the Hospital Anxiety and Depression Scale (HADS). In the former ICU patients, the population median HADS depression score was < 8 in both groups, consistently at each study follow-up visit. Authors concluded that throughout the follow-up, there were no differences in the mean depression scores or the proportion of patients reporting the presence of clinical depression.

Safety

Despite the non-pharmacological and non-invasive nature of VR interventions, there were some reports on adverse events. Among 25 aged care facility residents (Brimelow et al. 2022), there were two cases of mild adverse events (headache and "giddiness") and three cases of discomfort from wearing VR device were registered. Thus, the elderly population might be especially vulnerable to balance disturbances in the context of VR treatment. In a non-geriatric population, VR use might provoke adverse behavioral events. In the case report from Paul et al. (2020), a patient with diagnosis of depression and a history of substance misuse reported an improvement in his mood after VR therapy, but developed a behavioral pattern that resembled abusive usage of VR content.

Risk of bias within the studies

The studies under review did not calculate the risk of bias, but rather reported their limitations. Generally, the researchers evaluated their obtained results as experimentally observed outcomes of treatment involving the immersive VR technology, which could be helpful in designing new prospective trials with a larger number of participants.

Qualitative analysis

There was a considerable diversity in the study populations and treatment modalities presented across the selected studies. To synthesize the various findings, we used the method of narrative synthesis, which can be helpful in deriving a general conclusion from the existing heterogeneous data. All four studies considered the COVID-19 pandemic in the context of stress due to social distancing, lack of physical activities, and a fear of potential infection and death.

DISCUSSION

Since the onset of the COVID-19 pandemic, there have been only a very few studies assessing the efficacy of the VR modality for managing depressive symptoms. The studies that have been initiated in this period generally involved a population without assessment of the prevalence/ percentage of participants with clinical depression. This strong limitation demands us to conclude that the studies, conducted in times of global social isolation, did not strongly support an appropriate use and evaluation of the efficacy of VR-based methods use in the treatment of clinical depression. We suppose that the VR studies that were conducted prior to the pandemic have not yet been able to respond to the question related to the potential efficacy of VR-based therapy for depression. Furthermore, the time period from the beginning of the pandemic to the time of writing the report was too brief to arrange a more appropriate study design and VR content, or delivery of the VR equipment to the study participants.

In this regard, it is crucial to overview the pre-pandemic studies of VR-based interventions for depression. The latest scoping review (Baghaei et al. 2021) included only four studies (Dehn et al. 2018, Lin et al. 2020, Stamou et al. 2019, Suwanjatuporn & Chintakovid 2019), each of which having substantial limitations for evaluating the VR efficacy in depression treatment: (i) the studies had limited sample size, (ii) a change in the depressive state was not assessed within any longitudinal study design, (iii) there was no comparative data on the VR use for inactive control, (iv) studies were designed based on a sample of healthy population. Thus, there is a substantial gap in the research data on the clinical potential of VRbased interventions for treatment of depressive disorders.

According to Clark & Watson (1991), a deficit of positive emotions in combination with over-representation of negative emotions is one of the neuropsychological factors promoting the development of depression, while negative affect is hypothesized to be the common basis of vulnerability in relation to developing anxiety and depressive disorders (Clark & Watson 1991). According to the Research Domain Criteria (RDoC), negative and positive emotions are mediated by neuronal pathways involved in positive valence (e.g., the reward system) and negative valence (e.g., attention and salience networks, fear circuits involving the amygdala) (Kessel et al. 2017). In this context, research of the effects of VR-based interventions on positive and negative emotions may provide a clearer vision on the perspectives of VR efficacy in the treatment of depression.

