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Review

Virtual reality in the diagnostic and therapy for mental disorders: A systematic review

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ABSTRACT

Background: Virtual reality (VR) technologies are playing an increasingly important role in the diagnostics and treatment of mental disorders.
Objective: To systematically review the current evidence regarding the use of VR in the diagnostics and treatment of mental disorders.
Data source: Systematic literature searches via PubMed (last literature update: 9th of May 2022) were conducted for the following areas of psychopathology: Specific phobias, panic disorder and agoraphobia, social anxiety disorder, generalized anxiety disorder, posttraumatic stress disorder (PTSD), obsessive-compulsive disorder, eating disorders, dementia disorders, attention-deficit/hyperactivity disorder, depression, autism spectrum disorder, schizophrenia spectrum disorders, and addiction disorders.
Eligibility criteria: To be eligible, studies had to be published in English, to be peer-reviewed, to report original research data, to be VR-related, and to deal with one of the above-mentioned areas of psychopathology.
Study evaluation: For each study included, various study characteristics (including interventions and conditions, comparators, major outcomes and study designs) were retrieved and a risk of bias score was calculated based on predefined study quality criteria.
Results: Across all areas of psychopathology, k = 9315 studies were inspected, of which k = 721 studies met the eligibility criteria. From these studies, 43.97% were considered assessment-related, 55.48% therapy-related, and 0.55% were mixed. The highest research activity was found for VR exposure therapy in anxiety disorders, PTSD and addiction disorders, where the most convincing evidence was found, as well as for cognitive trainings in dementia and social skill trainings in autism spectrum disorder.
Conclusion: While VR exposure therapy will likely find its way successively into regular patient care, there are also many other promising approaches, but most are not yet mature enough for clinical application.
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1. Introduction

With an estimated lifetime prevalence of 29.2% worldwide (Steel et al., 2014), mental disorders constitute a major source for suffering and burden for society. Considering not only direct assessment and treatment costs, but also secondary costs (e.g., productivity losses due to early retirement or disability), the global economic costs resulting from mental disorders were around $US 2.5 trillion in 2010 and are expected

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to increase to $US 6 trillion in 2030 (Bloom et al., 2011). As such, mental disorders are estimated to account for 10.4% of all health costs worldwide (Bloom et al., 2011; Trautmann, Rehm, & Wittchen, 2016). Despite these tremendous investments into mental health, the need for treatment is still far from being met. In less developed countries, for instance, 76.3% to 85.4% of people with a mental disorder have been estimated to not receive treatment, while in higher developed countries, 35.5% to 50.3% of mentally-ill people receive no adequate treatment (Demyttenaere et al., 2004).

To mitigate cost increases while expanding access to evidence-based treatments, great effort is currently put into the development of new e-health technologies, such as telemedicine, healthcare applications, or virtual reality (VR; Bucci, Schwannauer, & Berry, 2019). The great hope propelling this endeavor is the assumed low-cost scalability of these technologies (Donker et al., 2019; Gordon, Landman, Zhang, & Bates, 2020; Murray et al., 2016). Once developed, a healthcare application, for instance, can be distributed to an arbitrary number of devices without significant increase of provision and maintenance costs. Such scalability also applies to VR, given that, with minimum additional equipment (e.g., a Google Cardboard, a Daydream VR, or Samsung Gear VR), almost every modern smartphone can nowadays be transformed into a VR device.

Besides this scalability benefit, however, VR offers many further advantages. First, as a technology that allows to implement immersive, interactive and experientially-rich virtual environments, VR appears predestined for exposure interventions. As in classical exposure therapy, patients can be specifically confronted with their anxiety and thereby learn to attenuate it by habituation and extinction (Wechsler, Kümpers, & Mühlberger, 2019). By means of VR, exposure situations can even be created that would not be viable in the real world (e.g., balancing on a tightrope between two skyscrapers). Second, given its power to simulate symptom-relevant 'realities', VR appears eminently suitable for developing new testing environments that are ecologically-valid and yet highly-standardized. Third, as a technique that might systematically feign reality, VR can impressively demonstrate how unveridical and malleable one's own 'sense of self' and 'sense of reality' often is (Metzinger, 2018), especially if one suffers from mental illness. Such experience-based psychoeducation could be particularly beneficial in mental disorders, in which the own self-model or reality-model is abnormally changed (e.g. in psychoses or body schema disorders), and where conventional interventions often fail.

While VR has been around since the 1960s, its clinical applicability has been studied since the 1990s. The initial research primarily focused on anxiety disorders and posttraumatic stress disorder, whereas little attention was paid to the usability of VR in other mental disorders. However, at the latest since the first affordable high-quality VR devices (esp. the Oculus Rift in 2013) entered the consumer market, a veritable VR research boom has set in. This systematic review examines the current evidence regarding the use of VR in the assessment and treatment of mental disorders. The areas of psychopathology investigated are specific phobias (SP), panic disorder and agoraphobia (P&A), social anxiety disorder (SAD), generalized anxiety disorder (GAD), posttraumatic stress disorder (PTSD), obsessive-compulsive disorders (OCD), eating disorders (ED), dementia disorders (DEM), attention-deficit/hyperactivity disorder (ADHD), depression (DEP), autism spectrum disorders (ASD), schizophrenia spectrum disorders (SSD), and addiction disorders (AD).

2. Methods

2.1. Protocol and registration

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Page et al., 2021) and pre-registered in the PROSPERO register (CRD42020188436). Please note that during the revision process of this review, our VR inclusion criterion was extended as compared to the originally specified VR criterion in the pre-registration.

2.2. Information sources and search strategy

Systematic literature searches on titles, abstracts and keywords were separately performed in PubMed for each area of psychopathology (original search date: 27th of July 2020; updated search: 9th of May 2022): SP, P&A, SAD, GAD, PTSD, OCD, ED, DEM, ADHD, DEP, ASD, SSD, and AD. For each psychopathology area, a conjunctive search query was made, whose first operand always was '(VR OR Virtual Reality)'. The second operand was disorder-specific and entailed a disjunctive set of target keywords relevant for the respecting area of psychopathology. Wherever possible, appropriate truncations were hereby used, to search for all variations of a word stem (e.g., depres* to search for depression and depressive). Moreover, the second operand also entailed NON-keywords to ignore inappropriate research items. A list of the search queries used for each area of psychopathology can be found in the Supplementary Material (SM 1).

2.3. Eligibility criteria

To be eligible, a study had to be published in English, be peer-reviewed, be related to the respective area of psychopathology, be VR-related and had to report original research data. A study was classified as psychopathology-related if it (1.) addressed the clinical characterization, assessment or treatment of a disorder, symptom or problem within the respective area of psychopathology and (2.) was conducted, at least in part, in a clinical sample for which clear psychopathology-specific inclusion criteria (e.g., DSM-V or ICD-10 criteria) were specified. A study was accepted to be a VR study if its authors themselves considered that study a VR study, except when only abstract symbols, videos, or static images were presented via a traditional computer screen or an augmented reality was implemented. Studies with a lowly-immersive, but interactive VR scenario occurring on a classic computer screen (e.g., a computer game) were thus included. Moreover, no inclusion restrictions were made with respect to population age, intervention type, study type, study outcomes, VR type, or comparators. Studies without locatable full texts were, in turn, excluded.

2.4. Study characterization and evaluation

For each study included, various study characteristics were retrieved and compiled in area-specific summary tables:

Study Type: Specifies whether the study was an assessment or therapy study. Studies that focused on symptom markers, putative etiological factors, or clinical characterizations, were thereby categorized as assessment studies. Studies that had both an assessment and therapy aspect were grouped into both types and are listed in the results section for both assessment and therapy studies.

Study Design: The study design used, given the following taxonomy: Randomized controlled trial (RCT), controlled clinical trial (CCT), case-control study, cohort study, cross-sectional study, single case study, or case series study. Studies were accepted as an RCT or CCT, if at least two clinical groups or conditions were statistically compared, even if a definite assignment of which group represented the control group/condition was missing. Studies with a crossover design were classified as an RCT in case of a randomized condition order and as a CCT in case of a non-randomized condition order.

Clinical Inclusion Criterion: The primary clinical instrument or criterion, upon which participants were accepted for the study. If multiple clinical inclusion criteria were mentioned, only the most established clinical instrument was chosen.

Study Interventions: Indicates which experimental interventions were performed, how long they lasted, and how often they were repeated.

Age Range: Categorizes the study samples into four age ranges: Children and adolescents (< 18 years), adults (≥ 18 years), cross-age (< 18 & ≥ 18 years) and unspecified.

Study Outcomes: Specifies the primary results of the study.

Risk of Bias (RoB): Quantitatively assesses the study quality, based on the following Yes/No-criteria:

1. Control-comparison: Was there a control group or within comparator to which the VR intervention was compared?
2. Ordering/assignment-control: Was assured that the interventions or intervention groups being compared were (pseudo-)randomized or counterbalanced?
3. Pre/post-comparison (only assessed in case of a therapy study): Was there a pre-measurement to which the post-measurement was compared, or for which the post-measurement was adjusted (e.g., relative change)?
4. Follow-up (only assessed in case of a therapy study): Was there a follow-up measurement after six weeks (the earliest), or later?
5. Registration: Was the study enrolled in an official study register?
6. Experimenter-blinding: Were the study conductors blinded with respect to the interventions or intervention groups being compared? This criterion was also assigned if only the diagnosis itself was blinded.
7. Analyst-blinding: Were the study evaluators blinded with respect to the interventions or intervention groups being compared?
8. Participant-blinding: Were the participants naive to whether they received an actual intervention or a control intervention?

Based on the Yes/No-criteria, a RoB score was derived by calculating the percentage of unfulfilled criteria. For both, assessment and therapy studies, a 0% RoB thus indicates a high study quality and a 100% RoB a low study quality. Missing information was marked as such in the summary tables.

VR Device: Specifies which type of VR device was used, based on a fixed taxonomy (cf. SM 2). Each study was thereby assigned to one of four head categories: Highly-immersive, semi-immersive, lowly-immersive or unspecified.

2.5. Data collection process

For each area of psychopathology, the eligibility assessment and study evaluation were each performed by two independent reviewers and disagreements between reviewers were resolved through discussion, or by consultation of a third reviewer. In case of ambiguity with a study, or if the full text of an article was non-accessible, the respective study authors were contacted.

3. Results

Across areas of psychopathology, a total of 9315 records were identified, from which 1284 full-text articles were accessed for further evaluation (for a PRISMA flowchart, see Figure 1). Of these, 721 articles were finally included in this review. The remaining 8594 papers were excluded, whereby the most common reasons for rejection were that studies were off-topic (e.g., usage of the abbreviation VR in another context) or conducted with healthy individuals only.

For each area of psychopathology, several characteristics of included studies are summarized in Figure 2. Most of the studies were found on SP (k = 100; 13.87%) and fewest on OCD (k = 10; 1.39%). Moreover, across areas of psychopathology, more therapy studies (k = 400; 55.48%) have been carried out than assessment studies (k = 317; 43.97%) or mixed studies (k = 4; 0.55%), but this ratio varied markedly between areas. While therapy studies, for instance, clearly predominated for anxiety disorders, ED and PTSD, assessment studies predominated for ADHD, ASD, SSD, and AD. Regarding assessed cohorts, clearly more studies were carried out with adults (k = 569; 78.92%) than with children/adolescents (k = 95; 13.18%) or cross-age populations (k = 50; 6.93%). Only for ADHD and ASD, this overall pattern deviated in that more studies were conducted with children/adolescents. Regarding study quality, similarly many RCTs (k = 249; 34.54%) and CCTs (k = 116; 16.09%) were carried out compared to other, less-rigorous study designs (k = 356; 49.38%). In consequence, the estimated overall RoB was moderate (*M* = 69.44%; *SD* = 19.12%), but highly varied between studies and areas of psychopathology. Whereas the lowest average RoB was found for GAD (*M* = 59.71%; *SD* = 9.93%), the highest RoB was

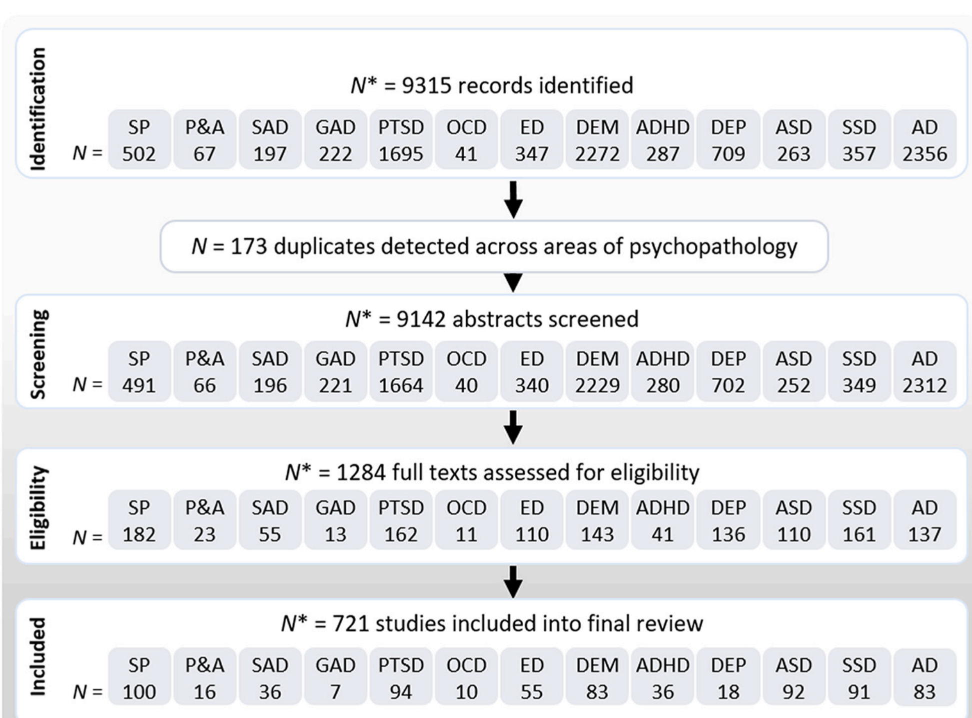

Fig. 1. PRISMA flow diagram of the article selection process.
Abbreviations: SP = specific phobias; P&A = panic disorder & agoraphobia; SAD = social anxiety disorder; GAD = generalized anxiety disorder; PTSD = posttraumatic stress disorder; OCD = obsessive-compulsive disorders; ED = eating disorders; DEM = dementia; ADHD = attention-deficit/hyperactivity disorder; DEP = depression; ASD = autism spectrum disorders; SSD = schizophrenia spectrum disorders; AD = addiction disorders. *Please note: A study was counted multiple times if it showed up multiple times in seperate area-specific literature searches.

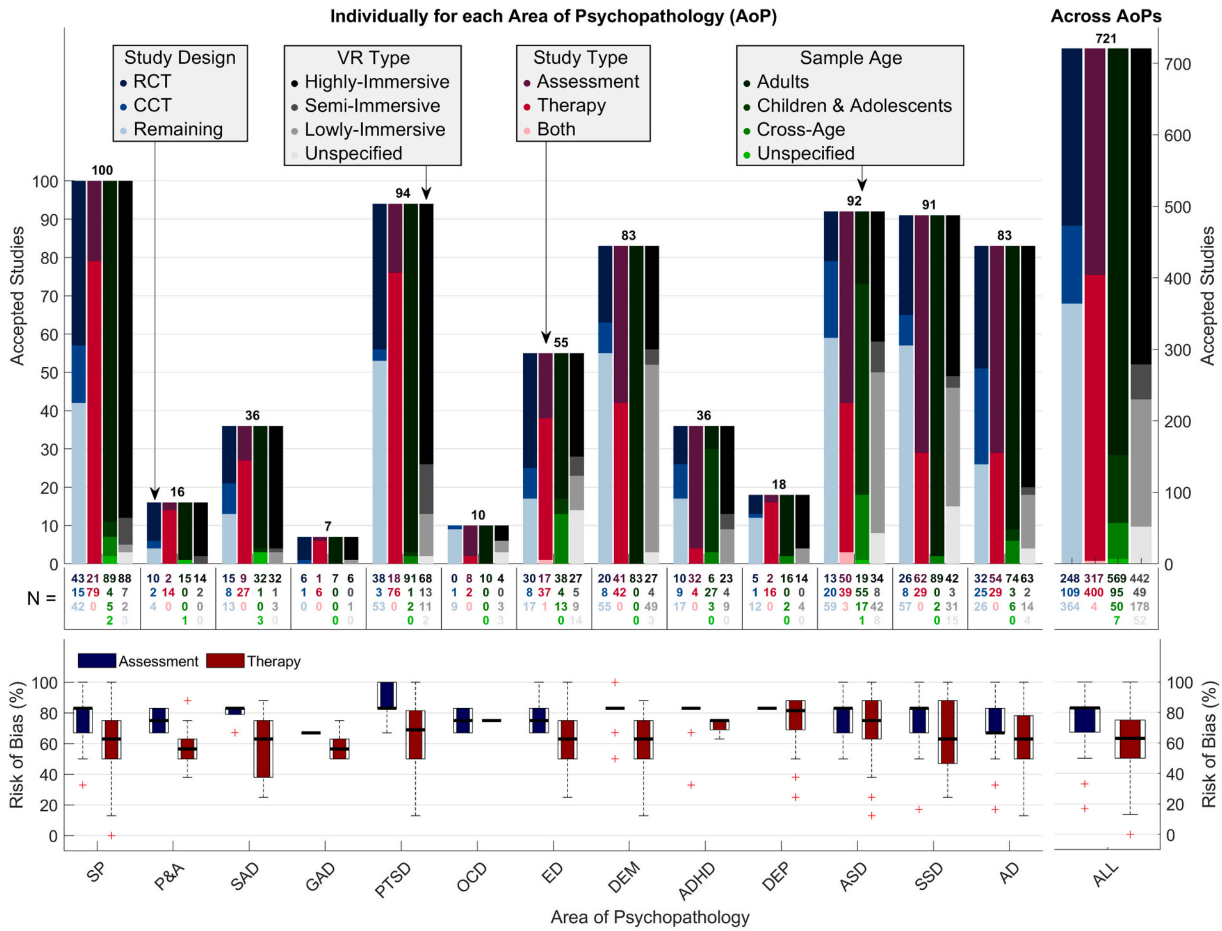

Fig. 2. Synopsis of included study designs, VR types, study types, sample age groups, and risk of biases (rRoB).
Upper panel. Number of included studies arranged according to study designs (blue shades), VR types (grey shades), study types (red shades) and sample age groups (green shades) for each area of psychopathology. Lower panel. Boxplots for all rRoB results in each area of psychopathology. *Abbreviations:* AoP = area of psychopathology; SP = specific phobias; P&A = panic disorder & agoraphobia; SAD = social anxiety disorder; GAD = generalized anxiety disorder; PTSD = posttraumatic stress disorder; OCD = obsessive-compulsive disorders; ED = eating disorders; DEM = dementias; ADHD = attention-deficit/hyperactivity disorder; DEP = depression; ASD = autism spectrum disorders; SSD = schizophrenia spectrum disorders; AD = addiction disorders.

determined for ASD (*M* = 75.94%; *SD* = 15.67%). Finally, regarding VR types, 61.30% of studies relied on highly-immersive VR devices (i.e., HMDs or CAVE systems), while 6.80% of studies used semi-immersive VR devices (e.g., stereoscopic glasses) and 24.69% lowly-immersive VR setups (i.p. computer screens).

An outline of the historical development of VR assessment and treatment studies by publication year and disorder is provided in Figure 3. As can be seen, since the first study was published in 1995, there has been an exponential growth of newly published studies in this field over the years. Moreover, while research activity began quite early in the area of SP, use of VR in the areas of DEP, GAD, and OCD was explored comparatively late.

3.1. *Specific phobias (SP)*

SP describe the marked fear or avoidance of a certain object or situation, which is overreaching with regard to the actual hazard of the feared object or situation (American Psychiatric Association, 2013). Typical subtypes of SP are the phobia of animals, natural environments, blood-injection-injuries, situations, and other phobias (Craske et al., 2017).

3.1.1. *Assessment studies*

Regarding SP, k = 21 assessment studies were found by the present review (cf. SM 3.1). Fear and anxiety ratings as well as physiological measures and behavioral cues were primarily examined as potential discriminators between healthy controls (HC) and phobic study participants.

