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Psychedelics and virtual reality: parallels and applications

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***Abstract*:** Psychedelic drugs and virtual reality (VR) each have the capacity to disrupt the rigidity and limitations of typical conscious experience. This article delineates the parallels among psychedelic and VR states as well as their potential synergistic applications in clinical and recreational settings. Findings indicate that, individually, psychedelics and VR are used in analogous ways to alter sensory experience and evoke awe. They are also both used in tandem with traditional therapies to treat a variety of mood disorders; their shared capacity to transiently alter perspective and disrupt rigid patterns of mental experience may underly their analogous and transdiagnostic therapeutic uses. In terms of their combined applications, a number of recreational users currently utilize psychedelics and VR together to enhance their experience. We propose that VR may be a useful tool for preparing hallucinogen-naïve participants in clinical trials for the sensory distortions experienced in psychedelic states. Given the critical role of "setting" in psychedelic treatment outcomes, we also detail how VR could be used to optimize the environment in psychedelic sessions. Finally, we provide considerations for future studies and detail how advancements in psychedelic and VR research can inform one another. Collectively, this article outlines a number of connections between psychedelics and VR, and, more broadly, is representative of growing scientific interest into the interactions among technology, psychopharmacology, and mental health.

Keywords: commentary, cyberdelics, perspective, psychedelics, virtual reality

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Introduction

Psychedelic drugs and virtual reality (VR) are each used to disrupt the rigidity of sensory experience,[1,2] as well as enhance outcomes with mental health treatments.[3,4] Classic psychedelics include lysergic acid diethylamide (LSD), psilocybin, mescaline, and ayahuasca/*N*,*N*-dimethyltryptamine (DMT; Table 1), and they induce their acute effects primarily through serotonin 5-HT2A receptor activation.[5] VR is defined as three-dimensional interactive environments, which users navigate *via* avatars.[6] The early discourse surrounding VR was linked with psychedelic culture and the drugs' capacity to markedly change mental experience – a reluctant connection for some in the technological community.[7] Many in the psychedelic community, on the other hand, embraced these connections and saw VR as a socially accepted tool to introduce the public to altered states.[8] Notably, Timothy Leary argued that cyberdelics – the fusion of psychedelic drugs and cyberculture – could reprogram the mind,[9] and went so far as to change his popular catchphrase "turn on, tune in, drop out" to "turn on, boot up, and jack in." Despite the early associations among psychedelics and VR, there has been a paucity of contemporary scholarly discussion in this area. This article addresses this gap by summarizing the parallels between psychedelics and VR, detailing their combined clinical and recreational applications, and discussing experimental considerations for future research.

Parallels

One connection between psychedelics and VR regards their ability to alter perceptual experience, notably visual processing. DMT, in particular, is a

Table 1. Overview of the classic psychedelic drugs.

Hallucinogen	Chemical class	Potential therapeutic applications	Therapeutic mechanisms
Ayahuasca/DMT	Tryptamine	Anxiety,[10] depression,[11] substance misuse[12]	Increased BDNF,[11] neurogenesis/plasticity,[13] MAO Inhibition[11]
LSD	Tryptamine	Anxiety,[14] depression,[15] substance misuse[16]	Amygdala and DMN alterations,[17] mystical experience[18]
Mescaline	Phenethylamine	No clinical applications studied to-date	
Psilocybin	Tryptamine	Anxiety,[19] depression,[20] OCD,[21] substance misuse[22]	Amygdala and DMN alterations,[23] mystical experience,[22] neurogenesis/plasticity[24]

BDNF, brain-derived neurotrophic factor; DMT, *N,N*-dimethyltryptamine; LSD, lysergic acid diethylamide; MAO, monoamine oxidase inhibitor; OCD, obsessive-compulsive disorder.

potent hallucinogen for immersing users into unique and vivid mental landscapes[25]; "visions" are a characteristic effect of other classic psychedelics as well, but take on increased salience in DMT reports. At higher doses, DMT visions can "completely replace ongoing mental experience",[26] and immerse individuals into what are subjectively described as "alternate universes".[27] Curiosity in exploring this visual phenomenology can be a motive for usage.[28] Likewise, a signature feature of VR is to immerse individuals into visual environments that transcend the limitations of their physical self.[29] This quality has recreational and therapeutic implications. For example, visual attractiveness of virtual worlds has been shown to influence entertainment value,[6] and virtual immersion into anxiety-provoking situations has been used in tandem with exposure therapy to enhance outcomes with anxiety disorders.[30] Altogether, research supports that immersion into new perceptual environments can be an important feature of psychedelic and VR experiences.