Notably, the VR modality has been investigated as a method for managing anxiety disorders. Numerous studies demonstrated that individuals with anxiety or depression might benefit from a VR intervention, which seems to be mediated by activation of neurobiological mechanisms of fear extinction (such as repeated exposure to fear provoking stimuli), or via correction of attentional bias in the processing of negative emotional stimuli (Li et al. 2021, Premkumar et al. 2021, Reeves et al. 2021, Urech et al. 2015, Wechsler et al. 2021, Zainal et al. 2021, Zolfaghari et al. 2022).

In a healthy population, VR-exposure showed promising results in inducing positive emotional states. For example, according to Magdin et al. (2021), the VR environment induced significantly stronger emotional states than did a control treatment with viewing of a standard LCD screen (Magdin et al. 2021). In another study, VR exposure during two weeks proved to be feasible, and showed effects on positive and negative emotions in healthy volunteers (Mahmud et al. 2022). Another study investigated the ability of VR games to induce positive emotions and diminish negative emotions, with consideration of the contribution to body movements (Pallavicini & Pepe 2020). The study of 36 healthy volunteers reported a statistically significant increase in the intensity of happiness feeling and a simultaneous decline in fear, sadness and perceived anxiety. The authors furthermore reported a greater efficacy of high body-involvement games compared to the low body-involvement games, both for eliciting positive emotions and in reducing negative emotions and state anxiety.

Few studies addressed the efficacy of VR-mediated induction of positive emotions in clinical samples. Herrero et al. (2014) conducted the study in a sample of 40 adult women with primary diagnosis of fibromyalgia, of whom 52.5% had a comorbid diagnosis of an anxiety disorder, and 65% having a depressive disorder, all according to the Structured Clinical Interview for DSM-IV Axis I Disorder (SCID-I) (Herrero et al. 2014). The VR

intervention was intended to induce positive emotions via a visual and audio virtual surrounding. A primary outcome measure was acute, pre-, post-induction change in mood. None of the participants reported worsening in their mood state, while 28% felt the same and other 72% reported improvement. Pre- vs post-test effects sizes (Cohen's d) were moderate for mood (-0.43), joy (-0.37), and vigor/energy (-0.38) and mild for motivation (-0.25). The effects of VR on anhedonia, as a representation of deficits in positive affect, was assessed in a study by Chen et al. (2020). The authors hypothesized that viewing positive scenes through VR might suppress anhedonic symptoms by inducing a more positive affect. Six participants diagnosed with moderate-to-severe depression were exposed to 13 sessions of viewing positive scenes in a controlled VR environment. The authors reported a significant decrease in self-reported anhedonia, depression, anxiety, and impairments in functioning from the baseline to one-month follow-up. Remarkably, that positive affect improved later across the course of treatment compared to negative affect, consistent with the generally more refractory nature of anhedonia.

CONCLUSIONS

Despite the obvious disruptions in healthcare systems due to widely implemented social distancing measures and high rise in cases of SARS-Cov-2 infection, only a very few studies having investigated the effectiveness of VR interventions for depression treatment since the onset of the COVID-19 pandemic. These VR-based studies had strong limitations in terms of our research question due to imprecise design, small sample size, and outcome assessments. However, these studies may draw some crucial directions for further evidence-based research of VR use and its efficacy in depression treatment.

Much as in the case of anxiety disorders, VR interventions for depression should target negative affect, which is the biologically-driven vulnerability factor. Similar to anxiety disorders, where the VR intervention targeted the negative affect – the biologically-driven vulnerability factor, in depression (with its inherent exaggerated negative affect and low positive affect) the VR modality could be used not only for management of the negative attentional bias but also for the induction of a positive emotional state and emotional resources/balance.

The reviewed studies demonstrated certain favorable effects of the VR-based interventions on inducing the positive emotions both in healthy participants and in clinical study samples in terms of depression treatment and depressive symptoms management. At the same time, most of the studies assessed only the immediate or shortterm effects of the VR-based interventions, whereas the long-term effects for depression remain unclear. Therefore, we emphasize the importance of further research using randomized prospective design to test the effectiveness and long-term impact of VR-modalities on managing negative affect and promoting the positive affect, as a key concept of recovery from depression, aiming to find path back to normality / emotional balance in people suffering from affective and mood disorders.