Two RCTs (Deppermann et al., 2016; Notzon et al., 2015) exposed their participants (same sample) to a VR-based spider scenario after transcranial magnetic stimulation or sham stimulation. Across conditions, a higher subjective anxiety, more disgust, and an elevated heart rate and skin conductance level was found in adults with arachnophobia (fear of spiders) compared to HC (Notzon et al., 2015). Additionally, the arachnophobia group showed an initially lower activation of the left inferior frontal gyrus (as measured by functional near-infrared spectroscopy) during an emotional Stroop task, which disappeared after the VR exposure (Deppermann et al., 2016).

Another three studies focused on aviophobia (fear of flying) and acrophobia (fear of height). One of these studies (Wiederhold, Jang, Kim, & Wiederhold, 2002) thereby employed a virtual plane scenario and reported larger skin resistance changes during exposure in individuals with aviophobia (fear of flying) than in HC, whereas another study (Diemer, Lohkamp, Mühlberger, & Zwanzger, 2016) confronted their participants with a 'virtual height challenge' and yielded no physiological differences between acrophobic (fear of height) and non-acrophobic participants, but stronger fear ratings in the acrophobic participants. The third study (Petrescu et al., 2020), in turn, found that anxiety levels during height exposure may be predicted using features extracted from heart rate and skin conductance measurements.

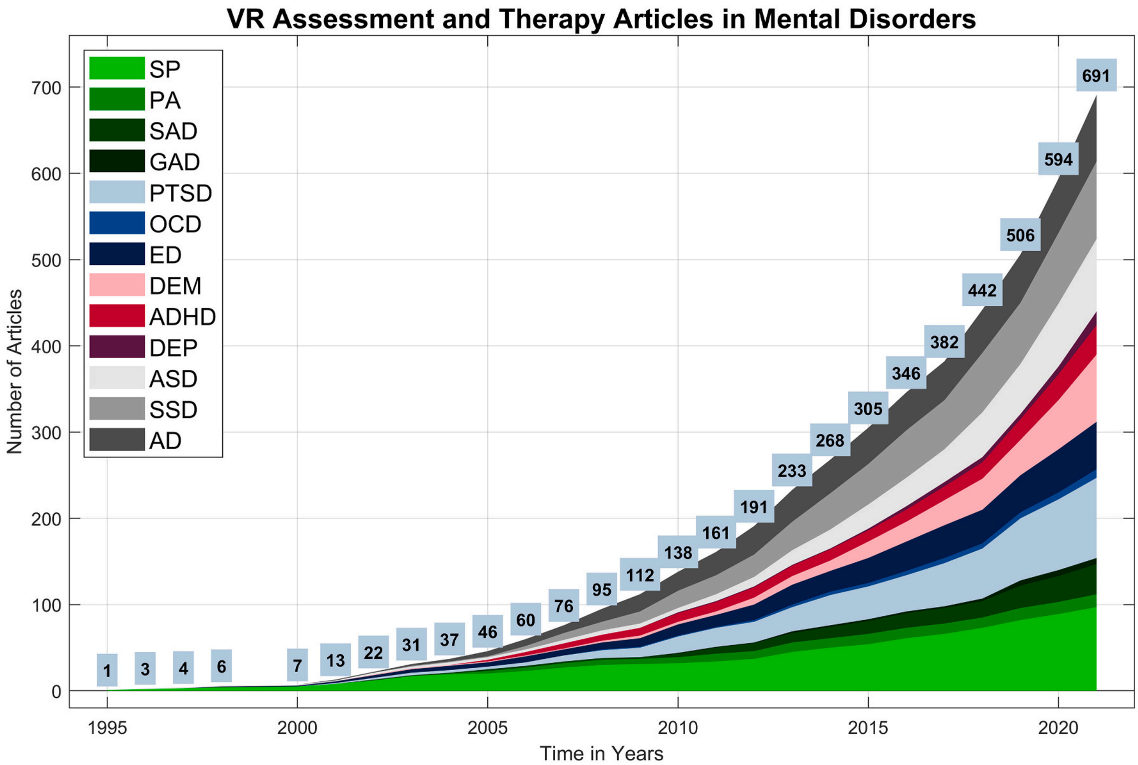

Fig. 3. Time course of publication activities.
Plot depicts the cumulative number of included studies published up to each respective year in each area of psychopathology from 1995 to 2021. *Abbreviations:* SP = specific phobias, P&A = panic disorder & agoraphobia; SAD = social anxiety disorder; GAD = generalized anxiety disorder; PTSD = posttraumatic stress disorder; OCD = obsessive-compulsive disorders; ED = eating disorders; DEM = dementias; ADHD = attention-deficit/hyperactivity disorder; DEP = depression; ASD = autism spectrum disorders; SSD = schizophrenia spectrum disorders; AD = addiction disorders.

A series of fMRI studies in small animal phobia showed that VR exposure leads to activations of fear-related brain areas (Clemente et al., 2014), that the intensity of brain activation and number of structures involved is higher in phobics than HC (Fumero et al., 2021), that 3D animated animal stimuli (spiders, lizards, cockroaches) elicit anatomically-similar (but weaker) brain activations as photorealistic 3D videos showing the same animals in persons with SP (Peñate et al., 2019), and that a higher number and greater proximity of fear related stimuli increases the neuronal phobic response (Fumero et al., 2021).

Several other studies found higher levels of anxiety (Gromer et al., 2018; Peperkorn, Alpers, & Mühlberger, 2014; Robillard, Bouchard, Fournier, & Renaud, 2003; Suied, Drettakis, Warusfel, & Viaud-Delmon, 2013; Taffou, Guerchouche, Drettakis, & Viaud-Delmon, 2013; Wilhelm et al., 2005), stronger physiological fear responses (Mühlberger, Bülthoff, Wiedemann, & Pauli, 2007; Wilhelm et al., 2005), or avoidance behavior (Gromer et al., 2018; Rinck et al., 2016), and a better fear discrimination (Mosig et al., 2014) in phobic participants compared to non-phobic participants. Moreover, in acrophobic patients, movement (Coelho et al., 2008) and wind simulation (Gromer et al., 2018) in VR were associated with higher fear. Additionally, both in individuals with acrophobia (Gromer, Reinke, Christner, & Pauli, 2019) and arachnophobia (Peperkorn & Mühlberger, 2013), sense of presence and the experience of fear in a virtual scenario were associated. Finally, Diemer et al. (2013) found that, in arachnophobic patients, physical panic symptoms triggered by VR spider exposure, but not subjective fear could be decreased by administering 100 mg of Quetiapine prior to exposure.

3.1.2. Therapy studies

With respect to VR therapy of SP, the present literature search identified k = 79 therapy studies (cf. SM 3.2; for previous reviews, see Botella, Fernández-Álvarez, Guillén, García-Palacios, & Baños, 2017; Thng, Lim-Ashworth, Poh, & Lim, 2020; Wechsler et al., 2019), most of which focused on VR exposure therapy (VRET). Similar to classical exposure therapy, VRET is a therapeutic intervention in which patients are virtually exposed to fear-provoking situations and then have to remain in that situation without applying safety-behavior until their fear declines due to habituation and/or extinction.

Acrophobia: Several controlled trials showed that acrophobia significantly decreased after VRET compared to a waiting-list control group (Krijn et al., 2004; Rothbaum, Hodges, Watson, Kessler, & Opdyke, 1996) or treatment as usual (TAU) (Freeman et al., 2018), even if VRET was administered self-guided via a smartphone using low-budget VR goggles (Bentz et al., 2021; Donker et al., 2019). Notably, these effects were even maintained until follow-up (Freeman et al., 2018; Krijn et al., 2004) and practice time, but not number of sessions, was associated with a stronger decrease in acrophobia symptoms (Donker, van Klaveren, Cornelisz, Kok, & van Gelder, 2020). A within-subject CCT by Emmelkamp, Bruynzeel, Drost, and van der Mast (2001), compared VRET to in vivo exposure in acrophobia and here VRET proved to be merely as effective. Moreover, another within-subject CCT by Levy, Leboucher, Rautureau, and Jouvent (2016) and Levy et al. (2016) compared therapist-guided VRET to remote VRET and reported both intervention types to be equally effective.

Another series of studies investigated whether VRET for acrophobia can be boosted by additional brain stimulation or pharmacological treatment. Regarding brain stimulation, one study (Herrmann et al., 2017) thereby reported an acceleration of VRET effects if the medial prefrontal cortex was stimulated by repetitive transcranial magnetic stimulation before VRET conduction, whereas another study (Bulteau et al., 2022) found no such acceleration effects after transcranial direct current stimulation of the ventromedial prefrontal cortex during VRET conduction. Regarding pharmacological treatment, in turn, some studies found no differences between VRET + pharmacological treatment and VRET + placebo treatment (Meyerbroeker, Morina, & Emmelkamp, 2018; Tart et al., 2013), whereas two controlled trials (de Quervain et al., 2011; Ressler et al., 2004) reported greater reduction of acrophobia after VRET + pharmacological treatment. In addition, in a secondary analysis of Tart et al. (2013), Smits et al. (2013) found that D-cycloserine administration after VRET led to a stronger symptom reduction than placebo administration, but only in participants who reported low fear at the end of the exposure session. If fear at the end of exposure was still high, in turn, the placebo group showed greater symptom reduction than the group receiving D-cycloserine.

Further three acrophobia studies revealed that VRET led to an overall reduction of symptoms and avoidance, regardless of whether coping self-statements or physical exercise before exposure were added (Jacquart et al., 2017; Krijn, Emmelkamp, Olafsson, Schuemie, & van der Mast, 2007; McInerney et al., 2021). Similarly, a case series study by Coelho, Santos, Silvério, and Silva (2006) reported positive effects of VRET in acrophobia. And finally, Bălan, Moise, Moldoveanu, Leordeanu, and Moldoveanu (2020) used machine learning algorithms to classify the patient's individual anxiety level during exposure based on physiological parameters, which can be used to adapt the intensity of exposure automatically.

Aviophobia: Three case-series (Czerniak et al., 2016; Ferrand, Ruffault, Tytelman, Flahault, & Négovanska, 2015; Wallach & Bar-Zvi, 2007) found supporting evidence for positive effects of VRET in aviophobia, but missed control interventions. Other, more rigorous studies, however, also confirmed a superiority of VRET over other control interventions: Two RCTs compared VRET with relaxation treatment (Mühlberger, Herrmann, Wiedemann, Ellgring, & Pauli, 2001), and cognitive therapy with VRET elements to sole cognitive therapy (Mühlberger, Wiedemann, & Pauli, 2003), and found found stronger symptom reductions after VRET; two other RCTs (Wiederhold et al., 2002; Wiederhold & Wiederhold, 2003) found that the ability to fly was greater after VRET compared to imaginal exposure therapy and that online biofeedback increased the efficacy of VRET; and another RCT (Krijn et al., 2007) found that both VRET and CBT were more effective than bibliography. Compared to computer-aided exposure therapy (Tortella-Feliu et al., 2011) and imaginal exposure (Rus-Calafell, Gutiérrez-Maldonado, Botella, & Baños, 2013), VRET was found to only be as effective at both post-treatment and follow-up. Another study revealed that treatment gains of VRET as well as for standard exposure therapy turned out to be maintained in the long term, even after a catastrophic, fear-relevant event (September 11, 2001) (Anderson et al., 2006). Moreover, an RCT by Shiban et al. (2017) indicated that VRET combined with diaphragmatic breathing can improve effective coping of fear for patients with aviophobia. Finally, examining adjunctive pharmacotherapy, two RCTs combining VRET with yohimibine hydrochloride (Meyerbroeker et al., 2018; Meyerbroeker, Powers, van Stegeren, & Emmelkamp, 2012) or propranolol administration (Meyerbroeker et al., 2018) found that adding specific medication was not more effective in reducing symptoms than VRET and placebo.

Arachnophobia: Four studies reported positive effects of VRET in arachnophobia (Botella et al., 2008; Bouchard, Côté, St-Jacques, Robillard, & Renaud, 2006; Piercey, Charlton, & Callewaert, 2012; Shiban et al., 2016) but lacked any control interventions. Supporting this preliminary evidence, two interventional studies found that VRET induced a stronger symptom reduction than no treatment (Garcia-Palacios, Hoffman, Carlin, Furness 3rd, & Botella, 2002) or neutral VR exposure (Minns et al., 2018). Moreover, another two RCTs (Michaliszyn, Marchand, Bouchard, Martel, & Poirier-Bisson, 2010; Miloff et al., 2019) reported significant reductions of arachnophobia and behavioral avoidance after both VRET and in vivo exposure therapy, although this effect was higher after in vivo exposure. Two case-series studies, in turn, showed that the gamified VRET program already tested by Miloff et al. (Miloff et al., 2019) induced a high sense of presence in the participants (Lindner, Rozental, et al., 2020) and was also effective when being self-administered (Lindner, Miloff, et al., 2020). Moreover, follow-up analyses of the same gamified program revealed that a higher alliance with the virtual therapist was associated with a higher change in spider fear (Miloff et al., 2020) and that active exposure maintenance led to continued improvement over a 1-year follow-up period (Lindner et al., 2021). Álvarez-Pérez et al. (2021) found that after eight weekly VR exposures to spider images, although subjective fear levels significantly decreased, a neural fear response was still observable, as indicated by similar fMRI amygdala activity pre and post treatment. Another RCT by Kleim et al. (2014) revealed that sleep following VRET led to higher reductions of arachnophobia and catastrophic fear-related cognitions compared to wakefulness after exposure. Rhythmic eye movements during VRET, on the other hand, did not increase its effectiveness, as shown by another RCT (Reitmaier et al., 2022). According to an RCT by Tardif, Therrien, and Bouchard (2019), adding tactile and haptic stimuli to a one-session VRET did also not increase its effectiveness. Further RCTs (Shiban, Pauli, & Mühlberger, 2013; Shiban, Schelhorn, Pauli, & Mühlberger, 2015) reported that the renewal of arachnophobia was more strongly prevented after multiple-context than single-context VRET. Moreover, it was found that a short fear activation procedure prior to the exposure had no additional attenuating effect on the return of fear 24 hours later (Shiban, Brütting, Pauli, & Mühlberger, 2015). In a secondary analysis of (Shiban et al., 2013), Portêlo, Shiban, and Maia (2021) found that the individual change in fear during VRET can be mathematically categorized, which may help predict treatment response. Three further case-series studies found potential predictors for short-term treatment response: demographics and pre-treatment clinical scores (Leehr et al., 2021), fear generalization and brain activity during a pre-treatment fear-conditioning paradigm (Roesmann et al., 2022), and changes in self-efficacy and dysfunctional beliefs during treatment (Côté & Bouchard, 2009).

Other phobia types: Further RTCs and case-series studies provided preliminary evidence for an effectiveness of VRET in driving phobia (da Costa, de Carvalho, Ribeiro, & Naro, 2018; Wald & Taylor, 2003; Walshe, Lewis, Kim, O'Sullivan, & Wiederhold, 2003), dental phobia (Gujjar, Sharma, & Jongh, 2017; Gujjar, van Wijk, Kumar, & de Jongh, 2019; Gujjar, van Wijk, Sharma, & de Jongh, 2018), blood-injection-injury phobia (Jiang, Upton, & Newby, 2020), fear of storms (Lima, McCabe-Bennett, & Antony, 2018), dog phobia (Farrell et al., 2021), phobia of enclosed spaces (Malbos, Mestre, Note, & Gellato, 2008), fear of falling in elderly patients (Levy, Leboucher, Rautureau, Komano, et al., 2016), and in phobias in autistic patients (Maskey, Rodgers, Grahame, et al., 2019; Maskey, Rodgers, Ingham, et al., 2019; Maskey, Lowry, Rodgers, McConachie, & Parr, 2014). Lastly, the present review identified nine single case studies that also reported positive effects of VRET and can be found in SM 3.2.

3.1.3. Conclusion

To sum up, a substantial number of studies on VR assessment and treatment of SP have been carried out. VR has thereby turned out to be suitable for inducing fear in phobic individuals and for discriminating phobic individuals from HC. Moreover, VRET emerges as a promising new therapy option for SP, with an overall effectiveness comparable to traditional exposure therapy (imaginal exposure and in vivo exposure). However, a cost advantage of VRET over traditional exposure therapy has yet to be demonstrated, for instance, by conducting further smartphone-based VRET studies.

3.2. Panic disorder and agoraphobia (P&A)

Panic disorder is characterized by reoccurring, unexpected panic attacks, followed by at least one month of concern, worrying or behavioral changes related to the attacks (American Psychiatric Association, 2013). Agoraphobia, in turn, is an intense fear or anxiety of situations where escape is difficult or help may not be reachable in the event of a panic attack (e.g., public transportation, open spaces), accompanied by avoidance of these situations (American Psychiatric Association, 2013). Both disorders often occur comorbidly.

3.2.1. Assessment studies

K = 2 studies were found that utilized VR for investigating P&A characteristics (cf. SM 4.1). One study (Viaud-Delmon, Warusfel, Seguelas, Rio, & Jouvent, 2006) compared the spatial performance of P&A adults with HC in a visual and an audiovisual virtual environment. In both virtual environments, no performance differences between patients and HC were found, but patients reported higher cybersickness scores. In the other study (Neueder, Andreatta, & Pauli, 2019), contextual fear conditioning was investigated in adults with acute panic attacks and HC, using virtual rooms as contextual stimuli. Greater contextual conditioning, stronger generalization of contextual anxiety, and higher levels of arousal and anxiety were found in patients than in HC.

3.2.2. Therapy studies

Regarding VR therapy in P&A, the present literature search yielded k = 14 studies (cf. SM 4.2; for previous reviews, see Carl et al., 2019; Meyerbröker & Emmelkamp, 2010; Wechsler et al., 2019), all of which investigated the effectiveness of VRET. Six RCTs (Botella et al., 2004, Botella et al., 2007; Y. H. Choi et al., 2005; Meyerbroeker, Morina, Kerkhof, & Emmelkamp, 2013; Pitti et al., 2008, 2015) studied the effects of a CBT program with VRET elements in comparison to CBT with traditional in vivo exposure and/or compared to a waiting list control condition. Both CBT interventions were found to be superior to the waiting list condition and equally effective on almost all clinical variables. In medicated patients, Pitti et al. (2008, 2015) even found a slight advantage for CBT with VRET and in vivo exposure compared to CBT with solely in vivo exposure, in that a greater symptom decrease at post-treatment (Pitti et al., 2008) and at follow-up (Pitti et al., 2015), and a higher rate of medication discontinuation at follow-up (Pitti et al., 2015) emerged. Y.-H. Choi et al. (Y. H. 2005), in turn, found similar pre-post effects in CBT with VRET and traditional CBT, while at follow-up, more medication discontinuation was observed in the traditional CBT condition. The traditional CBT group, however, received more exposure sessions than the VR group. Comparing mere VRET to VRET + cognitive therapy in an RCT, Malbos, Rapee, and Kavakli (2011, 2013) did not find any additive benefit of cognitive therapy. Moreover, as revealed by Meyerbroeker, Morina, Kerkhof, and Emmelkamp (2011), different forms of VR technology seem to produce similar results: Both VRET via HMD and VRET via CAVE were equally more effective in reducing P&A symptoms than no treatment. Also, even administered via a VR-based mobile self-help app, CBT with VRET elements turned out to be an effective treatment compared to a waiting list control condition (Shin, Oh, et al., 2021). To investigate the effects of VR interoceptive exposure, Pérez-Ara et al. (2010) compared VRET + VR interoceptive exposure to VRET + traditional interoceptive exposure and found that pre-post improvements were equal in both groups and maintained at follow-up. Finally, two case-series studies with small sample sizes also studied the effectiveness of VRET: While Lundin et al. (2022) found that 10 to 12 sessions of CBT with VRET elements led to a significant reduction in P&A symptoms, Kim et al. (2019) administered a two-session VRET with real-time heartbeat feedback to panic disorder patients, and did not find significant pre-post effects, but a trend for symptom improvement. Finally, a single case study (Whitney et al., 2005) found positive effects for a combination of VRET and physical therapy in an individual with agoraphobia.

3.2.3. Conclusion

In summary, based on the current literature, the effectiveness of VRET in P&A cannot yet be conclusively assessed. The few available studies, however, suggest a high effectiveness. Similarly, the question of the efficacy of VRET compared to in vivo exposure remains unresolved. While most studies report similar effects for both, there is some evidence for a slight superiority of VRET and some for in vivo exposure. However, within and between study variations in number and length of exposure sessions (cf. SM 4) impede any direct comparison. To confirm whether VRET is superior, inferior, or equally effective as traditional in vivo exposure therapy, more systematic research is needed.