Another commonality among psychedelics and VR is their capacity to evoke awe in users, which can also have cognitive and therapeutic implications. For instance, awe has been linked to increased curiosity, better academic outcomes, and enhanced wellbeing.[31,32] When used with proper preparation, support, and integration, psychedelic experiences have been described as awe-provoking and incredibly personally meaningful: in one study in which participants were given psilocybin, two-thirds subsequently rated their session among the five most meaningful experiences of their entire lifetime.[33] Hendricks postulated that awe is an important mechanism underlying psychedelics' therapeutic benefits, specifically by promoting unitive experiences as well as feelings of sacredness and gratitude.[34] In a qualitative analysis of participant accounts from a study examining psilocybin's potential for smoking cessation, Noorani and colleagues found that the patients' psilocybin sessions left an enduring sense of awe, and this diminished the relative importance of smoking in their lives.[35] Similarly, VR has emerged as a modern and accessible method of evoking awe.[36] One study found that awe-inducing VR environments were associated with an increased sense of perceived vastness, presence, and positive affect.[37] Quesnel and Riecke found that aesthetic beauty, themes of social connection, familiarity, and personalization of VR environments influenced the extent to which participants experienced awe.[38] Thus, psychedelics' and VR's potential to elicit awe is illustrative of another commonality between the two.

Researchers are also beginning to assess if, individually, psychedelics and VR can be incorporated into traditional mental health treatments to optimize therapeutic outcomes.[39,40] Indeed, in late 2018, psilocybin-assisted psychotherapy was designated to breakthrough therapy status for treatment-resistant depression by the United States Food and Drug Administration (FDA).[41] Preliminary evidence from a number of recent studies suggests that, in carefully screened and monitored volunteers, psychedelic-assisted psychotherapy can potentiate remission of depression,[3,11] anxiety,[10,14,19] obsessive-compulsive disorder (OCD),[21] end-of-life distress,[20] and substance misuse.[12,22] Mystical experiences,[18,42]

emotional breakthrough,[43] ego dissolution,[44] neuroplasticity,[45] neurogenesis,[13,24,46] and decreases in default mode network (DMN) activity have each been theorized to underlie the therapeutic benefits linked to psychedelics.[17,47] It should be noted, however, that there are several limitations to much of the current research, including unstandardized dosages, homogenous samples, expectancy effects, and small sample sizes.[23] In addition, while psychedelics are non-toxic (i.e., do not damage mammalian organ systems)[48] and have low potential for abuse,[49] the drugs are not risk-free as they can lead to psychologically challenging experiences for some individuals.[50] Even with robust therapeutic support, up to a third of participants experience transient fear or panic at some point during high-dose sessions.[33] Given the potential for these intense emotional reactions, individuals with predispositions towards psychotic symptoms are generally excluded from current trials. Finally, psychedelics alone do not seem to induce serotonin syndrome[51]; however, the combination of a selective serotonin reuptake inhibitor (SSRI) with a monoamine oxidase inhibitor (MAOI; such as that found in ayahuasca) can produce severe serotonin syndrome. Because of this, ayahuasca retreats typically require attendees to abstain from their current medications for a month before taking the drug.

VR has been utilized in research and clinical settings to assist in treating a number of overlapping conditions as psychedelic treatment, including depression,[4] anxiety,[30] OCD,[52] and substance misuse[53]; VR has also been incorporated into palliative care by simulating travel experiences for housebound individuals.[54] Potential risks linked to this treatment include nausea, dizziness, and seizures in epileptic patients.[55] VR has been argued to impart its therapeutic benefits through providing a benign, but vivid, setting, and to confront fears as well as by promoting memory reconsolidation completed through a safe environment and perspective.[56] Ratings of "immersion" and "presence" in virtual environments predict a number of positive outcomes when VR is combined with therapy,[57] suggesting that transcending one's typical perspective is a critical mechanism underlying its therapeutic efficacy. Many psychiatric disorders can be characterized by rigid beliefs about one's self and getting "stuck" in maladaptive narratives, moods, or habits.[58] Therefore, psychedelics' and VR's shared capacity to transiently alter perspective and disrupt rigid patterns of mental experience may be common mechanisms underlying their analogous and transdiagnostic therapeutic uses.