Limitations of the study

Despite the use of a well-defined search strategy, our study may still represent selection bias. In addition, the conclusions are constrained by the inherent limitations of the few existing studies which met our specific narrow-targeting inclusion criteria on the clinical investigations of VR use in depression treatment in the context of pandemic-related conditions.

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Conflict of interest:

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Contribution of individual authors:

- Natalia Borisova, Nathan Moore, Sridevi Sira Mahalingappa, Subodh Dave, Aleksandr Kolsanov, Daria Smirnova & Timur Syunyakov formulated the primary idea, elaborated the research hypothesis for narrative review, and fixed the keywords search algorithm based on the zoom-meet brainstorming sessions and the advice from Seri Abraham, Sergey Chaplygin, Roshelle Ramkisson, Giuseppe Tavormina, Tatiana Kozina & Andrey Vlasov.
- Natalia Borisova, Daria Smirnova & Timur Syunyakov designed the narrative review, searched and reviewed the literature and wrote the first draft of the manuscript.
- Natalia Borisova & Timur Syunyakov analyzed the data targeting narrative review approach.
- Nathan Moore, Sridevi Sira Mahalingappa, Paul Cumming, Roshelle Ramkisson, Giuseppe Tavormina & Aleksandr Kolsanov contributed to the detailed revision upon the agreement from other coauthors.
- Daria Smirnova & Timur Syunyakov share senior authorship of the manuscript.
- Natalia Borisova, Aleksandr Kolsanov, Sergey Chaplygin, Tatiana Kozina, Andrey Vlasov, Daria Smirnova & Timur Syunyakov develop and promote the scientific and technological topic of virtual reality application to neuropsychiatry in Samara State Medical University in collaboration with the research groups from Australia (Nathan Moore, Sridevi Sira Mahalingappa, Paul Cumming) and UK (Subodh Dave, Seri Abraham, Roshelle Ramkisson, Giuseppe Tavormina) to plan further advanced studies.