3.3. Social anxiety disorder (SAD)

SAD is characterized by a fear of negative evaluation by others that is out of proportion to the actual threat and leads to a broad impairment in social situations (American Psychiatric Association, 2013).

3.3.1. Assessment studies

K = 9 studies were found to deal with VR-based assessment of SAD (cf. SM 5.1; for previous reviews, see Emmelkamp, Meyerbröker, & Morina, 2020; Vanni et al., 2013). All of them compared socially anxious individuals to HC in different virtual social scenarios. In a virtual public speaking task, SAD individuals showed poorer performance, higher levels of distress and anxiety, a higher startle reactivity when the audience directed their gaze towards them, and less eye gaze towards the audience than HC (Cornwell, Heller, Biggs, Pine, & Grillon, 2011; Haena Kim et al., 2018). Consistent with this, Kishimoto and Ding (2019) also reported higher anxiety scores in SAD patients than in HC for their virtual public speaking task. However, here, group differences in anxiety even increased when participants received ambiguous feedback from the virtual audience than when they received negative feedback (Kishimoto & Ding, 2019). Likewise, administering a virtual cue exposure task, Felnhofer, Hlavacs, Beutl, Kryspin-Exner, and Kothgassner (2019) found both higher subjective fear ratings and higher physiological anxiety in SAD individuals than in HC. Moreover, Lange and Pauli (2019) found that high socially anxious participants avoided humanoid avatars to a greater extent than low socially anxious participants. Similarly, Reichenberger et al. (2019); Reichenberger, Pfaller, and Mühlberger (2020) examined approach behavior towards virtual agents in a social fear conditioning paradigm. While no group difference was found in the overall sample, a subgroup analysis revealed higher subjective anxiety ratings and, using eye tracking, hypervigilance and attentional avoidance in high socially anxious participants compared to low socially anxious participants. In line with this, Wieser, Pauli, Grosseibl, Molzow, and Mühlberger (2010) reported that high socially anxious participants showed more avoidance of gaze contact with male virtual avatars than low socially anxious participants. Lastly, Holmberg et al. (2020) exposed their participants to a series of VR-videos simulating real-life shopping center situations and found an increase in anxiety in SAD patients as compared to HC.

3.3.2. Therapy studies

Regarding VR therapy in SAD, k = 27 studies were found (SM 5.2; for previous reviews, see Carl et al., 2019; Kampmann, Emmelkamp, & Morina, 2016; Wechsler et al., 2019). Most of them focused on VRET, in which patients were exposed to a social situation within VR, for example giving a presentation in front of an audience. In some cases, the therapy contained additional CBT elements such as psychoeducation and/or cognitive techniques (Anderson et al., 2013; Bouchard, Dumoulin, et al., 2017; Kim, Eom, Kwon, Kyeong, & Kim, 2020; Price, Mehta, Tone, & Anderson, 2011; Zainal, Chan, Saxena, Taylor, & Newman, 2021). 15 of the 27 included studies were RCTs. Although these studies varied greatly in terms of the type and number of control groups, there are three recurring findings: First, eight RCTs found significant pre-post reductions in social anxiety symptoms (Anderson et al., 2013; Bouchard, Dumoulin, et al., 2017; Lindner et al., 2019; Price & Anderson, 2011, 2012; Reeves, Elliott, Curran, Dyer, & Hanna, 2021; Robillard, Bouchard, Dumoulin, Guitard, & Klinger, 2010; Zainal et al., 2021). Second, in most of these studies, VRET was superior to a waiting-list control group (Anderson et al., 2013; Bouchard, Dumoulin, et al., 2017; Price & Anderson, 2011; Reeves et al., 2021; Robillard et al., 2010; Zainal et al., 2021) but not to conventional in vivo exposure therapy (Anderson et al., 2013; Price & Anderson, 2011). And third, VRET-induced symptom improvements were maintained until follow-up (Anderson et al., 2013;

Bouchard, Dumoulin, et al., 2017; Reeves et al., 2021; Safir, Wallach, & Bar-Zvi, 2012; Zainal et al., 2021). Further evidence for a positive effect of VRET was found in three CCTs (Harris, Kemmerling, & North, 2002; Kim, Eom, et al., 2020; Klinger et al., 2005) and five case-series studies (Gebara, de Barros-Neto, Gertsenchtein, & Lotufo-Neto, 2016; Geraets et al., 2019; Hur et al., 2021; H. J. Kim et al., 2020; Price et al., 2011). However, one RCT (Kampmann et al., 2016) also revealed rather mixed results, in that it found greater improvements for in vivo exposure therapy compared to VRET in most outcome measurements (pre-post and follow-up) and sometimes even no difference between VRET and a waiting-list control group.

Another two studies compared different VR interventions: Whereas the first study reported only weak evidence for an increased effect of VRET combined with attentional guidance training, in which participants were instructed to look directly at the audience, compared to traditional VRET (Rubin, Muller, Hayhoe, & Telch, 2022), the other study reported an increased effect of VRET for public speaking with an audience compared to no audience (Reeves et al., 2021).

Further findings were that outcome expectancy (Price & Anderson, 2012), mindfulness (Burton, Schmertz, Price, Masuda, & Anderson, 2013), and social costs, self-focused attention and self-efficacy (Kampmann, Emmelkamp, & Morina, 2019) influence the effect of exposure therapy regardless of the type of exposure and that the working alliance between therapist and patient similarly increases during treatment in both VRET and exposure group therapy (Ngai, Tully, & Anderson, 2015). Moreover, regarding neural correlates, changes in brain activity in the prefrontal and orbitofrontal cortex (Lee, Choi, Jung, Hur, & Cho, 2021), as well as changes in activation in various brain areas in a self-referential stimuli processing task (Hur et al., 2021) were found after six sessions of VRET with additional CBT elements. Additionally, fewer dropouts from individualized VRET compared to exposure group therapy were found in an RCT by Johnson, Price, Mehta, and Anderson (2014). Concerning the optimal amount of VRET sessions, Jeong, Lee, Kim, and Kim (2021) retrospectively analyzed various anxiety-related outcomes in patients and reported that more than 10 sessions offer minimal benefit over fewer sessions when insufficient treatment response was achieved in the first 10 sessions. Moreover, investigating the influence of presence, Price et al.'s (2011) case-series indicated that the sense of realness is associated with fear experience during VRET and that a high sense of involvement positively influences treatment success. Furthermore, a case series with children found positive results regarding acceptance, feasibility and credibility for VRET (Sarver, Beidel, & Spitalnick, 2014). Finally, two studies promisingly probed a VR-based training with a dot-probe task (Urech, Krieger, Chesham, Mast, & Berger, 2015) and a self-led online VR-intervention (Lindner et al., 2019) as alternative VR therapy approaches in SAD, but their therapeutic efficacy has yet to be further verified.

3.3.3. Conclusion

To sum up, VR-based scenarios demonstrate their usefulness in both the diagnosis and treatment of SAD. Regarding VR assessment, socially anxious individuals indeed report more anxiety and show generally more SAD specific characteristics than HC. Regarding VR therapy, the results indicate that VRET can effectively reduce SAD symptoms and may be a promising addition or even alternative to conventional exposure therapy.

3.4. Generalized anxiety disorder (GAD)

Essential features of GAD are the existence of excessive anxiety and worry across multiple topics, events, or activities that last for at least six months (American Psychiatric Association, 2013).

3.4.1. Assessment studies

Only k = 1 study was found (Guitard, Bouchard, Bélanger, & Berthiaume, 2019) that dealt with VR assessment of GAD (cf. SM 6.1). Using a CAVE system, Guitard et al. (2019) briefly exposed their participants to a neutral non-catastrophic VR scenario, a standardized 'catastrophic' VR scenario (e.g., sitting in an ambulance room), and a personalized 'catastrophic' scenario in imagination. The result was that participants reported more anxiety towards the two catastrophic scenarios than towards the neutral non-catastrophic VR scenario, while no differences were found between the standardized 'catastrophic' VR scenario and personalized 'catastrophic' scenario in imagination.

3.4.2. Therapy studies

Regarding VR therapy in GAD, the present review identified k = 6 studies (cf. SM 6.2; for previous reviews, see Maples-Keller, Bunnell, Kim, & Rothbaum, 2017; Oing & Prescott, 2018), all of which applied VR-based relaxation and mindfulness scenarios as a therapeutic tool to reduce anxiety levels.

An RCT by Navarro-Haro et al. (2019) compared a group receiving mindfulness-based treatment (MBT) to a group receiving MBT + VR-based mindfulness skills training. In the additional VR-trainings, participants listened to mindfulness skills learning audios, while concomitantly they were exposed to a floating river scenario. Whereas a pre-post GAD symptom reduction was observed after both interventions, the dropout rate was significantly lower in the group receiving additional VR-training.

Two further RCTs (Gorini et al., 2010; Repetto et al., 2013) investigated the effects of VR-based relaxation, with or without biofeedback, in comparison to a wait-list control. In both studies, pre-post comparisons revealed a significant GAD symptom reduction for both VR-relaxation types, but the symptom reductions were larger when additional biofeedback was given.

Another three studies focused on neurophysiological effects of VR in GAD patients (Tarrant, Viczko, & Cope, 2018; Wang, Sit, Tang, & Tsai, 2020; Wang, Tsai, Tang, Wang, & Lee, 2019). In T.-C. Wang et al.'s (Wang, Sit, et al., 2020; Wang, Tsai, et al., 2019) RCTs, participants either cycled 20 min in front of a "virtual nature" or "virtual abstract paintings" scenario while their EEG-activity was being recorded. It was found that group cycling in virtual nature showed significantly enhanced alpha activity compared to the control group cycling in front of virtual paintings (Wang, Tsai, et al., 2019). Moreover, both groups showed significantly higher alpha activity after training, though it remains unclear to what extent VR was causative for this increase in alpha activity (Wang, Sit, Tang and Tsai, 2020). In addition, group cycling through "virtual nature" reported higher levels of stress-relief, restorative quality and restorative satisfaction, as compared to group cycling through the "virtual abstract paintings" (Wang, Sit, Tang and Tsai, 2020). The CCT by Tarrant et al. (2018), in turn, employed a mixed model repeated-measure approach, whereby EEG activity and state anxiety were measured at baseline (T1), after a five minute resting interval (T2), and after a five minute interval either containing a nature-based mindfulness VR experience (VR meditation) or an eyes-open resting period (T3). While in both conditions state anxiety decreased and EEG alpha increased, further electrophysiological changes (i.e., global and regional decreases in beta activity) only occurred during VR meditation.

3.4.3. Conclusion

In sum, VR research in GAD has so far mainly focused on VR-based relaxation and/or mindfulness trainings. While the few studies to date suggest that VR trainings might indeed be a valuable adjunct for conventional therapies, further studies are necessary to conclusively demonstrate a benefit of these VR trainings over classical relaxation and mindfulness approaches. Moreover, it would be intriguing to see whether also more GAD-specific and CBT-inspired VR interventions beyond mere relaxation trainings can be developed (e.g., a VR exposure scenario that combats 'intolerance of uncertainty').

3.5. Posttraumatic stress disorder (PTSD)

PTSD may occur among individuals with previous exposure to at least one traumatic stressor (e.g., witness of death, actual or threatened sexual violence). Characteristic psychopathological features are intrusive symptoms of re-experience (e.g., flashbacks, nightmares), avoidance of trauma-related stimuli, and negative alterations in cognition and mood (American Psychiatric Association, 2013).

3.5.1. Assessment studies

Regarding VR assessment of PTSD, the present review identified k = 18 studies (cf. SM 7.1; for a previous review, see Rizzo & Shilling, 2018). An RCT by Malta et al. (2020) found that after exposure to war-related VR scenarios, intentional thought suppression impaired memory recall and increased the frequency of involuntary memories. In line with this, Zlomuzica et al. (2018) reported a PTSD-related reduced episodic memory formation and utilization in a case-control VR-assessment study.

Another three case-control studies (J. Park et al., 2017; Van't Wout, Spofford, Unger, Sevin, & Shea, 2017; Webb, Vincent, Jin, & Pollack, 2015) and three case-series (Costanzo et al., 2014; Maples-Keller et al., 2019; Roy et al., 2013) presented VR trauma cues to elicit vegetative responses. Several physiological alterations, such as changes in skin conductance or heart rate were found among participants with full or sub-threshold PTSD.

Similarly, various studies combined VR with functional magnetic resonance imaging to detect altered activity patterns in several specific brain regions of interest. Whereas Roy, Costanzo, Blair, and Rizzo's (2014) case-control study and Rousseau et al.'s case-series (2019) found changes in regional brain activity during exposure to trauma stimuli before and after PTSD therapy, Wicking et al.'s (2016) case-control study detected activation differences in functional imaging between participants with and without PTSD during a VR fear conditioning and fear extinction procedure. Marusak et al. (2021) used a similar procedure and found evidence of impaired fear extinction recall in trauma exposed children. Moreover, in an RCT, Steuwe et al. (2014) implemented a VR fMRI paradigm and showed that simulated direct eye contact elicited increased subcortical activation in participants with PTSD.

The remaining studies each explored separate themes: A case-control study (Onakomaiya et al., 2017) focused on the relationship between PTSD and physical activity in patients with traumatic brain injury (TBI) and reported that those TBI patients who additionally suffered from PTSD, performed worse in VR-assisted physical tasks. Another cohort study of victims of assault let their participants undergo a virtual underground ride through London (VURLON) and demonstrated that PTSD symptoms in VR correlate positively with traditional measures of PTSD (Freeman et al., 2013; Freeman, Antley, et al., 2014). And finally, virtual scenes from conflict zones were found to induce stress in participants with PTSD (Kramer, Savary, Pyne, Kimbrell, & Jegley, 2013), while social avoidance in VR environments turned out to correlate with PTSD symptom burden (Myers et al., 2016).

3.5.2. Therapy studies

Regarding VR therapy in PTSD, the present review identified k = 76 studies (cf. SM 7.2; for previous reviews, see Botella, Serrano, Baños, & Garcia-Palacios, 2015; Deng et al., 2019; Kothgassner et al., 2019). Most of these focused on VRET featuring trauma-related cues as a treatment for PTSD. Similar to VRET for (other) anxiety disorders, VRET for PTSD is based on conventional exposure therapy concepts such as prolonged exposure therapy (Foa & Kozak, 1986) and shall facilitate a therapist-guided confrontation of traumatic memories within a context-related VR environment (Rizzo, Reger, Gahm, Difede, & Rothbaum, 2009). Trauma associated thoughts and feelings are re-experienced during therapy to promote concomitant memory extinction processes.

58 studies focused on VRET in veterans or active soldiers. Three large-scale RCTs, each of which had multiple follow-up analyses, were conducted by Reger et al. (2016), Rothbaum et al. (2014), and van Gelderen et al. (2020). The investigation by Reger et al. (2016) employed a VRET program based on a virtual Iraq/Afghanistan scenario to active soldiers with war-related PTSD. Major outcomes were that both the VRET program and the prolonged exposure active control group stronger reduced PTSD symptoms (Reger et al., 2016), resting heart rate (Bourassa et al., 2019), and persecutory delusions (Buck, Norr, Katz, Gahm, & Reger, 2019) than a wait-list control group, and that there were no group differences in respect to PTSD symptoms and drop-out rates between the VRET program and prolonged exposure active control group at post-treatment, but a superiority of prolonged exposure at follow-ups (Reger et al., 2016). The RCT by Rothbaum et al. (2014), in turn, let n = 156 veterans with PTSD undergo one of three combination treatments: VRET + D-Cycloserine treatment, VRET + alprazolam treatment, or VRET + placebo treatment. Important outcomes included a pre-post reduction of PTSD symptoms in all three groups even up to a 12 months follow-up (Rothbaum et al., 2014), that cortisol responses to trauma cues were lower after VRET + D-Cycloserine treatment than after VRET + alprazolam or placebo treatment (Rothbaum et al., 2014), that there was a negative association between post-treatment PTSD symptoms and outcome expectancy (Price et al., 2015), that the treatment response after VRET + D-Cycloserine treatment was especially high in participants with a high psychophysiological reactivity (startle response) at baseline (Norrholm et al., 2016), that the treatment response after VRET + alprazolam treatment was especially high in participants with a low stress hormone reactivity at baseline (Norrholm et al., 2016), that changes in re-experiencing symptoms preceded changes in other symptom clusters (avoidance/numbing/hyperarousal) (Maples-Keller, Price, Rauch, Gerardi, & Rothbaum, 2017), and that reductions in subjective distress across treatment sessions were associated with improved outcomes (Rauch et al., 2018). In the RCT by van Gelderen et al. (2020), on the other hand, veterans with treatment-resistant PTSD either received a motion-assisted VRET program or a non-trauma focused treatment. Important outcomes were, inter alia, a higher reduction of PTSD-symptoms in the VRET group at a 16-week follow-up (van Gelderen, Nijdam, Haagen, & Vermetten, 2020), higher pre-session and post-session cortisol levels in treatment responders than non-responders (van Gelderen, Nijdam, de Vries, Meijer, & Vermetten, 2020), and positive impacts of VRET in respect to openness, new learning, self-concept, closure, and reintegration (van Gelderen, Nijdam, Dubbink, Sleijpen, & Vermetten, 2020). Finally, besides these three large-scale RCTs, various further studies were conducted that mainly found significant PTSD-reductions after war-related VRET, although VRET was not always superior to control interventions (for a complete listing of study results, see SM 7).

A further single case study (Vlake et al., 2020) and RCT (Vlake et al., 2021) focused on traumatized patients due to intensive care unit treatment and applied VRET. Whereas the first study found a pre-post reduction in PTSD, anxiety, and depression symptoms, the second study also found a pre-post reduction of PTSD and depression-symptoms that was additionally higher than in an active control group (generic VR nature scenario).

Another five studies employed VRET in witnesses of the 2001 World Trade Center Attack. After promising results in a single case study (Difede & Hoffman, 2002), two CCTs compared VRET to a wait-list control group and found significantly lower post-treatment PTSD symptoms and a higher number of patients who did no longer meet the diagnostic criteria for PTSD in the exposure group (Difede et al., 2007; Difede, Cukor, Patt, Giosan, & Hoffman, 2006). Furthermore, administering 100mg D-cycloserine before each VR exposure session increased the symptom reduction and remission rate compared to placebo (Difede et al., 2014). In a secondary analysis of Difede et al. (2014), Peskin et al. (2019) found that the VRET-induced reduction in PTSD symptoms led to a reduction in depressive symptoms, and that this effect could be enhanced by D-cycloserine. Lastly, a further single case study employed a customized virtual bus ride scenario in a survivor of a terrorist attack and found a decrease in PTSD symptoms to full recovery (Freedman et al., 2010).

A further three studies focused on motor vehicle accidents, whereby Beck, Palyo, Winer, Schwagler, and Ang (2007) employed a VRET driving program for adults with PTSD due to a motor vehicle accident, Walshe et al. (2003) a VR-driving simulator for adults with driving phobia and/or PTSD due to a motor vehicle accident, and Kamkuimo Kengne, Fossaert, Girard, and Menelas (2018) a VRET program for a truck driver with a PTSD. The common finding was a pre-post reduction in PTSD symptoms. All three studies, however, lacked a control group.

The remaining five studies dealt with mixed trauma etiologies. Two of these implemented EMMA's world, an adaptive VR system that, embedded in a CBT program, aims to foster emotional processing in patients with PTSD (Botella et al., 2010; Guillén, Baños, & Botella, 2018). EMMA's world seemed to reduce PTSD symptoms (Botella et al., 2010) and patients expressed positive opinions about the intervention and high treatment satisfaction (Guillén et al., 2018), although no statistically significant differences between EMMA's world and classical CBT without VR were observed. Two further studies compared VR-based meditation to in vivo meditation in undergraduate students with varying degrees of PTSD symptoms (Mistry et al., 2020; Waller, Mistry, Jetly, & Frewen, 2021). Overall, they found that the order of the different types of meditation impacted positive experience (Mistry et al., 2020), but PTSD symptoms were a risk factor for experiencing negative affect during meditation (Mistry et al., 2020; Waller et al., 2021). Finally, a case-series study (Tielman, Neerincx, Bidarra, Kybartas, & Brinkman, 2017) found high usability for an online therapy program including a 3D world builder for recreation of traumatic memories in four patients with PTSD (veterans and childhood sexual abuse victims).