Next, it may be useful to directly compare the effect sizes between research integrating psychedelics or VR into therapy (Table 2). Aday *et al.*[23] compiled the effect sizes for long-term changes in depression after psychedelic-assisted psychotherapy, and found that η_p^2 ranged from 0.32 to 0.70, Hedges' g from 0.7 to 3.2, and Cohen's d from 0.82 to 2.3. Li and colleagues reviewed the research on VR therapy for depression and found an average Cohen's d of 0.67,[59] but this average was derived from just two studies. A later experiment combining a self-compassion regimen and VR found an effect size of Cohen's $d = 1.11$ for depression.[4] Aday *et al.*'s review of the long-term effects of psychedelic drugs also assessed changes in anxiety after psychedelic treatment[23]; these effect sizes ranged from $\eta_p^2 = 0.27$ to 0.28, Hedge's $g = 2.0$–3.2 and Cohen's $d = 0.5$–2.67. When reviewing the effects of VR therapy on anxiety, Opris *et al.* found a strong effect (i.e. Cohen's $d = 1.11$) for VR compared with a waitlist control, but no effect when compared with traditional evidence-based treatments (i.e. Cohen's $d = 0.16$).[60] The research on integrating psychedelics or VR into therapy for substance misuse, OCD, and end-of-life care is growing but still in its infancy, making it difficult to meaningfully compare data from the two paradigms. Nonetheless, this analysis suggests that incorporating psychedelics or VR may improve the efficacy of some therapeutic treatments, particularly in settings in which only small-to-moderate effects are achieved with traditional treatment approaches. Further research is needed to identify if incorporating both psychedelics and VR into a single therapeutic regimen would yield additive effects or if their overlapping mechanisms would limit further improvement. To inform this work, we will next address theoretical considerations of using psychedelics and VR together.

Combined applications

There are a number of ways psychedelics and VR can be combined to optimize the benefits of each. Already, a number of individuals use psychedelics and VR together for recreational enhancement. Entire online communities dedicated to the discussion of using VR while on psychedelics have emerged on popular websites such as Reddit. Indeed, at the time of writing, the psychedelics/VR Reddit forum had over 6000 members.[74]

Table 2. Effect sizes in therapy.