References

- 1. Aboujaoude E, Gega L & Saltarelli AJ: The retention challenge in remote therapy and learning seen through the lens of the COVID-19 pandemic. World Psychiatry 2021; 20:138-139. doi:10.1002/wps.20828
- Anderson M, Pitchforth E, Asaria M, Brayne C, Casadei B, Charlesworth A, et al.: Lse-lancet commission on the future of the nhs: Re-laying the foundations for an equitable and efficient health and care service after COVID-19. Lancet 2021; 397:1915-1978. doi:10.1016/S0140-6736(21)00232-4
- Astafeva D, Syunyakov T, Yashikhina A, Cumming P, Vlasov A, Chaplygin S, et al.: The efficacy of mobile phone-based interventions for the treatment of depression: A systematic meta-review of meta-analyses of randomized controlled trials. Psychiatr Danub 2022; 34(Suppl 8):S155-163
- Baghaei N, Chitale V, Hlasnik A, Stemmet L, Liang HN & Porter R: Virtual reality for supporting the treatment of depression and anxiety: Scoping review. JMIR Ment Health 2021; 8:e29681. doi:10.2196/29681
- Brandizzi M, Polselli A, Corigliano V, Tamorri SM, Venturini P, Azzoni A, et al.: Psychiatric emergencies during, after, and before the COVID-19 lockdown: What happened to our patients? A naturalistic observational study. Ann Gen Psychiatry 2022; 21:29. doi:10.1186/s12991-022-00408-z
- Brimelow RE, Thangavelu K, Beattie R & Dissanayaka NN: Feasibility of group-based multiple virtual reality sessions to reduce behavioral and psychological symptoms in persons living in residential aged care. J Am Med Dir Assoc 2022; 23:831-837, e832. doi:10.1016/j.jamda.2021.07.026
- Carrasco JP, Herraiz B, Sanchez LO, Luengo A, Fusalba OR & Aguilar EJ: COVID-19 lockdown influence in the psychiatric emergencies: Drastic reduction and increase in severe mental disorders. Rev Psiquiatr Salud Ment (Engl Ed) 2021; 14:117-118. doi:10.1016/j.rpsmen.2021.05.002
- Chen K, Barnes-Horowitz N, Treanor M, Sun M, Young KS & Craske MG: Virtual reality reward training for anhedonia: A pilot study. Front Psychol 2020; 11:613617. doi:10.3389/fpsyg.2020.613617
- 9. Chitale V, Baghaei N, Playne D, Liang HN, Zhao Y, Erensoy A, et al.: The use of videogames and virtual reality for the assessment of anxiety and depression: A scoping review. Games Health J 2022. doi:10.1089/g4h.2021.0227
- Clark LA & Watson D: Tripartite model of anxiety and depression: Psychometric evidence and taxonomic implications. J Abnorm Psychol 1991; 100:316-336
- 11. Dehn LB, Kater L, Piefke M, Botsch M, Driessen M & Beblo T: Training in a comprehensive everyday-like virtual reality environment compared to computerized cognitive training for patients with depression. Computers in Human Behavior 2018; 79:40-52. doi:10.1016/j.chb.2017.10.019
- 12. Di Lorenzo R, Pinelli M, Bertani D, Cutino A, Dragone D, Elia C, et al.: The impact of COVID-19 pandemic on psychiatric emergencies in two different settings: Emergency room and community mental health service. Front Psychiatry 2022; 13:894939.
 - doi:10.3389/fpsyt.2022.894939
- Fountoulakis KN, Apostolidou MK, Atsiova MB, Filippidou AK, Florou AK, Gousiou DS, et al.: Self-reported changes in anxiety, depression and suicidality during the COVID-19 lockdown in greece. J Affect Disord 2021; 279:624-629. doi:10.1016/j.jad.2020.10.061

- 14. Fountoulakis KN, Karakatsoulis G, Abraham S, Adorjan K, Ahmed HU, Alarcón RD, et al.: Results of the COVID-19 mental health international for the general population (COMET-G) study. European Neuropsychopharmacology 2022a; 54:21-40
- 15. Fountoulakis KN, Karakatsoulis GN, Abraham S, Adorjan K, Ahmed HU, Alarcon RD, et al.: The effect of different degrees of lockdown and self-identified gender on anxiety, depression and suicidality during the COVID-19 pandemic: Data from the international COMET-G study. Psychiatry Res 2022b; 315:114702. doi:10.1016/j.psychres.2022.114702
- 16. Herrero R, Garcia-Palacios A, Castilla D, Molinari G & Botella C: Virtual reality for the induction of positive emotions in the treatment of fibromyalgia: A pilot study over acceptability, satisfaction, and the effect of virtual reality on mood. Cyberpsychol Behav Soc Netw 2014; 17:379-384. doi:10.1089/cyber.2014.0052
- 17. Imperatori C, Dakanalis A, Farina B, Pallavicini F, Colmegna F, Mantovani F, et al.: Global storm of stressrelated psychopathological symptoms: A brief overview on the usefulness of virtual reality in facing the mental health impact of COVID-19. Cyberpsychol Behav Soc Netw 2020. doi:10.1089/cyber.2020.0339
- 18. Kessel EM, Kujawa A, Goldstein B, Hajcak G, Bufferd SJ, Dyson M, et al.: Behavioral observations of positive and negative valence systems in early childhood predict physiological measures of emotional processing three years later. J Affect Disord 2017; 216:70-77. doi:10.1016/j.jad.2016.10.044
- 19. Li H, Dong W, Wang Z, Chen N, Wu J, Wang G, et al.: Effect of a virtual reality-based restorative environment on the emotional and cognitive recovery of individuals with mild-to-moderate anxiety and depression. Int J Environ Res Public Health 2021; 18. doi:10.3390/ijerph18179053
- 20. Lin AJ, Cheng F & Chen CB: Use of virtual reality games in people with depression and anxiety. Proceedings of the 5th International Conference on Multimedia and Image Processing 2020; 169-174
- 21. Lovibond S & Lovibond P: Manual for the depression anxiety & stress scales. (2nd ed.). Sydney: Psychology Foundation, 1995
- 22. Magdin M, Balogh Z, Reichel J, Francisti J, Koprda Š & György M: Automatic detection and classification of emotional states in virtual reality and standard environments (lcd): Comparing valence and arousal of induced emotions. Virtual Reality 2021; 25:1029-1041. doi:10.1007/s10055-021-00506-5
- 23. Mahmud AAe, Zakaria H, Mohd Yusoff MZ, Nik Jaafar NR, Baharudin A & Mohd Tamil A: Brief virtual reality exposure therapy and its effects on negative and positive emotions among healthy working adults: A feasibility study. Alpha Psychiatry 2022. doi:10.5152/alphapsychiatry.2022.21781
- 24. Nadareishvili I, Syunyakov T, Smirnova D, Sinauridze A, Tskitishvili A, Tskitishvili A, et al.: University students' mental health amidst the COVID-19 pandemic in georgia. Int J Soc Psychiatry 2022; 207640221099420. doi:10.1177/00207640221099420
- 25. Pallavicini F & Pepe A: Virtual reality games and the role of body involvement in enhancing positive emotions and decreasing anxiety: Within-subjects pilot study. JMIR Serious Games 2020; 8:e15635. doi:10.2196/15635