3.5.3. Conclusion

In sum, while some VR-based investigations of PTSD have been carried out and have advanced our understanding of PTSD pathomechanisms, the focus of VR-based PTSD studies has so far clearly been on VRET. While these studies provide reliable evidence that VRET is effective, particularly as a treatment for war-related PTSD, a clear cost advantage and clinical benefit of VRET over traditional exposure therapy has yet to be demonstrated. Regarding cost efficiency, it would be particularly intriguing to examine, as to what extent VRET still remains effective when administered via low-cost smartphone-based HMDs. In addition, it appears advisable to conduct more investigations in individuals without a military background to add further evidence to VRET efficacy in non-combat PTSD forms.

3.6. Obsessive-compulsive disorder (OCD)

OCD is a debilitating psychiatric disorder characterized by obsessions (i.e., intrusive unwanted thoughts or images) and/or compulsions (i.e., ritualized repetitive behaviors) (American Psychiatric Association, 2013). Though the clinical presentation of OCD is highly heterogeneous, obsessions and compulsions typically fall into a small number of symptom dimensions, including contamination/cleaning, obsessions/checking, and symmetry/ordering (Mataix-Cols, Do Rosario-Campos, & Leckman, 2005).

3.6.1. Assessment studies

Based on the inclusion criteria of our literature search, k = 8 articles on VR assessment of OCD were found eligible (cf. SM 8.1; for a previous review, see Dehghan, Saeidimehr, Sayyah, & Rahim, 2022). Four of these studies stem from the same research group and employed the Virtual Multiple Errands Test (VMET), in which subjects are instructed to complete a list of specific tasks in a virtual supermarket, such as buying products (Cipresso et al., 2013; La Paglia et al., 2014; La Paglia, La Cascia, Rizzo, Riva, & La Barbera, 2012; Pedroli et al., 2019). In these studies, OCD patients and HC were compared regarding their cognitive functions (Cipresso et al., 2013; La Paglia et al., 2012; La Paglia et al., 2014; Pedroli et al., 2019). Overall, patients exhibited significantly worse VMET performances than HC in all studies (Dehghan et al., 2022), which correlated with performance in a neuropsychological battery.

The other four studies explored VR-based cue exposure (Cullen, Dowling, Segrave, Carter, & Yücel, 2021; K. U. Kim et al., 2008; van Bennekom, Kasanmoentalib, de Koning, & Denys, 2017; van Bennekom, de Koning, Gevonden, Kasanmoentalib, & Denys, 2020). In the CCT by Cullen et al. (2021), n = 22 OCD patients completed both, an in vivo and a VR-based exposure session in counterbalanced order. VR exposure comprised either a kitchen or a bathroom scenario in which subjects were instructed to touch dirty items. While pre-session anxiety was significantly larger for in vivo exposure, there were no differences in post-session anxiety, therapeutic allegiance, and heart rate between in vivo and VR exposure. Notably, engagement and adherence were significantly increased in VR compared to in vivo exposure.

The case-control study by Kim et al. (2008), in turn, investigated whether a computer-generated virtual environment is effective in inducing anxiety and provoking OCD symptoms. More specifically, n = 33 OCD patients and n = 30 HC performed a VR task that was designed to assess checking compulsions in a virtual home environment. Using a joystick, participants turned on a switch, opened a window, opened the front door, turned on the gas valve and gas burner, and operated a water supply according to a predefined storyline. After a distraction phase, participants were asked to turn off and check everything freely before leaving the house. OCD patients reported significantly higher levels of anxiety, showed a larger decrease in anxiety after checking, and exhibited longer checking times than HC. Furthermore, the level of anxiety reported by OCD patients correlated with immersive tendency, OCD symptom severity, the Beck Anxiety Inventory score, and checking time.

Finally, the two case-control studies by van Bennekom et al. (2017, 2020) employed a VR game with 15 OCD-related items that pertained to cleaning, checking, and ordering in a virtual house. In the first pilot study with n = 8 OCD patients and n = 8 HC, no significant differences were observed with respect to subjective emotional response, although patients exhibited nominally higher values (van Bennekom et al., 2017). As expected, OCD patients performed significantly more compulsions than HC. In the second, more recent study, van Bennekom et al. (2020) assessed n = 26 OCD patients and n = 26 HC using the same VR game. Here, patients reported significantly higher levels of anxiety and performed more compulsions. Differences in tension, uncertainty, and urge to control were not significant between groups, and there were no substantial correlations with symptom severity for all emotional response measures.

3.6.2. Therapy studies

Based on the inclusion criteria of our literature search, only k = 2 articles on VR therapy of OCD were found eligible, which focused on VRET (SM 8.2; for a previous review, see Dehghan et al., 2022). In the first study (Laforest, Bouchard, Bossé, & Mesly, 2016), three OCD patients with contamination symptoms received a 12-session CBT treatment (1 h per week) including eight sessions of VRET in a CAVE. The VRET consisted of touching walls and toilet bowls with varying degrees of filthiness. Symptom severity, anxiety and daily functioning were assessed throughout the intervention and follow-up information was gathered after four and eight months. Time-series data of OCD symptom severity revealed a significant improvement in all three participants, while global improvement was considered positive for only two of them.

The second study (Dua, Jagota, & Grover, 2021) examined a single male OCD patient, who received 60 sessions of VRET over the course of two months. Idiosyncratic anxiety-provoking stimuli (i.e., images of people and audio recordings of their names) were presented via a HMD and clubbed with response prevention. By the end of the therapy, OCD symptom severity showed a strong reduction, and the patient maintained 80 % improvement at follow-up.

3.6.3. Conclusion

In sum, VR research on OCD is still in its infancy. Although various outlook papers (Ferreri et al., 2019; Kim, Kim, Kim, Roh, & Kim, 2009; M Koran & Aboujaoude, 2018) highlight the potential benefits of VR assessment and therapy for OCD patients, only a few studies have actually employed VR devices for neurocognitive assessments and VRET so far. Regarding OCD assessment, the conducted VMET studies found that OCD patients exhibit significant deficits in cognitive functions, suggesting that VR-based tests may be ecologically valid tools for the neurocognitive assessment of OCD patients. Regarding OCD therapy, the conducted studies provide preliminary evidence for the notion that virtual cue exposure is effective in inducing an emotional response in OCD patients and that VRET reduces OCD symptom severity. Further research with larger sample sizes and more standardized VR scenarios is, however, clearly warranted.

3.7. Eating disorders (ED)

ED are characterized by persistent and severe disturbances in eating and eating-related behaviors, thoughts, and emotions (American Psychiatric Association, 2013). The three most common ED are anorexia nervosa (AN), bulimia nervosa (BN), and binge-eating disorder (BED). Main characteristics of AN and BN are intense fear of gaining weight or persistent behavior that interferes with weight gain (e.g., a restriction of energy intake) and a misperception of body shape and/or size. In BED, binge or out-of-control eating is accompanied by significant distress about eating, but lacks compensatory behaviors (American Psychiatric Association, 2013). Although not defined as mental disorders, overweight (BMI $\geq$ 25) and obesity (BMI $\geq$ 30) may also be associated with abnormal eating behaviors (McCuen-Wurst, Ruggieri, & Allison, 2018) and have therefore also been included into this review.

3.7.1. Assessment studies

Regarding ED, $k = 17$ mere assessment studies and $k = 1$ combination study were found by the present literature search (cf. SM 9.1; for a previous review, see Clus, Larsen, Lemey, & Berrouiguet, 2018). Most studies implemented VR for food cue exposure ($k = 10$), while other studies dealt with interpersonal distance ($k = 1$), spatial memory ($k = 3$) and body perception ($k = 4$).

Regarding cue exposure, a CCT (Gorini, Griez, Petrova, & Riva, 2010) indicated that food cues presented via VR-goggles to AN and BN patients elicited higher subjective and physiological emotional responses than 2D food pictures and comparable emotional responses as real food. Moreover, in two RCTs from one group and three follow-up analyses, VR exposure to high-caloric compared to low-caloric food elicited higher levels of anxiety, depression, body image distortion, body dissatisfaction, and subjective discomfort in adolescents and adults with AN, BN, and ED not otherwise specified (Ferrer-Garcia & Gutiérrez-Maldonado, 2011; Ferrer-Garcia, Gutiérrez-Maldonado, Caqueo-Urízar, & Moreno, 2009; Gutiérrez-Maldonado, Ferrer-Garcia, Caqueo-Urízar, & Letosa-Porta, 2006), but not in HC (Ferrer-Garcia et al., 2009; Gutiérrez-Maldonado, Ferrer-Garcia, Caqueo-Urízar, & Moreno, 2010). Notably, higher levels of anxiety and depression thereby predicted stronger body image distortion and body dissatisfaction (Ferrer-Garcia & Gutiérrez-Maldonado, 2010). In addition, exposure to a swimming pool environment also elicited anxiety, depression, and subjective discomfort in the same patients (Ferrer-Garcia et al., 2009; Ferrer-Garcia & Gutiérrez-Maldonado, 2011; Gutiérrez-Maldonado et al., 2006), but not in HC (Ferrer-Garcia et al., 2009). In another two case-control studies (Ferrer-Garcia et al., 2015; Ferrer-Garcia, Pla-Sanjuanelo, et al., 2017), patients with BED and BN experienced higher levels of craving and anxiety in response to virtual food exposure compared to HC, with external and emotional eating behavior style predicting the level of food craving and anxiety in the patients. Finally, in two further case-control studies (Perpiñá et al., 2013; Perpiñá & Roncero, 2016), participants were asked to “eat a forbidden meal” in a virtual kitchen. While all participants reported high ecological validity of the scenario, adolescents and adults with AN, BN, or ED not otherwise specified reported higher palatability, fear, attention, emotional involvement, and negative effects of eating compared to HC (Perpiñá et al., 2013; Perpiñá & Roncero, 2016) and compared to obese adults (Perpiñá & Roncero, 2016).

Regarding interpersonal distance, an RCT by Welsch, Hecht, Kolar, Witthöft, and Legenbauer (2020) implemented a stop-distance task in VR and found that adult females with ED required larger interpersonal distance to feel comfortable than HC. Moreover, both groups occupied a larger distance towards under- and over-weighted compared to normal-weighted avatars, with this effect being more pronounced in the ED group and being associated with body-related avoidance and depression.

With respect to spatial memory and learning, three studies employed respective VR-tasks to patients with ED (Cipolletta, Malighetti, Serino, Riva, & Winter, 2017; Cyr et al., 2016; Serino, Dakanalis, et al., 2015). Two of these revealed that spatial abilities such as spatial retrieval (Serino, Dakanalis, et al., 2015), navigation and mental rotation (Cipolletta et al., 2017) were worse in AN (and for spatial retrieval also BN) patients as compared to HC. The study by Cyr et al. (2016), in turn, found that adolescents with BN did not perform worse than HC during a reward-based spatial learning paradigm, but showed abnormal activation in fronto-striatal brain regions and the anterior hippocampus.

The remaining four studies dealt with the assessment of body image disturbances in AN (Fisher, Abdullah, Charvin, Da Fonseca, & Bat-Pitault, 2020; Mölbert et al., 2018; Porras-Garcia, Ferrer-Garcia, et al., 2020; Provenzano et al., 2019). Fisher et al.'s (2020) CCT compared two body size estimation approaches and found that VR-based avatar rating scales captured body estimation and dissatisfaction in adolescents with AN to a similar extend as a widely-used paper-based figure rating scale. In the case- control study by Mölbert et al. (2018), in turn, participants were repeatedly confronted with biometric self-avatars and non-biometric avatars in varying body volumes. Two important results were that while both women with AN and HC underestimated their own weight, HC showed a stronger desire to lose weight compared to women with AN. Likewise, Provenzano et al. (2019) confronted their participants with biometric self-avatars of varying body volume. In this study both women with AN and HC equally precisely estimated the size of their own bodies, but those women with AN were more desirous to have a thinner body. Finally, the case-control study by Porras-Garcia, Ferrer-Garcia, et al. (2020) () found that while a biometric full-body illusion induced higher anxiety and fear of gaining weight in women with AN than HC, the patients were less susceptible to the illusion, with a strong negative correlation between body image disturbance and illusion intensity.

3.7.2. Therapy studies

$K = 37$ mere therapy studies and $k = 1$ combination study were found in the present review (SM 9.2; for previous reviews, see Clus et al., 2018; Ferrer-García, Gutiérrez-Maldonado, & Riva, 2013). Most of these studies utilized VR to modify body image, often as part of a multidisciplinary treatment. Giuseppe Riva's group (Catholic University of Milan) developed the Experiential Cognitive Therapy, which combines cognitive-behavioral approaches and weight reduction programs with VR interventions addressing body experience disturbances, motivation for change, self-efficacy, self-acceptance, and eating control. In several RCTs, Riva's group administered this treatment intervention to patients with BED and/or obesity and observed improved short- and long-term outcomes such as reduced weight and/or enhanced eating behavior (Cesa et al., 2013; Manzoni et al., 2016; Riva et al., 2006; Riva, Bacchetta, Baruffi, & Molinari, 2001, 2002; Riva, Bacchetta, Cesa, Conti, & Molinari, 2003, 2004), body image and satisfaction (Riva et al., 2001, 2002, 2003, 2004, 2006), and self-efficacy (Riva et al., 2002, 2003, 2004; 2006), compared to CBT and/or standard weight reduction therapy alone or waiting list control groups. A single-case study (Riva, Cárdenas-López, Duran, Torres-Villalobos, & Gaggioli, 2012) and a small case series (Cárdenas-López et al., 2014) also reported positive effects for Experiential Cognitive Therapy in obese adults after bariatric surgery. Moreover, one multiple published single-case study (Riva et al., 1999; Riva, Bacchetta, Baruffi, Rinaldi, & Molinari, 1998a, 1998b; Riva, Bacchetta, Baruffi, Rinaldi, & Molinari, 1999) suggested benefits of Experiential Cognitive Therapy also for AN, while another RCT (Marco, Perpiñá, & Botella, 2013) indicated that a similar VR therapy intervention aiming to modify body image was superior to standard CBT in a sample of patients with AN, BN, or ED not otherwise specified. Another five studies (Keizer, van Elburg, Helms, & Dijkerman, 2016; Porras-Garcia et al., 2021; Porras-Garcia, Serrano-Troncoso, et al., 2020; Provenzano et al., 2019; Serino, Polli, & Riva, 2019) evaluated the effects of a full body illusion in patients with AN. By enabling participants to immerse into an embodiable virtual body, the therapy rationale was to modify the distorted body image and to increase body satisfaction. While one RCT (Porras-Garcia et al., 2021) and one CCT (Keizer et al., 2016) found that embodiment of a virtual body might reduce fear of gaining weight, body dissatisfaction (Porras-Garcia et al., 2021), and body size misestimating (Keizer et al., 2016; Porras-Garcia et al., 2021) in AN, Provenzano et al.'s (2019) CCT found no effects on body satisfaction for this patient population. The two single-case studies by Porras-Garcia, Serano-Troncoso, et al. (2020) and Serino et al. (2019), in turn, implicated potential benefits for body image and satisfaction, as well as for weight gain in AN. Another four studies utilized VRET to food cues to modify eating behavior. While one case-series study revealed that a treatment consisting of food exposure in VR and in real life in combination with CBT elements is feasible and reduces binging in adults with BN or BED (Nameth et al., 2021), one RCT and follow-up examination indicates superior short- and long-term benefits of VRET for reducing binge eating and food craving in patients with BN or BED and limited response to CBT, as compared to CBT (Ferrer-Garcia, Gutiérrez-Maldonado, et al., 2017*;* Ferrer-Garcia et al., 2019). A single-case study further shows improvements in ED symptoms and increases in BMI in a woman with AN after VRET intervention to food cues (Cardi et al., 2012).

A further set of studies focused on VR-assisted weight reduction in overweight adults. In a case-series study, social eating scenarios in VR were used for weight management skills training, leading to improved eating control in overweight adults (Thomas, Spitalnick, Hadley, Bond, & Wing, 2015). Similarly, less loss of control over eating was achieved through inhibitory control training in VR (Manasse, Lampe, Juarascio, Zhu, & Forman, 2021). Moreover, four further studies (Johnston, Massey, & Devaneaux, 2012; Phelan et al., 2021; Sullivan et al., 2013; Thomas, Goldstein, Bond, Hadley, & Tuerk, 2020) employed online programs to enhance weight loss interventions in overweight and obese adults. Two of these thereby revealed similar (Johnston et al., 2012) or less (Sullivan et al., 2013) amounts of weight loss for a VR compared to a face-to-face intervention, but benefits for physical activity, self-efficacy, and healthy eating behavior (Johnston et al., 2012), as well as stronger long-term weight loss and physical activity increases for the VR intervention (Sullivan et al., 2013). The other two RCT's, in turn, showed that adding VR to a standard weight loss program did not enhance weight loss at the end of the intervention (Phelan et al., 2021; Thomas et al., 2020), but might have longer-term benefits (Thomas et al., 2020).

In two further RCTs (Manzoni et al., 2009; Riva, Manzoni, Villani, Gaggioli, & Molinari, 2008), VR was utilized for relaxation or stress management in obese patients suffering from emotional eating. The first RCT revealed that, combined with an inpatient weight reduction program, VR-based relaxation training had similar positive effects on eating behavior as imagination-based relaxation training, while, at 3-month follow-up, it was more efficient to reduce emotional eating (Manzoni et al., 2009). The second RCT, in turn, revealed that, compared to a DVD-based stress management protocol, a VR-based protocol reduced anxiety levels to a larger extend (Riva et al., 2008).

Another series of studies examined VR-assisted weight management education. Providing weight management education via a virtual physician in a standardized but realistic way, two RCTs reported that the type of information provided (genetic vs. behavioral causes of overweight), the communication approach and racial identification of the physician, as well as the emotional state of the participants had different effects on confidence, perceived stigmatization and blame, and nonverbal behavior of overweight adults (Persky, Ferrer, & Klein, 2016; Persky & Street, 2015). In addition, three RCTs (McBride, Persky, Wagner, Faith, & Ward, 2013; Persky et al., 2021*;* Persky, McBride, Faith, Wagner, & Ward, 2015) used a virtual buffet to study the food choice of overweight parents for their child after receiving information on the child's behavioral and/or genetic risks of obesity. While the first RCT indicated that a combination of both risk information types leads to a reduced calorie choice in mothers (McBride et al., 2013), the second revealed higher perceived guilt for the child's lifestyle behavior and genetic obesity risk (Persky et al., 2015). Finally, the third RCT implied that even though receiving genetic risk information leads to higher calorie choices in the virtual buffet only in mothers and not in fathers, both reported feeding their child more junk food and fatty meat at 1-week follow-up (Persky et al., 2021).

The remaining five studies utilized VR to improve experiences related to physical activity. In one RCT, pleasure after short cycling sessions was increased in obese adults (Jones & Ekkekakis, 2019), while in one CCT, playing active video games on a treadmill led to high ratings of attractiveness and fun, and high exercise intensities in obese children and adolescents (Polechoński, Nierwińska, Kalita, & Wodarski, 2020). Moreover, an RCT showed that watching an avatar resembling the subject can help to increase daily energy expenditure in overweight older adults (Ruiz et al., 2012), whereas in another RCT no VR-related physical activity increases following a 1-week intervention were observed in overweight adults (Navarro, Cebolla, Llorens, Borrego, & Baños, 2020). Finally, one case-series (Paslakis et al., 2017) suggested that exposure to physical activity in VR decreases the urge to be physically active in AN and BN.

3.7.3. *Conclusion*

To conclude, there are increasing research efforts on employing VR in the assessment and treatment of ED. Regarding VR assessment, the studied subdomains and research approaches adopted are still too heterogeneous to reliably evaluate the diagnostic value of VR-based approaches. However, the existing studies suggest that, among other interventions, the use of virtual food cues and embodiable and/or biometric self-avatars could be helpful in objectifying ED symptoms such as body schema distortions. Regarding VR therapy, in turn, a sizable number of well-designed studies indicates superiority of Experiential Cognitive Therapy over standard therapeutic approaches such as CBT or educational programs. Most of the evidence, however, stems from the group of Guiseppe Riva, so that replication studies in independent samples would strengthen these findings.

3.8. *Dementia (DEM)*

DEM is a major neurocognitive disorder characterized by an impairment in one or more cognitive domains, such as complex attention, executive function, learning and memory, language, perceptual motor-function, and social cognition (American Psychiatric Association, 2013). Mild cognitive impairment (MCI), in turn, refers to a cognitive decline between normal cognition and DEM, but with preserved independent daily functioning (Hugo & Ganguli, 2014). Most common forms of DEM are Alzheimer's disease, vascular DEM, DEM with Lewy bodies, and frontotemporal DEM.