Authors	Drug	Dosage(s)	Study type	Measure(s)	Effect size(s)
Psychedelics					
Depression (10 studies)					
Agin-Liebes *et al.*[61]	Psilocybin	0.3 mg/kg	RCT	BDI; HADS-D	Cohen's $d = 1.27–1.97$
Barrett *et al.*[62]	Psilocybin	25 mg/70 kg	Open-label	POMS	$\eta_p^2 = 0.32$
Carhart-Harris *et al.*[63]	Psilocybin	10, 25 mg	Open-label	BDI; HAM-D; QIDS	Hedges' $g = 2.0–3.2$
Carhart-Harris *et al.*[64]	Psilocybin	10, 25 mg	Open-label	QIDS-SR16	Cohen's $d = 2.3$
Carhart-Harris *et al.*[3]	Psilocybin	10, 25 mg	Open-label	BDI; HAM-D; QIDS	Cohen's $d = 1.52–2.3$
Griffiths *et al.*[65]	Psilocybin	1 or 3 mg/70 kg, 22 or 30 mg/70 kg	RCT	BDI; HADS; HAM-D	Cohen's $d = 1.55$
Lyons and Carhart-Harris[66]	Psilocybin	10, 25 mg	Open-label	HAM-D; QIDS	Hedges' $g = 0.7$
Roseman *et al.*[67]	Psilocybin	10, 25 mg	Open-label	HAM-D; QIDS	Cohen's $d = 1.55$
Ross *et al.*[20]	Psilocybin	0.3 mg/kg	RCT	BDI; HADS	Cohen's $d = 0.82–1.32$
Stroud *et al.*[68]	Psilocybin	10, 25 mg	Open-label	QIDS	$\eta_p^2 = 0.67–0.70$
Anxiety (5 studies)					
Agin-Liebes *et al.*[61]	Psilocybin	0.3 mg/kg	RCT	HADS-A; STAI	Cohen's $d = 0.86–2.67$
Barrett *et al.*[62]	Psilocybin	25 mg/70 kg	Open-label	STAI	$\eta_p^2 = 0.27–0.28$
Carhart-Harris *et al.*[63]	Psilocybin	10, 25 mg	Open-label	STAI-T	Hedges' $g = 2.0–3.2$
Carhart-Harris *et al.*[3]	Psilocybin	10, 25 mg	Open-label	STAI	Cohen's $d = 1.2–2.2$
Ross *et al.*[20]	Psilocybin	0.3 mg/kg	RCT	HADS-A; STAI	Cohen's $d = 0.8–1.49$
VR					
Authors	**Study details**			**Measure(s)**	**Effect size(s)**
Depression (4 studies)					
Falconer *et al.*[4]	Combined self-compassion/VR therapy			PHQ-9; Zung SDS	Cohen's $d = 1.11$
Gamito *et al.*[69]	VR exposure therapy in war veterans			BDI	Cohen's $d = 1.16$
Li *et al.*[70]	VR games for children with cancer			CES-DC	$\eta_p^2 = 0.06$
Li *et al.*[59]	Reviewed 2 VR therapy studies			BDI; HAM-D	Cohen's $d = 0.67$
Anxiety (5 studies)					
Botella *et al.*[71]	VR exposure therapy for panic disorder			ASI; PDSS	$\eta_p^2 = 0.67–0.72$
Krijn *et al.*[72]	VR exposure therapy for fear of flying			FAM; FAS	Cohen's $d = 1.82–2.13$
Opris *et al.*[60]	Reviewed 23 VR exposure therapy studies			Varied	Cohen's $d = 1.11$
Wallach *et al.*[73]	VR CBT for public speaking anxiety			FNE; SSPS	Cohen's $d = 0.92–1.50$

ASI, Anxiety Sensitivity Index; BDI, Beck Depression Inventory; CBT, cognitive behavioral therapy; CES-DC, The Center for Epidemiological Studies Depression Scale for Children; FAM, Flight Anxiety Modality questionnaire; FAS, Flight Anxiety Situations questionnaire; FNE, Fear of negative evaluation; HADS-A, Hospital Anxiety and Depression Scale (Anxiety); HADS-D, Hospital Anxiety and Depression Scale (Depression); HAM-A, Hamilton Anxiety Rating Scale; HAM-D, Hamilton Depression Rating Scale; PDSS, Panic Disorder Severity Scale; PHQ-9, Patient Health Questionnaire-9; QIDS, Quick Inventory of Depressive Symptomatology; QID-SR16, Quick Inventory of Depressive Symptomatology (Self-Report); RCT, randomized controlled trial; SSPS, Self-statements during public speaking; STAI, State-Trait Anxiety Inventory; STAI-T, State-Trait Anxiety Inventory (Trait); VR, virtual reality; Zung SDS, Zung Self Rating Depression Scale.

Members of these communities have anecdotally reported feeling greater presence and immersion into virtual worlds while on psychedelic drugs. Users have combined psychedelics with both competitive games as well as open world VR, which is less linear and allows players to explore virtual worlds more freely. While there has yet to be scientific inquiry into the use of VR with psychedelics, these naturalistic reports can be a valuable springboard for further research – Reddit and similar websites have been demonstrated as inexpensive sources for high-quality data and as cultural forums that can be facilitators of research ideas.[75,76]