- 26. Panfil AL, Lungeanu D, Tamasan S, Bredicean C, Papava I, Smirnova D, et al.: Suicidality related to the COVID-19 lockdown in romania: Structural equation modeling. Front Psychiatry 2022; 13:818712. doi:10.3389/fpsyt.2022.818712
- 27. Paul M, Bullock K & Bailenson J: Virtual reality behavioral activation as an intervention for major depressive disorder: Case report. JMIR Ment Health 2020; 7:e24331. doi:10.2196/24331
- Premkumar P, Heym N, Brown DJ, Battersby S, Sumich A, Huntington B, et al.: The effectiveness of self-guided virtualreality exposure therapy for public-speaking anxiety. Front Psychiatry 2021; 12:694610. doi:10.3389/fpsyt.2021.694610
- 29. Reeves R, Elliott A, Curran D, Dyer K & Hanna D: 360 degrees video virtual reality exposure therapy for public speaking anxiety: A randomized controlled trial. J Anxiety Disord 2021; 83:102451. doi:10.1016/j.janxdis.2021.102451
- 30. Riva G, Bernardelli L, Castelnuovo G, Di Lernia D, Tuena C, Clementi A, et al.: A virtual reality-based self-help intervention for dealing with the psychological distress associated with the COVID-19 lockdown: An effectiveness study with a two-week follow-up. Int J Environ Res Public Health 2021; 18. doi:10.3390/ijerph18158188
- 31. Sasangohar F, Bradshaw MR, Carlson MM, Flack JN, Fowler JC, Freeland D, et al.: Adapting an outpatient psychiatric clinic to telehealth during the COVID-19 pandemic: A practice perspective. J Med Internet Res 2020; 22:e22523. doi:10.2196/22523
- 32. Smirnova D, Cumming P, Sloeva E, Kuvshinova N, Romanov D & Nosachev G: Language patterns discriminate mild depression from normal sadness and euthymic state. Front Psychiatry 2018; 9:105. doi:10.3389/fpsyt.2018.00105
- 33. Smirnova D, Cumming P, Sloeva E, Kuvshinova N, Romanov D & Nosachev G: Language patterns discriminate mild depression from normal sadness and euthymic state. Front Psychiatry 2018; 9:105. doi:10.3389/fpsyt.2018.00105
- 34. Smirnova D, Syunyakov T, Bragin D, Fedotov I, Filatova V, Ignatenko Y, et al.: Interactions between anxiety levels and life habits changes in general population during the pandemic lockdown: Decreased physical activity, falling asleep late and internet browsing about COVID-19 are risk factors for anxiety, whereas social media use is not. Psychiatr Danub 2021; 33(Suppl 9):119-129
- 35. Stamou G, Garcia-Palacios A & Botella C: The combination of cognitive-behavioural therapy with virtual reality for the treatment of post-natal depression. Proceedings of the 31st Australian Conference on Human-Computer-Interaction 2019; 599-603
- 36. Stewart DE & Appelbaum PS: COVID-19 and psychiatrists' responsibilities: A wpa position paper. World Psychiatry 2020; 19:406-407. doi:10.1002/wps.20803