3.8.1. *Assessment studies*

In the present review, a total of k = 41 studies were found to investigate VR assessment of DEM (cf. SM 10.1; for previous reviews, see Yao Liu et al., 2019; Wang, Yin, et al., 2020), with most of them comparing one or more pathologic groups to healthy individuals in a case-control design and only few RCTs comparing different interventions.

One series of studies focused on spatial navigation deficits in MCI and Alzheimer's disease and employed various VR-based navigation tasks. A recurring finding here was that both patients with MCI (da Costa et al., 2021; Howett et al., 2019; Weniger, Ruhleder, Lange, Wolf, & Irle, 2011) and Alzheimer's disease (Allison, Fagan, Morris, & Head, 2016; Davis, Ohman, & Weisbeck, 2017; Morganti, Stefanini, & Riva, 2013; C.-F. Tsai et al., 2021) showed considerable spatial navigation deficits compared to HC. VR navigation skills were also found to correlate strongly with real-world navigation skills, and both skill types allowed to discriminate patients with MCI and early Alzheimer's disease (Cushman, Stein, & Duffy, 2008). Other important results were: First, patients with MCI performed better in a VR orientation task than patients with mild Alzheimer's disease (Moussavi, Kimura, & Lithgow, 2022). Second, higher sensitivity and specificity for discriminating biomarker-positive from biomarker-negative MCI patients was demonstrated for a VR-based compared to a paper-based navigation task (Howett et al., 2019). Third, patients with multiple domain MCI turned out to perform worse compared to those with single domain MCI in a VR reorientation task (Caffò et al., 2018). And fourth, only patients with multiple domain MCI or mild Alzheimer's disease, but not those with single domain MCI, were discriminated from HC by a VR navigation task (Mohammadi, Kargar, & Hesami, 2018).

Another series of studies focused on memory impairments in MCI and Alzheimer's disease. One finding was that while traditional and VR-based list learning revealed similar performances in HC, the VR-based test was more sensitive in detecting patients with mild Alzheimer's disease (Widmann, Beinhoff, & Riepe, 2012). In addition, Sauzéon et al. (2016) employed a "VR Human Object Memory for Everyday Scenes test" and found that their task discriminated only weakly between healthy young and elderly people, but well between healthy elderly and Alzheimer's disease patients. Further findings were: firstly, that navigation and memorization tasks in a virtual town showed a reduced prospective memory performance in patients with mild Alzheimer's disease as compared to HC (Lecouvey et al., 2019); secondly, that recall and recognition abilities after a virtual car drive simulation were worse in patients with Alzheimer's disease than in MCI and, moreover, that both performed inferior to HC (Plancher, Tirard, Gyselinck, Nicolas, & Piolino, 2012); thirdly, that patients with amnestic MCI and patients with Alzheimer's disease each show distinct deficits in a VR-based spatial memory paradigm (Serino, Morganti, Di Stefano, & Riva, 2015); and fourthly, that VR-based spatial memory evaluations appear to have potential to discriminate amnestic and non-amnestic MCI subtypes (Caffò et al., 2018).

In addition, there have been several study outcomes on more global cognitive functions and functional abilities in MCI and Alzheimer's disease: First, VR-based evaluations of functional abilities allowed to better discriminate between patients with MCI and HC than a questionnaire assessment (Seo, Kim, Oh, Ryu, & Choi, 2017) and to even discriminate between MCI and mild Alzheimer's disease patients (Tarnanas et al., 2013). Second, an assessment approach based on serious gaming revealed no group differences between amnestic MCI patients and HC in executive functioning, but in memory performance (Cabinio et al., 2020). Third, in particular spatial allocentric memory turned out effective in the discrimination between MCI and HC in a "Virtual Action Planning Museum" task (Tarnanas et al., 2015; Tarnanas, Laskaris, & Tsolaki, 2012) and in a virtual car scenario (Plancher et al., 2012). And finally, a virtual supermarket environment effectively discriminated HC and MCI (Yan et al., 2021), but yielded no significant differences between MCI subtypes (Eraslan Boz et al., 2020; Zygouris et al., 2015).

Another five studies focused on VR assessments in Parkinson's disease. Important outcomes here were: First, a VR-based evaluation of executive functioning yielded decreased performances in Parkinson patients as compared to HC (Borgnis et al., 2022). Second, a virtual kitchen task differentiated between impairments related to early Parkinson`s disease and early manifest Huntington's disease (Júlio et al., 2020). Third, a virtual supermarket task successfully discriminated between HC and Parkinson patients with and without MCI (Cipresso et al., 2014). Fourth, a short VR functional capacity assessment of patients with Parkinson's disease found those with MCI to have higher error rates and higher completion times than those without MCI (Turner, Atkins, & Keefe, 2021). And fifth, patients with amnestic MCI and Parkinson's disease MCI showed higher accuracy and distance scores than patients with Alzheimer's disease in a serious games global cognition evaluation (Bottiroli et al., 2021).

Finally, k = 12 assessment studies had a primary focus on feasibility aspects or used a less rigorous design with small samples on the basis of which no robust conclusions can be drawn (for a complete overview of all included assessment studies, see SM 10.1).

3.8.2. Therapy studies

As regards VR therapy studies in DEM, the present review identified k = 42 studies (cf. SM 10.2; for previous reviews, see Kim, Pang, & Kim, 2019; Yao Liu et al., 2019; Strong, 2020). Most of these examined VR-based cognitive trainings, combinations of VR-based cognitive trainings and physical trainings, or serious VR game approaches related to one or several specific cognitive functions or instrumental activities of daily living.

One series of studies focused on VR-based treatment approaches in patients with MCI and mostly found positive effects: First, VR-based combined cognitive (e.g., taking a virtual train) and physical training (e.g., practicing virtual tai chi) induced stronger improvements on global cognition, verbal delayed memory recall, instrumental activities of daily living (Liao, Tseng, Lin, Wang, & Hsu, 2020), and divided attention (Liao, Chen, Lin, Chen, & Hsu, 2019) than traditional physical and cognitive training. Second, VR cognitive-motor rehabilitation stronger enhanced cognitive functioning and attention than conventional cognitive rehabilitation (Park, Jung, & Lee, 2020). Third, administration of a virtual bike tour improved executive functions (Anderson-Hanley et al., 2018). Fourth, gains in episodic memory were stronger after a VR-based than a traditional therapy-led memory training (Man, Chung, & Lee, 2012). Fifth, cognitive functioning enhanced with both VR-based cognitive rehabilitation training and traditional rehabilitation training, but the former yielded stronger improvements (Torpil, Şahin, Pekçetin, & Uyanık, 2021). Sixth, virtual cognitive rehabilitation improved memory, language and visuoconstructional abilities stronger than cognitive TAU (Manenti et al., 2020). Seventh, multi-domain virtual cognitive training enhanced visuospatial function and quality of life (Kang et al., 2021). Eighth, multisession VR problem-solving training improved memory, concentration, and balance skills better than traditional occupational therapy (Hwang & Lee, 2017), and VR game-based cognitive training improved working memory performance better than a non-VR educational program (Thapa et al., 2020). Ninth, stronger improvements in abstract thinking and motor skills were evident after virtual tai chi than after usual daily physical activities (Hsieh et al., 2018). And tenth, cognitive functioning improved in both patients with MCI and HC after virtual cognitive training (Hyeyoung Kim et al., 2021; Maeng et al., 2021). However, one RCT by Park et al. (2020) also revealed less promising findings and did not deduce any differences in cognitive improvement between a VR culture-based cognitive training and a waiting list control group in patients with MCI. Notably, however, Park et al.'s RCT (2020) had a lower duration of VR exposures per week compared to the previous studies (Anderson-Hanley et al., 2018; Hwang & Lee, 2017; Liao et al., 2019, 2020; Manenti et al., 2020; Park, Jung, & Lee, 2020; Thapa et al., 2020; Torpil et al., 2021).

Another two RCTs and one CCT report on therapy approaches of patients with Alzheimer's disease and other major neurocognitive disorders. The RCT by Oliveira et al. (2021) found VR-based cognitive stimulation to improve the patients' global cognition, but not executive functioning compared to TAU, and Serino et al.'s (2017) RCT found spatial memory to be enhanced after virtual city navigation training in patients with Alzheimer's disease, but executive functioning to be improved only in HC. In line with these findings, Panerai et al.'s (2021) CCT was conducted on patients with major neurocognitive disorders and compared cognitive group training with combined cognitive group training and virtual cognitive training and found the combined training procedure to be superior in the improvement of cognitive functioning.

A further series of studies examined VR-assisted therapy approaches in Parkinson's disease. An RCT thereby found improvements in activities of daily living and motor function when routine physical therapy was supplemented by VR motor functioning training (Kashif et al., 2022). Likewise, an extensive CCT combining in-clinic and home-based VR rehabilitation reported increased functional mobility, balance, global cognitive function, memory, and quality of life in patients with Parkinson's disease (Isernia et al., 2020). Moreover, another CCT found that Parkinson's patients with additional cognitive impairments showed enhancements in global cognitive functioning and visuospatial abilities after VR-based cognitive training compared to a pen-and-paper cognitive training group (Maggio et al., 2018). Also, multi-dimensional VR-based treatment was found to have a positive effect on multiple cognitive domains based on a sufficient level of preserved general cognitive functioning, while the etiology itself (stroke vs. Parkinson's disease vs. multiple sclerosis) turned out to be less of a factor (Di Tella et al., 2020).

The remaining k = 21 studies, including k = 12 case-series and k = 2 single-case studies, focused on feasibility evaluations of several VR therapy environments or applied less rigorous study designs as for instance based on small sample sizes (for a complete overview of all included therapy studies, see SM 10.2).

3.8.3. Conclusion

To summarize, there is promising indication that VR-based assessments separate DEM and MCI conditions from healthy states. In addition, there exists some evidence that such assessments also discriminate between MCI and Alzheimer's disease, mostly based on spatial navigation and memory tasks. VR-based assessments thereby seem to not only provide an ecologically more valid environment but also appear to provide higher accuracy than traditional test environments. However, before VR-based DEM assessments can be used within regular patient care, a considerable amount of validation work is still to be performed. Regarding VR therapy, the studies reviewed provide promising indications that VR interventions might help improve cognitive functioning in MCI and mild forms of Alzheimer's disease or Parkinson's disease. Especially in more severe forms of DEM, however, further research is required before these interventions can ultimately be classified as being effective. Also, while there are indications that a higher level of immersion entails higher ecological validity, many of the included studies did not use fully immersive technology such as HMDs. However, with respect to the studies compared, no substantial differences in outcome between the devices used were revealed.The degree to which fully immersive technology can also be applied to more severe forms of DEM remains to be addressed in future research.

3.9. Attention-deficit/hyperactivity disorder (ADHD)

ADHD is a neurodevelopmental disorder characterized by inattention and/or hyperactivity-impulsivity (American Psychiatric Association, 2013). ADHD not only occurs during childhood and adolescence (5%), but persists in about half of the cases into adulthood (2.5% of adults worldwide) (Faraone et al., 2015).

3.9.1. Assessment studies

Overall, k = 32 studies were found to deal with VR-based assessments of ADHD (cf. SM 11.1; for a previous review, see Parsons, Duffield, & Asbee, 2019). Of these, 20 studies dealt with different virtual classroom (VC) implementations, within which participants performed VC-embedded cognitive tests, such as a continuous performance task (VR-CPT), while distracting events were concomitantly happening within the VC.

One series of VC studies thereby investigated whether the VR-CPTs are able to differentiate between children/adolescents with and without ADHD. Overall, the finding was that the VR-CPTs differentiated well between both populations (Areces, Dockrell, García, González-Castro, & Rodríguez, 2018; Areces, Rodríguez, García, Cueli, & González-Castro, 2018) and similarly to conventional CPTs (Adams, Finn, Moes, Flannery, & Rizzo, 2009; Bioulac et al., 2012; Neguț, Jurma, & David, 2017; Parsons, Bowerly, Buckwalter, & Rizzo, 2007; Pollak et al., 2009; Rodríguez, Areces, García, Cueli, & González-Castro, 2018). Notably, a machine learning model applied by Yeh et al. (2020) achieved a mean cross-validation classification accuracy of 83.2%, with features comprising VR-CPT and head rotation parameters. Regarding the impact of distractions, in turn, study results have so far been inconsistent: Whereas Adams et al. (2009) found a higher distractor-related impact on the cognitive performance in participants with ADHD compared to HC, Hong, Kim, Kwon, Eom, and Kim (2022) found that only HC were affected by distractions.

Another series of VC studies examined medication effects on the VR-CPTs. An RCT by Pollak, Shomaly, Weiss, Rizzo, and Gross-Tsur (2010) compared intra-individual CPT performance differences after intake of methylphenidate (MPH) and placebo, and revealed that while the VR-CPT detected an omission error drop after MPH intake, two other conventional CPT variants missed this MPH-induced attention increase. Similarly, a CCT confirmed the ability of the VR-CPT in detecting the performance difference following MPH use among individuals with ADHD (Jang et al., 2020). Likewise, a case-control study by Mühlberger et al. (2016) found that unmedicated children/adolescents with ADHD exhibited higher reaction time variabilities in the VR-CPT than medicated children/adolescents with ADHD and HC. Moreover, Díaz-Orueta et al. (2014) reported that their VR-CPT implementation successfully differentiated medicated from unmedicated children/adolescents with ADHD in a variety of assessed metrics, including processing speed, motor activity, and quality of attentional focus.

The remaining VR-CPT studies addressed other aspects besides test discriminability and medication influences: Mangalmurti et al. (2020) focused on head-actigraphy aspects and found that field-of-view shifts partially mediated the existence of an association between deficits in focused attention and hyperactivity-impulsivity symptoms; Eom et al. (2019) examined social aspects of VR-CPT performances and found that adding a virtual teacher to the VC that gave task-related instructions improved attentional processing in children/adolescents with ADHD, but not in HC; Areces, Rodríguez, García, Cueli, and González-Castro (2021) explored the influence of anxiety levels on attentional performance and revealed that state anxiety was effective in predicting performance scores in the VR-CPT; Ide-Okochi, Matsunaga, and Sato (2022) investigated participants' gaze characteristics during distraction and showed that children/adolescents with ADHD and/or autism focused on the virtual teacher longer than HC; and finally, Boo, Alpers-Leon, McIntyre, Mundy, and Naigles (2021) examined structural language use during a speaking task in children/adolescents with ADHD and/or autism and revealed that they produced less complex structural language than HC.

In another series of studies, road traffic behavior was examined in adolescents/adults with ADHD, using VR driving simulators and virtual road-crossing scenarios. Compared to HC, three studies thereby found riskier driving behaviors among adults with ADHD (Bernstein, Roye, Calamia, & De Vito, 2019; Knouse, Bagwell, Barkley, & Murphy, 2005) as well as less safe road-crossing behavior in ADHD adolescents (Clancy, Rucklidge, & Owen, 2006). Four RCTs, in turn, examined the effect of different stimulants on driving performance in ADHD patients: While Cox et al. (2008) found no performance change after MPH or amphetamine intake in a VR driving simulator as compared to placebo intake, Barkeley et al. found that ADHD adults even drive safer after taking MPH (Barkley, Murphy, O'Connell, & Connor, 2005) and atomoxetine (Barkley, Anderson, & Kruesi, 2007), but not after alcohol intake

(Barkley, Murphy, O'Connell, Anderson, & Connor, 2006).

The remaining six studies presented a variety of different VR-implementations. The first study (Camacho-Conde & Climent, 2020) examined a new virtual aquarium task and reported that adolescents with ADHD performed significantly worse than HC in various attention measures. The second study (Fang, Han, & Luo, 2019) examined the task performances of children with ADHD in three different VR tasks (Position Tracking Task, Stroop Task and Recognition Task) and found that, across tasks, they showed significantly worse performances than HC. In the third study(Dahan & Reiner, 2017), a VR motor task was conducted and it was found that patients with ADHD showed different motion characteristics compared to HC. Utilizing a VR spatial navigation task, the fourth study (Farran et al., 2019), in turn, investigated the relationship between motor and spatial domains. No relationship was, however, found in the individuals with ADHD. The fifth study (Silva & Frère, 2011) investigated the influence of color on attentional performance in ADHD patients and HC and found that a decrease in performance was observed when the VR game was presented with blue/yellow hints instead of green/red hints across groups. Finally, to increase the naturalistic level of VR tasks, the sixth study (Seesjärvi et al., 2021) developed several VR scenarios that represented everyday tasks, and found that ADHD children executed more movements and goal-irrelevant actions compared to HC.

3.9.2. Therapy studies

In regard to VR therapy in ADHD, k = 4 studies were found eligible (cf. SM 11.2). The first study was an RCT by Bioulac et al. (2020) and evaluated the effectiveness of a multi-session VC-based cognitive remediation training compared to MPH treatment and psychotherapy. Results revealed that, after interventions, the cognitive remediation group showed improved performance in the VR-CPT compared to the MPH (commission errors) and psychotherapy group (correct hits). The second study was a case series study (Shema-Shiratzky et al., 2019) employing a combined motor-cognitive training task with VR that required participants to walk on a treadmill while completing a virtual cognitive task. Here, parent reports indicated a reduction in ADHD children's social problems as well as an improvement in psychosomatic behavior after training. The third study (Baumann et al., 2020) compared a novel with an already familiar virtual environment in their effect on improving memory consolidation and provided evidence that ADHD children/adolescents had enhanced memory consolidation in the novel environment, while no such enhancement effect was found in HC. Finally, the fourth study (Rodrigo-Yanguas et al., 2021) developed a VR serious game to provide cognitive training for children/adolescents with ADHD. Pilot results here were that ADHD patients enjoyed playing the game.

3.9.3. Conclusion

In summary, the reviewed assessment studies cover a range of possible applications of VR in the investigation of ADHD. In particular, the VR-CPT studies provide good evidence that by means of VR, neuropsychological test environments can be developed that may allow to discern children/adolescents with ADHD from typically developing children/adolescents, as well as medication states from non-medication states. Moreover, VR driving simulators also prove useful as a reliable tool to study the driving performance of individuals with ADHD. However, before these VR-based tests can actually be used within regular patient care, there is a need to prove their superiority over traditional assessment tools, to be further validated, and to be norm-referenced. Moreover, the development of VR-based assessment tools for ADHD is mainly focused on children and adolescents, whereas research in adults with ADHD has, to date, still been scarce. Regarding VR therapy in ADHD, our review only deduced four studies. While the results of these studies are encouraging, there is a clear need for further investigations on VR therapy approaches for ADHD. For example, it would be interesting to investigate whether existing neurofeedback approaches can be further improved by VR, e.g., by making the neurofeedback tasks to be performed ecologically more valid and less abstract.

3.10. Depression (DEP)

DEP is characterized by the appearance of five or more core symptoms, at least one of them being a consistent depressed mood or a loss of interest or pleasure over at least two weeks (American Psychiatric Association, 2013). Among others, additional symptoms consist of insomnia/hypersomnia, avolition, feelings of worthlessness or recurrent thoughts of death.

3.10.1. Assessment studies

Regarding VR assessment, k = 2 studies were found concerning depression (cf. SM 12.1), both of which examined characteristics of cognitive processes. While Cornwell et al. (2010) found depressed patients to have increased difficulties in spatial navigation in a virtual water maze, Camacho-Conde et al. (2021) reported worse attentional performance in dual tasks embedded in a VR environment compared to HC.

3.10.2. Therapy studies

Regarding VR therapy of DEP symptoms, k = 16 studies were found (cf. SM 12.2). Three of these studies are RCTs examining the efficacy of a virtual garden that is withered in the beginning and grows increasingly colorful as the participant completes simple tasks, aiming to counter helplessness and underline self-efficacy. This paradigm was found to elevate the decrease of depression severity in elderly women (Szczepańska-Gieracha, Cieślik, Serweta, & Klajs, 2021) and to show larger effects than autogenic training in depressed patients with coronary artery disease (Szczepańska-Gieracha, Jóźwik, Cieślik, Mazurek, & Gajda, 2021) and COPD (Rutkowski, Szczegielniak, & Szczepańska-Gieracha, 2021).

Two further studies investigated VR-based behavioral activation in DEP (Colombo et al., 2022; Paul, Bullock, & Bailenson, 2022). The RCT by Paul et al. (2022) compared traditional behavioral activation and TAU to VR-based behavioral activation in an adult population with major depression and found a decrease of symptom severity in both behavioral activation groups, with the TAU group yielding no significant improvement. In line with this, also Colombo et al. (2022) employed a virtual behavioral activation scenario and found a higher activity level as well as decrease of depression symptoms.