Combining psychedelics and VR could also have uses in therapeutic settings. For instance, simulating psychedelic hallucinations in VR may be a valuable method of preparing hallucinogen-naïve participants for the strong sensory distortions commonly experienced in psychedelic states. Suzuki *et al.* developed VR technology that produces visual phenomenology described as qualitatively comparable with the effects of classic psychedelic drugs, which could be co-opted for preparing participants.[77] This technology's use as a tool to experimentally alter consciousness has the potential to open new avenues of psychological research. VR may also be useful during psychedelic sessions by optimizing the therapeutic setting, which is widely argued to be integral to the drugs' benefits.[78,79] That is, psychedelics seem to be unique drugs in that the context they are taken in can dramatically alter their acute and long-term effects. As psychedelic research progresses, scientists may delineate which settings are most effective for therapeutic benefits, and these can be simulated in VR. In addition, it is not uncommon for individuals on psychedelic substances to want to immerse themselves into nature while under the influence of the drugs, and psychedelics have been shown to increase nature relatedness.[66] Currently, clinical trials are conducted in secured laboratories or hospitals, which do not allow for participants to be outside in natural environments. VR could synthetically circumvent this problem by simulating natural scenes that participants could explore and immerse themselves into.

Experimental considerations for future research

Although this synthesis of the literature revealed a number of connections and potential applications with psychedelic drugs and VR, there are additional ethical concerns, experimental limitations, and open questions that should be addressed. Delineation of these factors can inform future research combining psychedelics and VR. First, given the proverbial nature/technology dichotomy and divide, some in the psychedelic community may be resistant to incorporating artificial devices into psychedelic experiences that have been described as primitive, noetic, and sacred.[80] Many cultures around the world revere hallucinogenic plants for their spiritual and medicinal properties[81]; thus, researchers should proceed respectfully and be attendant to cultural concerns. In addition, an important distinction to keep in mind for future researchers considering combining psychedelic drugs and VR is that the perceptual changes are generated internally with psychedelics and externally with VR. While confounding internally and externally driven perceptual changes may be a transient and benign experience in healthy volunteers, it is conceivable that this could pose risk for patients with psychotic conditions characterized by pre-existing self/other and internal/external distortions. This distinction also has phenomenological – and potentially therapeutic – implications as internally driven changes by psychedelics may have a noetic quality, whereas changes triggered by VR could be perceived as artificial because they were generated by another person/technology. Speculatively, it is possible that psychedelic treatment could serve as an alternative or adjunct to VR therapy in cases where altered perspective is desired, but the virtual environment is perceived as too contrived for immersion.

A limitation to the current research is that, while VR technology can simulate some of the visual effects of psychedelic drugs, it is clear that further research and development is needed for VR to replicate the nuances of the drugs' perceptual effects. In particular, refining VR-induced synesthesia is an area of study that is growing and can be coalesced with psychedelic research.[82] Furthermore, future researchers should assess if these parallels and combined applications differ across various types of psychedelic drugs, as well as identify which virtual environments are most conducive to psychedelic therapy. VR offers a unique paradigm for testing the effects of environmental conditions on psychedelic experiences because researchers can systematically alter precise parameters of the environment and replicate them across experiments. Given the critical role of "setting" in psychedelic

experiences and long-term outcomes,[23,77] VR could be a valuable tool for studying how to optimize treatment effects.

A final consideration concerns using theoretical advancements discovered in psychedelic research to shape VR research (and vice versa). For example, recent studies indicate that psychedelics alter an individual's perspective and sense of self in part by inhibiting activity in the DMN – which is thought to be fundamentally involved in maintaining one's sense of self.[83] Could it be, then, that VR might alter perspective through the same mechanism? If so, could VR be used to induce ego dissolution, which has been related to decreased DMN activity and positive changes in affect?[84] These remain open and intriguing empirical questions.

Conclusion

The findings presented here demonstrate numerous connections among psychedelic and VR states as well as several combined uses. Some of these parallels and applications date to the inception of VR technology but have received limited scholarly attention. Psychedelics and VR are both used to alter sensory experience, evoke awe, and are used in combination with traditional therapies to treat a variety of psychiatric conditions. VR can simulate the visual phenomenology of psychedelic states, which may be useful for preparing participants in clinical trials with the drugs. VR could also be used to optimize and tailor the therapeutic setting during psychedelic sessions. Finally, a number of recreational users currently utilize psychedelics and VR together to enhance their experience. Altogether, it is apparent that the connections between psychedelics and VR have important implications for psychological research. These findings are in line with recent increased scientific interest into the interactions among technology, psychopharmacology, and mental health.

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