- 37. Suwanjatuporn A & Chintakovid T: Using a virtual reality system to improve quality of life of the elderly people with depression. 2019 IEEE International Conference on Consumer Electronics - Asia (ICCE-Asia) 2019; 153-156. doi:10.1109/ICCE-Asia46551.2019.8941607
- Urech A, Krieger T, Chesham A, Mast FW & Berger T: Virtual reality-based attention bias modification training for social anxiety: A feasibility and proof of concept study. Front Psychiatry 2015; 6:154. doi:10.3389/fpsyt.2015.00154
- 39. Vlake JH, van Bommel J, Wils EJ, Bienvenu J, Hellemons ME, Korevaar TI, et al.: Intensive care unit-specific virtual reality for critically ill patients with COVID-19: Multicenter randomized controlled trial. J Med Internet Res 2022; 24:e32368. doi:10.2196/32368
- 40. Vrublevska J, Perepjolkina V, Martinsone K, Kolesnikova J, Krone I, Smirnova D, et al.: Determinants of anxiety in the general latvian population during the COVID-19 state of emergency. Front Public Health 2022; 10:854812. doi:10.3389/fpubh.2022.854812
- 41. Vrublevska J, Sibalova A, Aleskere I, Rezgale B, Smirnova D, Fountoulakis KN, et al.: Factors related to depression, distress, and self-reported changes in anxiety, depression, and suicidal thoughts during the COVID-19 state of emergency in latvia. Nord J Psychiatry 2021; 75:614-623. doi:10.1080/08039488.2021.1919200
- 42. Wasserman D, Iosue M, Wuestefeld A & Carli V: Adaptation of evidence-based suicide prevention strategies during and after the COVID-19 pandemic. World Psychiatry 2020; 19:294-306. doi:10.1002/wps.20801
- 43. Wechsler TF, Pfaller M, van Eickels RE, Schulz LH & Muhlberger A: Look at the audience? A randomized controlled study of shifting attention from self-focus to nonsocial vs. Social external stimuli during virtual reality exposure to public speaking in social anxiety. Front Psychiatry 2021; 12:751272. doi:10.3389/fpsyt.2021.751272
- 44. Zainal NH, Chan WW, Saxena AP, Taylor CB & Newman MG: Pilot randomized trial of self-guided virtual reality exposure therapy for social anxiety disorder. Behav Res Ther 2021; 147:103984. doi:10.1016/j.brat.2021.103984
- 45. Zhang SX, Miller SO, Xu W, Yin A, Chen BZ, Delios A, et al.: Meta-analytic evidence of depression and anxiety in eastern europe during the COVID-19 pandemic. Eur J Psychotraumatol 2022; 13:2000132. doi:10.1080/20008198.2021.2000132
- 46. Zolfaghari E, Ridout B, Medlow S, Campbell A, Coggins A, Murphy M, et al.: Exploring the use of virtual reality to manage distress in adolescent patients in emergency departments: A feasibility study. Emerg Med Australas 2022. doi:10.1111/1742-6723.13945

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