Another set of studies explored the possibility to support exploration behavior by means of VR. Li et al. (2021) developed five VR environments with or without interaction to explore, all of which reduced negative emotions in mildly depressed adults. Likewise, Habak et al. (2020) created a VR environment that starts off as an empty room with the possibility of opening several doors and windows. Exploration behavior was thereby rewarded with positive imagery that actively changes the environment. Resulting pre-post improvements of hopelessness and positive mood were revealed. Finally, two further case series suggested VR exploration of positively valenced environments to decrease depressive symptoms (Chen et al., 2020; Fernandez-Alvarez et al., 2021), whereby one of these studies utilized individualized positive autobiographical memory to virtually transport the patients to a specific place they have a positive connection to (Fernandez-Alvarez et al., 2021), while the other employed standardized content.

Two further studies probed VR-based stress management programs. In the first study (Shah et al., 2015) patients with major depressive disorder and bipolar disorder completed a VR-based stress management program that included face-to-face psychoeducation and viewing VR relaxation videos. While a pre-post comparison showed significant reductions in subjective stress, depression, and anxiety symptoms, objective physiological measures of stress showed no significant differences across measurement points. The second study (Stamou, García-Palacios, Woodford, Suso-Ribera, & Botella, 2021) targeted women with postnatal depression and combined traditional CBT with a VR session, in which the patients fulfilled tasks surrounding a virtual house while being confronted with several stressors. The intervention resulted in a decrease of hopelessness and depressive symptoms, with the effect size increasing specifically after VR treatment.

Another two case series examined the benefit of VR games in motor, cognitive and balance training in depressed elderly as well as chronic pain patients (House et al., 2016; Yang, Lee, & Kim, 2017). Both studies thereby suggested an improvement of depressive symptoms together with increased motor control.

The remaining three studies each addressed separate topics: Falconer et al. (2016) implemented a VR-based compassion training. From baseline to a four-week follow-up, self-criticism decreased significantly, and self-compassion increased significantly. In addition, overall depressive symptomatology decreased significantly in four patients. Flores, Linehan, Todd, and Hoffman (2018), in turn, investigated whether a VR-assisted mindfulness skills training is effective in reducing depression in two patients with spinal cord injury. In several sessions, both patients were immersed into a virtual scenic environment, in which they underwent the illusion of floating down a river while listening to mindfulness skills training instructions. Both patients reported feeling less depressed after each VR intervention. Finally, Migoya-Borja et al. (2020) implemented a VR-based chatbot psychoeducation tool to increase awareness of depressive symptoms. In the VR session, patients were immersed into a virtual bar where they sat across a same-sex avatar with whom they held a peer-to-peer conversation about their depressive symptoms. Pre-to- post comparisons revealed a decrease in depressive symptoms for patients with lower baseline scores and an increase in depressive symptoms for patients with higher baseline scores.

3.10.3. Conclusion

Since only a few studies on VR-assisted assessments of DEP have yet been carried out, the potential diagnostic benefit that VR might offer for better characterizing DEP cannot yet be determined. Given that DEP not only affects cognition but also behavior, it would be of great interest to examine how patients with DEP behave differently in VR environments compared to HC (e.g., with respective to gaze behavior, personal distance behavior, or exploration behavior). Regarding VR therapy, the overall finding of decreased DEP symptoms after various VR interventions suggests that the development of VR-based therapeutic approaches for treating DEP might be promising (e.g., VR-based behavioral activation and exploration). In the future, more studies including adequate comparators are warranted.

3.11. Autism spectrum disorders (ASD)

Autism is a pervasive neurodevelopmental disorder with an early childhood onset and varying degrees of severity. The symptoms and individual characteristics are multifaceted and vary from persistent deficits in social communication and interaction to restricted, repetitive, and stereotyped behavior, interests, or activities (American Psychiatric Association, 2013). While the DSM-IV divided autism into autistic disorder, Asperger disorder, and pervasive developmental disorder not otherwise specified (American Psychiatric Association, 2013), the DSM-5 now defines the term autism spectrum disorder (ASD) as a syndrome without subtypes (American Psychiatric Association, 2013).

3.11.1. Assessment studies

As regards VR assessment of ASD, the present literature search revealed k = 50 mere assessment studies and k = 3 combination studies (cf. SM 13.1). Eight of these examined the general acceptance and usability of VR environments in individuals with ASD. Three studies thereby found that ASD patients did not experience any adverse or serious side effects (McCleery et al., 2020) and were generally willing to immerse themselves using HMDs (Newbutt et al., 2016; Strickland, Marcus, Mesibov, & Hogan, 1996). In line with these finding, also Newbutt, Bradley, and Conley's (2020) CCT confirmed a high HMD acceptability among children and adolescents with ASD, using the HTC Vive as the most preferred model. A study by Parsons, Mitchell, and Leonard (2004), in turn, found that adolescents with ASD could grasp and use a computer-based virtual café environment similarly well as HC. Moreover, Fitzgerald et al. (2018) reported that a paper folding project was easier solved by two adults with ASD when an instruction video for this task was presented via a classical monitor than via an HMD. By contrast, Malihi et al.'s (2020b) RCT compared the phenomenal experiences towards a bus passenger scene either being played via an HMD or a classical monitor, and found that adolescents with ASD reported more spatial presence, naturalness and preference towards the HMD-based presentation-mode. Furthermore, IQ and anxiety were positive and negative predictors for sense of presence, respectively (Malihi et al., 2020a).

Ten further studies dealt with sensorimotor processing in ASD. Greffou et al.'s (2012) study found that, compared to HC, ASD children demonstrated a postural hypo-reactivity in response to a color-oscillating virtual tunnel, while ASD adults did not present such peculiarities. Biffi et al. (2018), in turn, implemented a virtual treadmill and found various peculiarities with respect to gait patterns and motor performances for children with ASD compared to HC. Differences in motor performance between patients with ASD and HC were also found in a VR-based whole body movement task in children and adolescents (Fears et al., 2022) and a virtual racquetball task in adolescents and adults (Arthur et al., 2021). In line with this, Alcañiz et al.'s studies reported that machine-learning algorithms could discriminate children with ASD from HC based on their movement behavior (Alcañiz, Marín-Morales, et al., 2020) or electrodermal activity (Alcañiz, Chicchi Giglioli, et al., 2020) when being exposed to multimodal VR stimulation scenarios. Cook, Swapp, Pan, Bianchi-Berthouze, and Blakemore's (2014) study investigated interference effects of action observation and found that, unlike HC, high-functioning adults with ASD did not display interference effects towards real human, virtual human or virtual robot movements. Simões et al. (2020), in turn, let their participants undergo a stop-distance paradigm in both a real and virtual environment and found that adolescents with ASD showed a more consistent interpersonal distance regulation behavior across environments than HC. In a dyadic sensorimotor interaction task (Zapata-Fonseca, Froese, Schilbach, Vogeley, & Timmermans, 2018), adults with high-functioning ASD performed equally well as HC. Finally, Valori, Bayramova, McKenna-Plumley, and Farroni (2020) presented a new VR-compatible self-turn task based on a swivel chair for investigating body-related spatial orientation of ASD patients and HC.

Another 17 studies focused on gaze patterns during virtual social interactions in ASD. In a computer-based task in which participants interacted with a virtual avatar narrating a story, adolescents with high-functioning ASD showed more difficulty correctly interpreting an ambiguous story, less fixations on the avatar face (Grynszpan et al., 2012), and a higher task-completion time (Kuriakose & Lahiri, 2015) than HC. Notably, however, eye-tracking based feedback and adaptation of task difficulty improved face-region gaze fixations (Lahiri, Bekele, Dohrmann, Warren, & Sarkar, 2013, 2015; Lahiri, Trewyn, Warren, & Sarkar, 2011; Lahiri, Warren, & Sarkar, 2011) and task performance (Lahiri et al., 2013, 2015) in ASD patients. Moreover, preliminary evidence also supports the efficacy of task difficulty adaptation based on physiological anxiety measures (Kuriakose & Lahiri, 2017). Three studies investigating VR-based facial emotion recognition found no difference in accuracy between adolescents with ASD and HC (Bekele et al., 2013, Bekele et al., 2014; K. U. Kim et al., 2015), but differences in gaze patterns (Bekele et al., 2013), and higher response latency and lower response confidence in ASD (Bekele et al., 2014). Differences in gaze patterns between ASD patients and HC were also found in a computer-based face preference task (Feng et al., 2018), in a virtual shopping mall (Alcañiz et al., 2022), and when listening to a teacher in a virtual classroom (Ide-Okochi et al., 2022) or to a virtual pronunciation tutor (F. Chen, Wang, Peng, Yan, & Pan, 2019), but not in a virtual supermarket navigation task (Mouga et al., 2022). Furthermore, three studies found that it was possible to train a machine learning classifier to differentiate between an autistic and non-autistic group based on eye-tracking parameters (Alcañiz et al., 2022; Lin et al., 2022) and based on nonverbal behaviors during social interaction (Robles et al., 2022).

Employing VR-based social scenarios, further findings include lower performance in a multiplayer social interaction game (Krishnappa Babu & Lahiri, 2020), lower performance (Amat et al., 2021) and a different pattern of memory consolidation (Mundy, Kim, McIntyre, Lerro, & Jarrold, 2016) in a joint attention task, less mimicry in a virtual avatar imitation game (Forbes, Pan, & de C Hamilton, A. F., 2016), less response to social bids by a virtual avatar (Kumazaki et al., 2019), lower social information processing (Russo-Ponsaran et al., 2018) and less complex language in a virtual classroom conversation task (Boo et al., 2021) in ASD patients compared to HC, as well as different brain activity patterns in a virtual approach scenario between the groups (Pitskel et al., 2011). In addition, a case-series by Amaral, Simões, Mouga, Andrade, and Castelo-Branco (2017) found that a VR-embedded and P300-based brain computer interface may be feasible to train joint-attention skills in adults with high-functioning ASD.

Another three studies focused on visual processing in ASD. The first study (Trepagnier, Sebrechts, & Peterson, 2002) thereby employed a visual processing task and found that adults with ASD showed impairments in face recognition compared to HC, while their object recognition was comparably well or even superior. The second study (T. Parsons & Carlew, 2016) compared different variants of the Stroop task: A paper-and-pencil based version, a computerized version, and a VR version with and without distractors. The result was that the ASD group performed significantly worse than the HC group only on the VR-based Stroop task with distractors. Similarly, the third study (Koirala et al., 2021) found a virtual maze task to be more sensitive at detecting visual and haptic processing differences between ASD and HC children than a traditional sensory profile questionnaire.

Finally, six studies administered virtual driving simulators to adolescents and young adults with ASD. Three of these were thereby case-series studies implementing a machine-learning approach based on EEG (Fan et al., 2015; Fan, Wade, Key, Warren, & Sarkar, 2018) and other physiological features (Zhang et al., 2017) and found high classification accuracies for task engagement level, enjoyment, frustration, boredom and difficulty (Fan et al., 2015, 2018) and for cognitive load (Zhang et al., 2017). The remaining three studies compared driving-performance of ASD patients and HC: While Patrick et al. (2020) did not find group-differences, the other two studies found a higher variability in speed and lane positioning (Patrick et al., 2018) as well as a lower overall performance (Selander, Strand, Almberg, & Lidestam, 2021) in ASD patients.

3.11.2. Therapy studies

Regarding VR therapy, k = 39 mere therapy studies and k = 3 combination studies were identified in the present review (cf. SM 13.2; for previous reviews, see Aresti-Bartolome & Garcia-Zapirain, 2014; Mesa-Gresa, Gil-Gómez, Lozano-Quilis, & Gil-Gómez, 2018). Four of these focused on individualized VRET of SP in ASD and found it effective in ASD children/adolescents (Maskey et al., 2014; Maskey, Rodgers, Grahame, et al., 2019) and adults (Maskey, Rodgers, Ingham, et al., 2019; Meindl, Saba, Gray, Stuebing, & Jarvis, 2019).

Eight further studies dealt with VR-based teaching of practical skills. Two CCTs in adolescents and young adults with ASD found that VR-driving simulator training led to a higher increase in tactical driving performance (Cox et al., 2017) and in parent-rated positive attitudes towards driving (Ross et al., 2018) than routine driving-training. In Simões, Bernardes, Barros, and Castelo-Branco's (2018) study, in turn, adolescents and adults with ASD learned the process of taking buses to reach a specific destination using HMDs, which resulted in an increased process knowledge and reduced anxiety levels, as measured by electrodermal activity. In Miller, Wiederhold, Miller, and Wiederhold's (2020) study, n = 5 children with ASD underwent three sessions of VR air travel training, whereby four of the five investigated children improved their air travel skills from before to after the intervention. Similarly, two studies found that VR-based pedestrian training in three children (Dixon, Miyake, Nohelty, Novack, & Granpeesheh, 2020) and 10 adults (Saiano, Garbarino, Lumachi, Solari, & Sanguineti, 2015) with ASD led to a generalization of the learned skills to a natural environment. Kuper, Ksobiech, Wickert, Leighton, and Frederick (2020), in turn, developed a VR-based training on wiring electrical sockets and reported that the training increased the self-efficacy of adults with ASD. Finally, Bossenbroek et al. (2020) tested a multi-session VR biofeedback game to reduce anxiety and disruptive classroom behavior and found that ASD children profited from this serious game in various measures.

Another four RCTs (Smith et al., 2014, 2021; Smith et al., 2015; Strickland, Coles, & Southern, 2013) and three case-series studies (Burke et al., 2018; Burke, Li, Grudzien, & Garcia, 2021; Kumazaki et al., 2021) administered job interview trainings with VR-elements in adolescents and/or young adults with ASD (and other disabilities). Compared to a group that did not receive specific job-interview training, the VR training group showed a significant increase in job interview skills (Smith et al., 2014, 2021; Strickland et al., 2013) and more access to jobs at follow-up (Smith et al., 2021; Smith, Fleming, Wright, Losh, et al., 2015). Furthermore, VR-based job interview training led to an increase in self-efficacy (Burke et al., 2021) and self-confidence (Kumazaki et al., 2021).

Further ten studies probed VR-assisted social skills trainings in ASD. In an RCT, Soltani Kouhbanani, Khosrorad, Zarenezhad, and Arabi (2021) compared the efficacy of Risperidone treatment and a combination of Risperidone with an at home behavioral training program for parents and children (TEACCH) with VR-elements in ASD. Both treatments led to a similar improvement in behavioral problems and social skills at post-treatment, but at follow-up the combined approach was superior. A CCT by Yuan and Ip (2018) implemented six virtual daily life situations to teach emotional and social skills and reported that children with ASD showed higher scores on emotion expression and regulation as well as social interaction and adaptation after training compared to a waiting-list control group. Similarly, three case-series studies in adolescents (Mitchell, Parsons, & Leonard, 2007; Stichter, Laffey, Galyen, & Herzog, 2014) and young adults (Kandalaft, Didehbani, Krawczyk, Allen, & Chapman, 2013) also found improvements in appropriate social behavior (Mitchell et al., 2007), social cognition and communication skills (Kandalaft et al., 2013; Stichter et al., 2014) after computer-based, daily-life social competence trainings. Moreover, Y. J. D. Yang et al. (Yang et al., 2017; Yang et al., 2018) found that after 10 sessions of a VR-based social cognition training, adults with high-functioning ASD showed improved emotion recognition, which were associated with changes in brain regions connected to socio-cognitive and socio-emotional processing (Y. J. D. Yang et al., 2018). Also, pre-treatment brain activity predicted treatment response (Yang, Allen, et al., 2017). An RCT by Frolli et al. (2022) compared VR-based (3D-videos) and traditional emotion recognition training (cardboard images) in children with ASD. While, after training, no group difference regarding the recognition of primary emotions was found, the VR group showed higher scores in the recognition of secondary emotions and situational emotions. Krishnappa Babu and Lahiri (2020), in turn, tested a virtual social interaction platform in pairs of children and adolescents with ASD and pairs of HC. Over two sessions, task performance and gaze pattern improved in ASD patients. In a pilot study by Cai et al. (2013), on the other hand, children and adolescents with ASD were taught to act as dolphin trainers in a virtual 3D dolphinarium, in order to amend their nonverbal communication skills.

Four studies focused on VR-based training of joint attention skills. In a study by Amaral et al. (2018), adolescents and adults with high-functioning ASD were asked to identify virtual target objects based on the gaze direction of an avatar while receiving EEG-based neurofeedback. Although the rate of automatic responses to joint attention cues did not improve from before to after the training, some secondary neuropsychological measures related to mood, anxiety, and depression symptoms indicated improvements. However, the other three studies that implemented different VR-based joint attention trainings in children and adolescents with ASD did report improved joint attention skills after training (Amat et al., 2021; Cheng & Huang, 2012; Ravindran, Osgood, Sazawal, Solorzano, & Turnacioglu, 2019).

Other promising VR-based therapeutic approaches in ASD include VR-based motor trainings (de Moraes et al., 2020; Hocking et al., 2022), word learning (Saadatzi, Pennington, Welch, & Graham, 2018) and pronunciation training (F. Chen et al., 2019), contextual processing training (M. Wang & Reid, 2013), visuo-spatial cognition and attention training (De Luca et al., 2021; De Luca et al., 2021), a brain-computer interface for college students with ASD (White et al., 2016), and a pretend-play training (Herrera et al., 2008).

3.11.3. Conclusion

Overall, a comparatively large number of studies examined VR-based diagnostic and therapeutic approaches in a variety of domains in ASD. However, more than half of the identified studies used VR technologies with a rather low degree of immersion (e.g., classic computer screens). Additionally, the methodological quality of many studies appears limited. Future research should focus on RCT designs with follow-up periods and ideally investigate clinical samples of different age groups and varying degrees of severity. While previous studies yielded overall promising results, it remains an open question whether VR can effectively complement the traditional approaches in ASD. From a psychotherapeutic perspective, the development of VR-based measures and interventions to foster empathy and socio-emotional competencies in individuals with ASD seems particularly promising for future research.

3.12. Schizophrenia spectrum disorders (SSD)

The schizophrenia spectrum encompasses a set of subclinical conditions and mental disorders that range from mild psychotic symptoms to severe schizophrenia (SCZ). Typical SCZ symptoms are positive symptoms such as hallucinations and delusions, and negative symptoms, such as diminished emotional expression, cognitive impairments or anhedonia (American Psychiatric Association, 2013).

3.12.1. Assessment studies

In the present review, k = 62 studies were found to investigate VR as a tool to characterize SSD (cf. SM 14.1; for previous reviews, see Rus-Calafell, Garety, Sason, Craig, & Valmaggia, 2018; Veling, Moritz, & van der Gaag, 2014). Of these, 11 studies relied on a virtual underground scenario in which participants found themselves situated in a virtual underground ride through London (VURLON) together with other passengers (avatars). This scenario was applied to various SSD populations and was well-tolerated (Fornells-Ambrojo et al., 2008; Freeman, Pugh, Vorontsova, Antley, & Slater, 2010; Stinson, Valmaggia, Antley, Slater, & Freeman, 2010; Valmaggia et al., 2007). Moreover, persecutory ideation towards VR avatars was more likely inducible in SSD populations as compared to HC (Freeman et al., 2010; Valmaggia, Day, Kroll, et al., 2015; Valmaggia, Day, Garety, et al., 2015), in persons with high trait paranoia (Valmaggia et al., 2007), and in persons with a high risk for psychosis who additionally had a history of childhood bullying (Valmaggia, Day, Kroll, et al., 2015) or social defeat (Valmaggia, Day, Garety, et al., 2015), while perceived ethnic discrimination was not a significant predictor in this population (Shaikh et al., 2016). Also, persecutory ideation towards VR avatars increased if the VURLON was undergone under normal than lowered head height (Freeman et al., 2014) and under low than high self-confidence (Atherton et al., 2016), whereas performing power postures before VURLON exposure had no influence on persecutory ideation (Brown, Waite, Rovira, & Freeman, 2020). Lastly, Fornells-Ambrojo et al. (2013) conducted a thematic analysis based on an interview after VURLON exposure and, inter alia, found that participants with persecutory delusions are less likely in active hypothesis-testing, but instead consider affect as evidence of persecutory intention.

Another eight studies build upon a virtual bar scenario (VBS), in which the participants were exposed to various avatars and social stress levels. Across various SSD populations, momentary subjective distress, persecutory ideation (Veling, Pot-Kolder, Counotte, van Os, & van der Gaag, 2016), and spatial distance taking (Geraets et al., 2017) towards the avatars increased as a function of VR-induced social stress. Moreover, spatial distance taking was lower in adults with a psychosis as compared to HC (Brinkman et al., 2011; Veling, Brinkman, Dorrestijn, & van der Gaag, 2014). In addition, paranoid ideation during VR exposure was positively associated with childhood trauma (Veling, Counotte, Pot-Kolder, van Os, & van der Gaag, 2016), real-world paranoia (Veling, Brinkman, et al., 2014), negative self-esteem (Jongeneel, Pot-Kolder, Counotte, van der Gaag, & Veling, 2018), and with various cognitive biases (Pot-Kolder, Veling, Counotte, & van der Gaag, 2018b). Also, cybersickness due to VBS exposure turned out to be moderated by the participants' anxiety level (Pot-Kolder, Veling, Counotte, & van der Gaag, 2018a).

Another 11 studies explored virtual social interactions in SSD. One case-series on patients with SCZ and schizoaffective disorder confirmed a high sense of presence, experiential verisimilitude, and acceptance towards virtual social environments (Rus-Calafell, Gutiérrez-Maldonado, & Ribas-Sabaté, 2013). Another RCT demonstrated conversation deficits during VR in female adults with SCZ, which improved under antipsychotic medication (K.-M. Park et al., 2009). A further RCT indicated a trend for higher paranoia after VR-induced social rejection (Hesse, Schroeder, Scheeff, Klingberg, & Plewnia, 2017). Likewise, four studies indicated that adults with SCZ kept less eye contact (S.-H. Choi et al., 2010; Han, Shin, Yoon, Jang, & Kim, 2014) and more distance (S. H. Park et al., 2009) to avatars during (negative) casual conversations than HC, and the distance taking towards avatars decreased the higher the SCZ negative symptomatology was (Ku et al., 2006). Another case-control study revealed that adults with SCZ rated the emotional valence and arousal expressed by angry avatars as lower and their own anxiety towards happy avatars as higher than HC (I.-H. Park et al., 2009). In addition, three studies found that when confronted to avatars, adults with SCZ show a worse social perception (Kim et al., 2007), including social gaze interpretation (Caruana, Seymour, Brock, & Langdon, 2019), and report higher levels of intimacy towards distant avatars (Park, Shin, Han, Shin, & Kim, 2014) compared to HC.

A further 15 studies investigated spatial navigation and source memory deficits in SSD and applied various 3D city scenarios (Buchy, Hawco, Joober, Malla, & Lepage, 2015; Han, Young Kim, & Kim, 2012; Hawco et al., 2015; Zawadzki et al., 2013), several virtual maze scenarios (Fajnerová et al., 2014; Folley, Astur, Jagannathan, Calhoun, & Pearlson, 2010; Kargar, Askari, Khoshaman, & Mohammadi, 2019; Mohammadi, Hesami, Kargar, & Shams, 2018; Siemerkus, Irle, Schmidt-Samoa, Dechent, & Weniger, 2012; Sorkin, Weinshall, Modai, & Peled, 2006; Spieker, Astur, West, Griego, & Rowland, 2012; Weniger & Irle, 2008; Wilkins et al., 2013), a virtual park scenario (Kargar et al., 2019; Mohammadi, Hesami, et al., 2018; Weniger & Irle, 2008), an immersive variant of the Wisconsin Card Sorting Task (Ku et al., 2003) and a virtual courtyard scenario (Wilkins et al., 2013) to SSD patients and HC. The recurring result across most studies is that patients with a SSD typically display worse spatial cognition performances than HC (for a systematic review, see Cogné et al., 2017).

The remaining 17 studies investigated cognitive deficits and alterations in SSD. Four of these, administered and validated a new "VR functional capacity assessment tool" (VRFCAT) that confronts participants to various routine tasks of daily living. Important outcomes were that patients with a SSD performed significantly worse in most of the administered subtasks (Ruse et al., 2014; Ventura et al., 2020), that the VRFCAT correlated with other functional performance tests

(Lindenmayer et al., 2020; Ruse et al., 2014; Ventura et al., 2020) and that it showed a similar factor structure in SSD patients than HC (Harvey et al., 2020). Two further VR-based assessment tools were reported for the detection of prospective memory problems (Man et al., 2018) and a general cognitive assessment (Miskowiak et al., 2021), both of which correlated with existing neuropsychological tests. Another series of studies implemented virtual supermarket scenarios in order to assess executive (Aubin, Béliveau, & Klinger, 2018; Greenwood et al., 2016; Huang et al., 2021; Josman, Schenirderman, Klinger, & Shevil, 2009) and social functioning (Canty, Cao, Neumann, & Shum, 2021). While Greenwood et al. (2016) and Aubin et al. (2018) report similar task performances during VR and real-world shopping, Josman et al. (2009) found their virtual supermarket task to converge with an existing executive functioning test (BADS). Canty et al. (2021), in turn, found that theory of mind abilities selectively decline with SSD chronification. Another two studies implemented a VR scenario, in which participants had to self-administer medications according to a treatment plan (Baker, Kurtz, & Astur, 2006; Kurtz, Baker, Pearlson, & Astur, 2007). Compared to HC, patients with SCZ performed significantly worse on self-administrating the medications. Having implemented a VR scenario in which participants had to recollect items and faces, a further study found that patients with SCZ not only showed a worse memory accuracy towards faces than HC, but also a higher confidence into their false memories (Dietrichkeit, Grzella, Nagel, & Moritz, 2020). Moreover, a study by Thirioux, Tandonnet, Jaafari, and Berthoz (2014) implemented a virtual tightrope walker scenario and revealed that the incapacity to spontaneously take a heterocentered visuo-spatial perspective relates with a high negative SCZ symptomatology. In addition, Lee et al. (2021) administered a VR visuotactile reaction time paradigm and reported that adults with SCZ show a reduced peripersonal space compared to HC. Lastly, Synofzik, Thier, Leube, Schlotterbeck, and Lindner (2010) implemented a VR-based pointing movement task and found evidence that misattributions of agency in SCZ are due to inaccurate predictions of sensory action outcomes.

3.12.2. Therapy studies

Regarding VR-based therapy in SSD, k = 29 studies were found to meet the defined inclusion criteria (cf. SM 14.2; for previous reviews, see Bisso et al., 2020; Rus-Calafell et al., 2018). Of these studies, four focused on VR-assisted CBT interventions. Three RCTs evaluated VR-assisted CBT against paranoid ideation in patients with a psychosis and, inter alia, found reduced paranoid symptoms (Geraets et al., 2020; Pot-Kolder et al., 2018) and low extra costs (Pot-Kolder et al., 2020) relative to TAU. Freeman et al.'s (2016) RCT, in turn, compared a VR-assisted safety-behavior avoidance intervention against mere VR exposure in adults with persecutory delusions and reported a stronger reduction in delusional conviction and real-world distress for the safety-behavior avoidance intervention.

Another six studies focused on 'AVATAR therapy', a new therapy intervention, in which patients interact with, and thereby disempower a virtual representation of their presumed persecutor. A few important outcomes of AVATAR therapy are, inter alia, a significant improvement of auditory verbal hallucinations (AVH), depressive symptoms, persecutory beliefs and quality of life from pre- to post-intervention (Dellazizzo, Potvin, Phraxayavong, & Dumais, 2020; Dellazizzo, Potvin, Phraxayavong, & Dumais, 2021; Dellazizzo, Potvin, Phraxayavong, Lalonde, & Dumais, 2018), a persistent improvement of auditory verbal hallucinations, depressive symptoms and quality of life at follow-up (Dellazizzo et al., 2021; du Sert et al., 2018; Rus-Calafell et al., 2020) and a higher pre-post reduction of affective symptoms compared to CBT (Dellazizzo et al., 2021), a higher pre-post improvement in auditory verbal hallucinations, persecutory beliefs, depressive symptoms and quality of life compared to TAU (du Sert et al., 2018). Moreover, a single case study reported hemodynamic changes (as measured by fNIRS) throughout the therapy course (Liang et al., 2021).

Thirteen further studies examined VR-based social skills training (SST) in adults with a SSD. Besides confirming a general feasibility and acceptance (Ku et al., 2007; Nijman et al., 2020; Thompson et al., 2020), important findings were a pre-post improvement in emotion recognition (Nijman et al., 2020; Rus-Calafell, Gutiérrez-Maldonado, & Ribas-Sabaté, 2012; Thompson et al., 2020; Wade et al., 2018), social anxiety and discomfort, general psychopathology, avoidance and social functioning (Rus-Calafell et al., 2012; Rus-Calafell, Gutiérrez-Maldonado, & Ribas-Sabaté, 2014), negative symptomatology (Adery et al., 2018; Rus-Calafell et al., 2012, 2014), anxiety and depression (Thompson et al., 2020), and theory of mind skills (Vass et al., 2021; Vass, Simon, Fekete, Kis, & Simon, 2021). In addition, a superiority of VR-assisted SST over traditional SST was reported with respect to conversational skills and assertiveness (K.-M. Park et al., 2011). Also, a pre-post improvement of social performances and psychotic symptoms after a VR-assisted vocational skill training alone (Sohn et al., 2016) was found as well as a better cognitive functioning and work performance after a prevocational training + VR-assisted vocational training compared to prevocational training alone (Tsang & Man, 2013). Likewise, it was found that SSD patients undergoing a specific SST for job interviews showed a better job interview performance after the training and received more job offers at a 6-month follow-up than SSD patients that only received TAU (Smith et al., 2015).

Another four studies probed different VR-assisted cognitive trainings for SSD. Amado et al. (2016) implemented a 12-session therapy program in which SCZ patients had to orientate themselves within a virtual city to plan every-day tasks and found a pre-post improvement in attention and memory. Similarly, La Paglia et al. (2013) implemented a "Virtual Attention and Executive-Function Training" using different scenes (park, valley, beach and supermarket) and found that adults with SCZ showed improvements in various neuropsychological measures. Moritz et al. (2014), in turn, implemented a virtual street task, in which SCZ adults had to recognize pedestrians and their facial affects, and, inter alia, reported a pre-post reduction of paranoia. Finally, Chan, Ngai, Leung, and Wong (2010) developed an "Interactive Rehabilitation Exercise System" in which elderly adults with SCZ had to catch virtual balls and chase a star underwater. This showed greater improvement in general cognitive function and memory skills compared to TAU.

The remaining two case series focused on VR-assisted physical exercise (Jo, Rossow-Kimball, Park, & Lee, 2018) and relaxation training (Rault, Lamothe, & Pelissolo, 2022) in patients with a SSD. Whereas Jo et al. (Jo et al., 2018) found a pre-post improvement in some physical fitness measures, Rault et al. (2022) found an anxiety reduction.

3.12.3. Conclusion

In summary, while there have been multiple studies assessing VR-technology as a tool to characterize SSD populations, there have been considerably less studies investigating VR as a tool for treating SSD. In part, this supposed imbalance, however, diminishes if one considers that multiple assessment studies were sometimes published on single experiments (cf. SM 14.1). The most important assessment finding is arguably that persecutory delusions and spatial orientation problems can be systematically elicited and thus be studied by VR technology, while AVATAR therapy is positioning itself as a promising new non-pharmacological therapeutic strategy for the treatment of auditory hallucinations and associated persecutory delusions.

3.13. Addiction disorders (AD)

While substance-related addiction describes a recurring desire to continue taking a drug despite consistent harmful consequences, behavioral addictions are characterized by compulsive, repetitive involvements in a rewarding behavior (e.g., pathological gambling, food consumption, internet use) despite persistent adverse consequences (Zou et al., 2017).

3.13.1. Assessment studies

Regarding VR assessment in AD, k = 54 studies were found in the present review (cf. SM 15.1; for previous reviews, see Hone-Blanchet, Wensing, & Fecteau, 2014; Segawa et al., 2020).

Nicotine: K = 28 articles dealt with characterizing nicotine addiction. Most of them employed virtual environments (e.g., an apartment, pub, or convenience store) with entailing nicotine cues (e.g. lighters, ashtrays, or cigarette packets) and, inter alia, investigated craving and/or physiological responses by comparing them to a control condition where no nicotine-related cues were present, or to a control group. Some of these studies thereby also included olfactory nicotine cues into their scenarios (Acker & MacKillop, 2013; Carter, Bordnick, Traylor, Day, & Paris, 2008; García-Rodríguez, Weidberg, Gutiérrez-Maldonado, & Secades-Villa, 2013; Thompson-Lake et al., 2015; Traylor, Bordnick, & Carter, 2008, 2009; Traylor, Parrish, Copp, & Bordnick, 2011).

Regarding craving, a reoccurring result in smokers is that virtual 3D environments with nicotine cues elicited higher craving compared to exposure to both 2D nicotine-related pictures (Lee et al., 2003; Lee, Lim, Wiederhold, & Graham, 2005) and neutral VR environments without nicotine cues, such as an empty room with an art gallery (Bordnick et al., 2004; Bordnick, Traylor, Graap, Copp, & Brooks, 2005), a bus, a waiting room and a library (Liu, Andrade, Schulze, Doran, & Courtney, 2022), an aquarium (Bordnick, Graap, Copp, Brooks, & Ferrer, 2005), screens with nature scenes (Acker & MacKillop, 2013; Traylor et al., 2008, 2009, 2011), a mountain landscape (Tamburin et al., 2021; Zandonai et al., 2021), an entire virtual office (Lee et al., 2005) or a neutral street and apartment route (Baumann & Sayette, 2006). Another study investigated craving in smokers by comparing three virtual scenarios: A pub, active cigarette smoking, and dart playing (García-Rodríguez et al., 2013). Notably, the craving effect increased if participants were not only exposed to nicotine cues but beyond that "smoked" a virtual cigarette.

Another finding for recent smoke quitters is that detailed realistic VR environments elicited stronger craving compared to less realistic scenarios while it was the other way around for current smokers (de Bruijn, de Vries, Bolman, & Wiers, 2020). In addition, in multi-modal VR environments which included visual, auditory, and olfactory nicotine cues simultaneously, craving levels and thinking about cigarettes were enhanced after exposure compared to neutral, non-smoking related environments (Thompson-Lake et al., 2015). Likewise, craving in cigarette smokers increased more rapidly when various smoking cues were presented, while in VR environments with only a few smoking cues, craving solely increased gradually (Pericot-Valverde, García-Rodríguez, Gutiérrez-Maldonado, Ferrer-Garcia, & Secades-Villa, 2011).

Moreover, six other studies, including two large-scale RCTs (García-Rodríguez, Pericot-Valverde, Gutiérrez-Maldonado, Ferrer-Garcia, & Secades-Villa, 2012; Kotlyar, Vogel, Dufresne, Mills, & Vuchetich, 2020), also implemented virtual cue exposure scenarios and also reported successful induction of craving (for a complete listing, see SM 15.1).

Regarding physiological responses, increases in skin conductance (Bordnick, Graap, et al., 2005), heart rate (García-Rodríguez et al., 2013; Thompson-Lake et al., 2015), pre-frontal cortex activity (Lee et al., 2005), posterior EEG alpha power (Tamburin et al., 2021), and ocular fixations (Gamito et al., 2011; Liu, Stamos, Dewitte, van Berlo, & van der Laan, 2022) were found in cigarette smokers in response to virtual nicotine cue exposure.

Furthermore, one study used VR scenarios with and without rewards to assess the influence of nicotine on conditioning in participants with varying degrees of nicotine dependence and reported partial evidence of nicotine affecting learning, extinction, and reinstatement (Palmisano, Hudd, McQuade, de Wit, & Astur, 2018). Lastly, by using a VR-based assessment of executive functions, one study reported lower executive functioning in placebogum-chewing smokers abstaining for two hours from nicotine compared to nicotine gum-chewing smokers, whereas no significant differences were found between a healthy placebo gum group and a healthy nicotine gum group (Jansari, Froggatt, Edginton, & Dawkins, 2013).

Cannabis: One study by Bordnick et al. (2009) investigated cannabis dependence by exposing adult cannabis smokers to a multisensory, cannabis-related virtual cue environment. Results revealed that craving and attention towards cannabis cues were elevated after cue exposure compared to a neutral control condition. In another study by Weinstein et al. (2008) cannabis dependents went through a VR maze under influence of tetrahydrocannabinol (THC) or without. Under influence of THC, participants had more collisions in the maze and showed increased brain activity in frontal cortical areas and anterior cingulate cortex (associated, e.g., to motor coordination) and decreased activity in occipital lobes (associated, e.g., to visual motor integration).

Alcohol: K = 8 studies focused on VR-based investigations of alcohol misuse. Similar to the nicotine studies, the focus was thereby on investigations aimed at assessing whether drinkers are influenced by virtual environments with alcohol cues. Also for this drug, a cue-induced craving effect was found across studies, in that alcohol-related virtual cue rooms (e.g., a virtual bar or party scenario), increased craving in alcohol dependents (Bordnick et al., 2008), abstinent alcohol dependents and social drinkers (Lee et al., 2008) binge drinkers (Ryan, Kreiner, Chapman, & Stark-Wroblewski, 2010), and heavy drinkers (Simon, Etienne, Bouchard, & Quertemont, 2020), as compared to neutral VR scenarios devoid of alcohol cues or a control group. Moreover, social drinkers were additionally influenced by social pressure, resulting in increasing craving levels during the presence of virtual avatars (Lee et al., 2008). Likewise, similar to virtual nicotine exposure, heavy alcohol drinkers experienced stronger craving in high compared to low ecologically valid scenarios (Simon et al., 2020). In Ghiţă et al.'s (2019) study, the authors exposed alcohol dependents and social drinkers to a neutral VR room and various drug related VR rooms. Craving increased in both groups, but the alcohol-related cue rooms (a bar, pub, restaurant, apartment) induced greater anxiety and craving than the neutral room (empty room with a glass of water). Lastly, Hernández-Serrano et al. (2021) found a positive correlation between alcohol use disorder (AUD) severity and craving during VR exposure.

The remaining two studies investigated executive motor functions with the help of VR scenarios (Chicchi Giglioli, Pérez Gálvez, Gil Granados, & Alcañiz, 2021; Quoilin, de Timary, & Duque, 2021). By use of a VR cooking task, Chicchi Giglioli et al. (2021) found that patients with AUD needed more time to complete the task and made more errors (e.g., burn food) than HCs, and beyond that, the VR paradigm discriminated reliably between AUD patients and HCs.

Stimulants: Two studies were found on cocaine (Saladin, Brady, Graap, & Rothbaum, 2006; Tau et al., 2014). The study by Saladin et al. (2006) compared a virtual cocaine environment against a neutral environment (a virtual 3D aquarium) and found increased craving and an elevated heart rate in cocaine dependents after being exposed to the cocaine environment. The study by Tau et al. (2014), in turn, compared adult abstinent cocaine dependents with a HC group while performing a virtual spatial learning task. They found, inter alia, deviations in the medial temporal lobe, which is associated with spatial learning.

Another eight studies were found on methamphetamine (meth). Two of these (Tan et al., 2019; Y. G. Wang, Shen, & Wu, 2018) exposed meth dependents to a VR meth-cue video in which actors simulated a real-life situation of drug use. Wang et al. (2018) thereby found a larger heart rate variability (HRV) in the patient group compared to HC as well as a positive correlation between HRV and cue-induced craving. Likewise, in meth dependents, Tan et al. (2019) confirmed an increase in craving and found higher skin conductance levels for meth-cue videos than for neutral videos and decreased EEG gamma activity in specific brain areas that predicted the changes of skin conductance level. Similar to other drugs, four studies also employed virtual meth-related cue environments (C.-C. Chen et al., 2022; Culbertson et al., 2010; Ding, Li, Li, Li, & Liu, 2020; Tsai et al., 2021). Others, in turn, implemented a VR visual analog scale (J. Wang, Lu, Zheng, & Zhang, 2021) to assess craving in meth dependents or used a VR competitive cycling exercise (Qi et al., 2021) to test its impact on neurocognitive functions of meth dependents in withdrawal.

With respect to MDMA, only one study was found (Kloft, Otgaar, Blokland, Toennes, & Ramaekers, 2022). In this study, a VR experiment was conducted with healthy adults with MDMA experience to investigate the effects of the substance on the formation of false episodic memories. The results showed no heightened vulnerability after MDMA consumption compared to placebo.

Likewise, there was merely one study on opioids (Scherbaum, Haber, Morley, Underhill, & Moustafa, 2018) in which participants with a history of heroin addiction were compared to HC in executing a virtual delay discounting task. Results showed greater levels of delay discounting leading to elevated non-optimal choices in former heroin addicts, probably due to a diminished ability to evaluate different options.

Gaming and Gambling: Regarding gaming, two RCTs were found (Lee et al., 2020; Shin et al., 2018). The study by Shin et al. (2018) explored craving in adults and adolescents with internet gaming disorder (IGD) by means of a virtual internet café. Compared to HC, craving was significantly enhanced in patients with IGD in response to the gaming related VR scenario. Moreover, there was a positive correlation between symptom severity and induced craving in patients with IGD, but not in HC. The study by Lee et al. (2020), in turn, aimed to support adults with IGD to recognize their gaming-related behavior patterns by simulating everyday situations in which they had to choose leisure activities or manage their consumption. Among other things, they found that adults with IGD selected fewer leisure activities than HC and preferred digital or gaming-related activities to other types of activities.

Regarding gambling, two studies were found (Lister, Nower, & Wohl, 2016; Young, Wohl, Matheson, Baumann, & Anisman, 2008). The study by Young et al. (2008) implemented a virtual casino and found that gamblers with a high risk of gambling addiction experienced higher levels of craving when they won a great gain instead of several smaller profits. Lister et al. (2016), in turn, exposed moderate-problem, low risk, and non-problem gamblers to a virtual slot machine and found a positive association between gambling goals (i.e., the importance a gambler places on achieving goals in the context of gambling) and chasing behavior (i.e. to what extent they continued playing the slot machine).

3.13.2. Therapy studies

Regarding VR therapy in AD, the present review identified k = 29 studies (cf. SM 15.2; for a previous review, see Amista, Kim, & Kim, 2017). Most of these studies applied virtual cue exposure therapy (VCET), a subform of VRET in which participants are exposed to drug-relevant cues whilst being hindered to consume the respecting drug. The underlying therapy rationale is to extinguish conditioned associations between drug-relevant cues and the drug itself in order to decrease cue-induced craving and relapsing (Culbertson, Shulenberger, De La Garza, Newton, & Brody, 2012).

Nicotine: K = 15 articles were found to deal with treating nicotine addiction. Two studies investigated the effect of a virtual online chatroom regarding smoking cessation for teenagers and found a decrease in cigarette consumption after seven weekly sessions (Woodruff, Conway, Edwards, Elliott, & Crittenden, 2007; Woodruff, Edwards, Conway, & Elliott, 2001). Krebs et al. (2009), in turn, tested the VR coping skill (VRCS) game they developed for recent smoke quitters and reported that participants conceived the trained coping skills helpful in reducing their urges to smoke.

Most other studies applied VCET either as a standalone intervention (Choi et al., 2011; Goldenhersch et al., 2020; Pericot-Valverde, Secades-Villa, Gutiérrez-Maldonado, & García-Rodríguez, 2014), in combination with CBT (Culbertson et al., 2012; Pericot-Valverde, Secades-Villa, & Gutiérrez-Maldonado, 2019), or nicotine replacement therapy (Bordnick, Traylor, Carter, & Graap, 2012; Kaganoff, Bordnick, & Carter, 2012). Overall, results supported that VCET can advance the current treatment of nicotine-dependence, since outcomes showed, inter alia, a decrease in subjective craving (Bordnick et al., 2012; Choi et al., 2011; Culbertson et al., 2012; Pericot-Valverde, García-Rodríguez, Ferrer-Garcia, Secades-Villa, & Gutiérrez-Maldonado, 2012; Pericot-Valverde, García-Rodríguez, Gutiérrez-Maldonado, & Secades-Villa, 2015), lower smoking rates (Bordnick et al., 2012; Culbertson et al., 2012; Goldenhersch et al., 2020; Machulska et al., 2021) even at six months follow-up (Bordnick et al., 2012), a decrease in physiological cue reactivity (Choi et al., 2011), higher abstinent rates (Girard, Turcotte, Bouchard, & Girard, 2009; Goldenhersch et al., 2020), and a higher motivation to quit (Caponnetto, Maglia, Lombardo, Demma, & Polosa, 2018) over the course of VCET.

Notably, however, in the study by Machulska et al. (2021), the decrease of daily cigarette consumption found after VR exposure did not remain significant after a seven-week follow-up measurement. Also, in the study by Pericot-Valverde et al. (2019) comparing VCET combined with CBT to CBT alone, no significant group differences were found in treatment retention and abstinent rates despite the found craving reduction in the VCET + CBT group. Instead, the relapse rate of the VCET + CBT group turned out to be higher compared to the CBT group after 12-month follow-up.

Cannabis: For cannabis dependency, no therapy-related experiments were identified by this literature search.

Alcohol: K = 8 studies were found on treating alcohol dependence. Of these, five applied varying types of VCET (Ghiţă et al., 2021; Hernández-Serrano et al., 2020; Kim & Lee, 2019; Lee et al., 2009; Son et al., 2015). More specifically, in the study by Hernández-Serrano et al. (2020), a combination of psychotherapy, pharmacotherapy and multisensory VCET showed a decrease in craving, while psychotherapy and pharmacotherapy alone did not. Lee et al.'s (2009) study, conversely, employed VCET with additional olfactory stimuli and an aversive phase (drinking kefir, a tart drink, and seeing and hearing a vomiting person), but without combining it with CBT. Also here, VCET proved to be more effective in decreasing craving in AUD patients than classical CBT. The study by Son et al. (2015) implemented a similar VCET paradigm but solely focused on VCET-induced brain changes. A decreased brain metabolism compared to baseline measurement in the right lentiform nucleus and right temporal lobe in adults with AUD was found, allegedly due to a reduced craving. Kim and Lee's (2019) RCT, in turn, compared the effect of approaching virtually presented non-alcohol-related situations and avoiding alcohol-related situations among heavy social drinkers. Interestingly, those participants trained to avoid alcohol-related situations showed a stronger decrease in implicit approach tendencies toward alcohol (but not in explicit craving for alcohol) than those participants who received a sham training. Finally, the case-study by Ghiţă et al. (2021) reported that after six sessions of VCET and TAU, craving and anxiety decreased when comparing pre-to-post measurements.

The remaining three studies investigated varying VR-based serious games (Caballeria et al., 2021; Gamito et al., 2021; Pennington, Reavis, Cano, Walker, & Batki, 2022). Two of these reported moderate to high usability and acceptance rates regarding VR-based serious gaming (Caballeria et al., 2021; Pennington et al., 2022). Moreover, in the study by Pennington et al. (2022), which employed an executive function training game where heavy drinking veterans with traumatic brain injuries used a stationary bike to navigate through a virtual wildlife environment and completed tasks, an increase in inhibition-switching and visual scanning was additionally found. Finally, in the study by Gamito et al. (2021), a VR-based cognitive training incorporating various activities of everyday life combined with TAU increased attention and cognitive flexibility compared to TAU-only in AUD patients.

Stimulants/Opioids: While no therapy studies were found on cocaine dependence, two were identified on meth dependence (Qi et al., 2022; Wang, Liu, & Shen, 2019) and one on opioid use (Hargett et al., 2022). In the first meth study, TAU (physiotherapy and psychotherapy) was compared to TAU combined with meth-related VCET (Wang, Liu, & Shen, 2019). Meth dependents who received additional VCET showed a larger decrease in craving and heart rate variability indices. In the second meth study, a VR cycling competition enhanced cortical activation and functional network efficiency in meth dependents (Qi et al., 2022). In the opioid study (Hargett et al., 2022), in turn, orthopedic/trauma in-patients with opioid tolerance or opioid use disorder received a VR meditation session, which led to a significant decrease in self-reported pain.

Gaming and Gambling: Two therapy studies were found on gaming (Park et al., 2016; Shin, Kim, et al., 2021) and one on gambling (Bouchard, Robillard, et al., 2017). In the study by Park et al. (2016), adults with online gaming addiction either received gaming-related VCET or CBT. After treatment, both groups showed reduced gaming addiction, but there were no group differences on this measure. A major advantage of using VR therapy instead of CBT, however, was substantial time saving. Shin, Kim, et al. (2021), in turn, used VR to simulate a dispute with parents about gaming to trigger negative emotions in patients with internet gaming disorder (IGD) and attempted to train their coping skills to manage those conflicts. Finally, Bouchard, Robillard, et al. (2017), inter alia, compared VCET to classical cue exposure therapy during CBT. During VCET, patients with gambling disorder experienced a virtual visit to a casino, whereas classical cue exposure therapy involved merely imagining such a scenario. An urge to gamble was successfully induced in both groups, however, VCET was not more effective than classical cue exposure therapy.

3.13.3. Conclusion

In sum, the reviewed assessment studies provide good evidence that VR cue exposure can reliably provoke craving towards a drug or a rewarding behavior. Particularly frequently, this finding has been shown for nicotine and alcohol dependence, but also for cannabis, stimulants, gaming and gambling there is at least one study each supporting this finding. Likewise, given this promising potential to induce craving, several VCET interventions have been proposed that mostly suggest an effectiveness of VCET in AD, especially in nicotine addiction. Many of these studies, however, lack sufficient methodological rigor and further large-scale RCTs with follow-up examinations appear necessary to prove VCET's effectiveness in AD. Moreover, to bring VCET into regular patient care, a cost advantage and clinical benefit of VCET over traditional cue exposure therapy or CBT has yet to be demonstrated.

4. Discussion

In this review, we examined the current state of research regarding the use of VR in the diagnostic and treatment of mental disorders. In total, we screened k = 9315 studies, out of which k = 721 studies were finally included in our review. Across studies and areas of psychopathology, we observed high variability with respect to both methodological rigor and application maturity.

4.1. Methodological rigor of studies

Regarding methodological rigor, many studies revealed a rather high RoB (on average: 69.44%). Recurrent methodological weaknesses include predominant usage of study designs with low evidence levels (e.g., 49.38% of studies lacked an RCT or CCT design), missing study preregistration, no or non-adequate comparators, missing follow-up investigations, missing concealment, no proper randomization or counterbalancing, salami publications (i.p. for SSD, PTSD and ED), inadequately described or non-standardized diagnostics of clinical samples, insufficient demographic descriptions, and undefined primary and secondary outcome parameters. Moreover, in some studies, the clinical motivations and/or study rationales appear vague or clinically uninformed.

When evaluating these methodological weaknesses, two aspects should, however, be considered: First, clinical VR is still an evolving field involving various different professions, each with their own scientific standards, viewpoints, and strengths and weaknesses. While an IT research group, for instance, might create fascinating VR worlds but struggle to conceptualize clinically-sound assessment or therapy programs, a clinical research group might offer such programs but fail to implement them technically. Hence, compliance with all currently set standards for a clinical VR study is challenging, costly, and hardly feasible without an interdisciplinary research team. Second, our review includes early VR studies published at a time when scientific standards were generally not as high as today (e.g., with respect to study preregistration and concealment). These studies in particular have a high RoB, while more recent studies typically have rather low RoBs. Hence, the quality of studies has improved markedly over the years, and the research community is now increasingly able to focus its attention not only on the complicated technical realization of VR applications, but also on their rigorous clinical testing.

4.2. Application maturity of VR interventions and future directions

Regarding VR therapy, the most compelling evidence certainly exists for the application of VRET in PTSD, SP, P&A and SAD. As reviewed, various RCTs and CCTs have been carried out, which largely, but not exclusively, indicate comparable effects of VRET to classical exposure therapy or TAU. While final evidence gaps have yet to be closed, especially for SAD and P&A, it is expected that VRET will now increasingly find its way into regular patient care. In this context, VRET might prove particularly useful in therapeutic situations where classical exposure therapy is difficult to carry out (e.g. exposition of war traumata). Moreover, in therapeutic situations where VRET and classical exposure therapy have similar efficacy, VRET may prove more cost-effective, assuming that VRET will soon also be applicable via smartphone-based HMDs (Donker et al., 2019). However, both therapeutic and economic benefits of VRET compared to traditional exposure therapy and TAU have yet to be demonstrated.

Similarly promising is also the use of VCET for AD. Concededly, clearly fewer RCTs have been carried out here to provide final evidence. The therapeutic rationale of VCET, however, is quite similar to VRET and the AD studies conducted so far predominantly demonstrate positive treatment effects, or, in the case of assessment studies, successful induction of craving in response to VR cue exposure. As with VRET, VCET might be particularly useful in situations where classical therapy approaches are unfeasible (e.g., a real exposition to methamphetamines). A next step could be to conduct large-scale RCTs with follow-up studies to investigate VCET as an effective and potentially more cost-saving alternative to traditional AD therapies.

Also promising is Riva et al.'s (1998a) Experiential Cognitive Therapy program for ED. In this program, VR is not developed as a stand-alone therapy method, but as a complementary therapy component within a larger existing ED treatment concept. In our view, this approach is advantageous and directional as not all complex treatment needs of an ED are addressed by VR alone, but VR is merely employed where it is particularly appropriate. Establishing VR as a complementary tool within larger treatment programs (e.g., within the scope of digital psychoeducation programs, or as one CBT module) rather than as a stand-alone intervention is, in our opinion, a reasonable approach that could also prove beneficial in other complex symptomatologies.

Regarding the remaining areas of psychopathology, the proposed therapeutic interventions are less mature. A veritable research gap, for instance, exists for OCD. While for anxiety disorders, we identified k = 126 therapy studies and another k = 76 therapy studies for PTSD, we merely found k = 2 therapy studies for OCD. This lack of research is remarkable, given that exposure therapy is the first-line treatment for OCD, similar to anxiety disorders or PTSD. Admittedly, the treatment mechanisms of OCD do not consist solely in habituation to a feared stimulus or situation, but also rely on learning self-determined behavior and regaining confidence in one's own senses and actions. This requires a greater focus on immersive interactions or manipulations of the virtual environment, such as tactile feedback, which is more difficult to implement than simple exposure scenarios for anxiety disorders. These technical hurdles, however, should be surmountable, and VRET should then prove to be a feasible and attractive treatment option also for OCD. In any case, based on the current state of the literature, it cannot be inferred whether VRET is effective or ineffective for OCD.

Similarly surprising is the scarcity of VR studies for DEP (k = 18), considering the high prevalence of affective disorders. Admittedly, unlike for anxiety disorders or PTSD, the therapeutic potential of VR for DEP is not as obvious. In our view, this problem could be mitigated by not attempting to treat DEP as a whole through VR, but instead developing symptom-specific VR interventions. For example, for the treatment of rumination and (self-deprecating) negative thoughts, VR interventions could be developed that 'experientially enrich' existing therapy techniques, such as cognitive restructuring, thought-stopping, mindfulness meditation, or cognitive defusion.

Across disorders, VR could certainly also help in the further development of experienced-based psychotherapy approaches. Within emotion-focused therapy, for instance, patients explore their different ego parts and juxtapose them scenically through chair dialogues (Greenberg, 2010). One background assumption behind this practice is that dysfunctional ego parts can best be recognized and modified, if they not only become cognitively but also emotionally co-activated during therapy. Such an experience-based juxtaposition of different ego parts could perhaps also be induced by VR, for instance by confronting the patient with different and simultaneously presented biometric self-avatars, that each represent a different ego part, and into each of which the patient may embody, depending on the current role-play situation.

Regarding VR assessment, slightly less studies were found (k = 317) than for VR therapy (k = 400), whereas k = 4 studies targeted both. The studies found, however, provide promising cross-pathology evidence that VR is principally well predestined for assessing and characterizing clinical populations. In line with general VR findings outside the clinical domain (Slater, 2009), many of the reviewed studies impressively demonstrate that individuals often behave similarly in virtual and actual environments. To exemplarily recap a few striking findings: Patients with SSD keep more distance to virtual avatars (Park, Ku, Kim, et al., 2009), Alzheimer's disease biomarker-positive patients with MCI exhibit more navigation difficulties in virtual three-dimensional environments than biomarker-negative patients with MCI (Howett et al., 2019), and patients with OCD experience significantly higher levels of anxiety than HC after conducting a virtual checking task (K. U. Kim et al., 2008). From our perspective, these findings clearly raise justified hope that VR can be used to create highly ecologically valid and symptom-relevant test environments that at the same time remain well controllable and standardisable.

Unfortunately, most reviewed studies confine themselves to such general proof-of-concept investigations, while only few studies actually present VR-based tests. Two of the few exceptions are the virtual daily living test for MCI (Seo et al., 2017) and the various classroom studies for ADHD (Mühlberger et al., 2016; Rodríguez et al., 2018). Undoubtedly, these VR-based tests have the potential to augment existing test diagnostics that are often considered ecologically invalid due to their abstract nature. And yet, even here, the respective test developments are still in their infancy, since the respecting tests have so far neither been standardized nor systematically been examined with regard to quality criteria. Compared to the intensive research on VR therapy interventions, there is still some backlog in the development of VR-based test procedures. In our opinion, however, it is the further development of VR-based testing procedures that could prove particularly worthwhile, as VR-based assessments could significantly change current (neuro) psychological testing.

Regarding addressed cohorts, clearly fewer studies were conducted with children/adolescents (k = 95; 13.18%) or cross-age populations (k = 50; 6.93%) than with adults (k = 569; 78.92%). In part, this effect can probably be explained by the fact that many HMDs are not approved for use by children/adolescents. Nevertheless, we see a research gap here, because it is the younger generation that is particularly open to new digital technologies such as VR and that could therefore especially benefit from VR interventions.

4.3. Limitations of the review

There are several limitations to this review. First, VR studies not listed on Pubmed (MEDLINE) and/or published in a language other than English were not included in our review. We suspect that this mainly affects feasibility studies and studies with a rather low study impact.

Second, our review does not entail any inferential meta-analyses, but remains limited to descriptive statistics and narrative syntheses of the retrieved studies. The main reason for this is that, in most areas of psychopathology, the studies were too heterogeneous or too few in number to pool them in a meta-analysis. Also, for some areas of psychopathology, extensive disorder-specific meta-analyses already exist (Cieślik, Mazurek, Rutkowski, Turolla, & Szczepańska-Gieracha, 2020). Therefore, conducting less-detailed meta-analyses in the present transdiagnostic review would have provided little additional insight.

Third, not necessarily a limitation but a characteristic, our review grounds on a rather wide conceptual understanding of VR, in that we included all studies which by their own standards identified as a VR study, except when only videos, abstract symbols, or static images were presented via a non-immersive display or when an augmented reality was implemented. Accordingly, our review not only reports on studies with highly-immersive VR setups (e.g., virtual environments presented over a HMD), but also with lowly-immersive VR setups (e.g. virtual environments presented over a classical computer screen) which have equal merit and use cases. As a consequence, our review maps quite comprehensively the entire VR research state in the domain of clinical psychology, but at the expense of pooling study results across quite different VR setups and applications.

4.4. Conclusions

In summary, our review reveals that VR offers promising and manifold opportunities to develop or advance assessment and treatment procedures for mental disorders. Regarding assessment, the virtual classroom studies for ADHD stick out in particular, since they impressively demonstrate that new reliable and ecologically valid neuropsychological tests can be realized by VR. This raises hope that VR could overcome the often conflicting requirements of high test standardization and ecological validity in classical test diagnostics. Regarding therapy, the highest evidence and application maturity certainly exist for VRET in PTSD and anxiety disorders. Thus, VR interventions can be expected to play an increasing role in future regular patient care. No less innovative are many of the proposed interventions in the other areas of psychopathology (i.p. for ED, SSD and AD), but their level of evidence is still too insufficient and requires further rigorous study. Finally, the question of cost-effectiveness of VR applications compared to established clinical procedures will increasingly have to be addressed. However, should smartphone-based HMDs prove sufficiently viable for performing clinical VR applications, VR technology will not need to shy away from this comparison.

Author contributions

Conceptualization and Methodology: AW, KK, BS & NB. Project administration: NB. Supervision: AW, KK, BS, SL, AP & NB. Literature search and data extraction: AW, KK, BS, JP, AM, AT, LP, NBL, ML, LA, KB, MS, MST, MCP, MG, FR, ME, HL, HF, SJ & NB. Writing psychopathology-specific section drafts: AW, KK, BS, JP, AM, AT, LP, ML, LA, KB, MS, MST, MCP, MG, FR, ME, HL, HF & NB. Validation and finalizing original manuscript: AW, KK, BS & NB. Revision and editing of manuscript: All authors.

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Availability of data

For each area of psychopathology, the whole literature search was conducted and documented in Mendeley. The respecting .bib-files can be found in the supplementary materials (cf. SM 16). All retrieved information from the different studies are listed in the area-specific summary tables (SM 3 - SM 15).

Supplementary data to this article can be found online at https://doi.org/10.1016/j.cpr.2022.102213.

Declaration of Competing Interest

The authors declare no competing financial interests.

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