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The Biophilic-Neuroplasticity Synergy in Biofeedback-Integrated VR for Anxiety: A Systematic Review and Proposed Mechanism

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Abstract. Background: Anxiety disorders are extremely widespread, and the existing therapies are limited to a high extent. Biofeedback-based virtual reality (BF-VR) has become an up-and-coming digital intervention that is associated with immersive exposure/relaxation and incorporating physiological self-regulation. This systematic review is summarising the evidence on the effectiveness of BF-VR in reducing anxiety, and discussing the put forward Biophilic-Neuroplasticity Synergistic Mechanism (BNSM). The PRISMA-guidelines allowed identifying 16 studies (2013-2025) to be included in the analysis at hand. A narrative synthesis identified evidence constantly that was available on the effectiveness of BF-VR versus waitlist controls, and its non-inferiority to conventional biofeedback as regards physiological results, and a better user experience. BF-VR was highly effective in anxiety symptom reduction compared to waitlist controls as well as non-inferior to conventional biofeedback based on physiological outcomes (e.g. HRV) and with a superior user experience. More importantly, biofeedback was proved to be added value, in comparison to VR. All the studies involved biophilic (nature-rich) environments. We suggest a synergistic effect: the bio-philic VR lowers defensive arousal to primed neuroplastic response and biofeedback-based self-regulation actively has a way of developing adaptive brain circuits. The interaction that supports this learning is the closed-loop interaction. BF-VR is an active and successful anxiety treatment. Besides the efficacy consolidation, the BNSM is a new, testable model that is proposed by the review as a future study. This process is in urgent need of being transformed into a specific digital treatment method through direct neuroplasticity measurement and optimal biophilic design.

Keywords: Biofeedback-integrated virtual reality, Effective, Anxiety, Biophilic design, Biophilic-Neuroplasticity Synergistic Mechanism (BNSM)

1. Introduction

They are anxiety disorders, one of the most common psychiatric disorders at a global level, with an immense burden on the quality of life and occupational performance of individuals, as well as the general well-being of society [1,2]. The first-line interventions, mainly including cognitive-behavioural therapy (CBT) and pharmacotherapy (e.g. SSRIs) are, however, related to severe

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limitations [3,4], The latter are the presence of side effects, risk of dependency, high prices, poor accessibility, and ineffective adherence, which is why an effective approach to innovative, scalable, and involving therapeutic alternatives is urgently needed.

Against these challenges, the digital health technologies have come across as a new avenue of treatment. The use of virtual reality (VR) has gained popularity in anxiety disorders treatment as it enables the patient a controlled environment where he/she can safely be exposed to and practice relaxation. The efficiency of VR is documented; it is possible to adjust exactly the anxiety-inducing organisms [5]. Simultaneously, there has been a biofeedback (BF) - an approach that provides the subject with the chance to successfully manage the physiological processes through the real-time data - that has been incredibly efficient in promoting self-control and the decrease in the arousal level [6]. The virtual reality with biofeedback (VR-BF) system is one of the promising combinations of two approaches that are being initiated by scientists [7]. These closed systems have been developed to modify the virtual world based on the physiological status of the user, a move that is aimed at enhancing the commitment and therapeutic efficacy even more than the one achievable by any given technology individually.

However, this sphere is yet nothing but an infantile one. Increasingly, there is an understanding of the general efficacy of VR with anxiety disorders. However, it is yet to have one extensive synthesis that would explicitly address biofeedback-implanted VR. What is more important, even the simplest mechanisms which allow explaining the effectiveness of BF-VR are yet to be conceived, and the systematic review of the existing literature is very much needed. The theoretical mechanism hypothesis, which is the most impressive, is presented in the present investigation, the Biophilic-Neuroplasticity Synergistic Mechanism (BNSM) hypothesis. Biophilic (nature-related) virtual reality (VR) spaces are predicted to suppress defensive arousal, thereby causing the brain priming process to be immersed [8]. Alongside with it, self-control through biofeedback has been discovered to be capable of redefining brain circuits through the process of neuroplasticity [9]. This potential combination of biophilia and neuroplasticity may be the modification of our understanding of digital interventions which we have not been thinking about before; however, it is yet to be tested.

Thus, the current research paper will focus on a systematic review that will be carried out with two main objectives in place, the first of which is to summarize the existing body of empirical research into the effectiveness of BF-VR interventions in reducing anxiety symptoms in adults, and the second one, to systematically synthesize and assess both direct and indirect evidence of the proposed biophilic-neuroplasticity synergistic mechanism. In its current form, the review will use the convergent synthesis approach, combining the results of different types of studies with varying designs, such as randomized controlled trials, mechanistic studies, technical validation and user experience reports, with the aim of offering a holistic assessment of the potential of the intervention.

2. Methods

Although it is acknowledged that the background of information on the biofeedback-enhanced virtual reality (BF-VR) application in anxiety is slowly evolving yet remains to its early stages. As a result, we will actively promote and incorporate the results on a variety of study designs. This method will enable an effectiveness signaling of the efficacy, as well as the mechanistic, technical validity, and acceptability to the user. All these factors combined are the basis of clinical practice.

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2.1. Research strategy

This system review was based on PRISMA statements [10]. All the studies that were relevant and published within the period between January 2013 and 31 May 2025 were searched in the following electronic databases: PubMed, Web of Science Core Collection, PsycINFO, Scopus and IEEE Xplore. The plan was designed on four main ideas, including (a) virtual reality technology, (b) biofeedback technology, (c) anxiety disorders, and (d) neuroplasticity and physiological regulatory processes. Besides, reference lists of included studies and applicable review articles were sifted through manually to complement the electronic search and come up with any other potentially eligible publication.

2.2. Inclusion criteria

PICOS (Population, Intervention, Comparison, Outcomes, Study design) framework was used to define eligibility:

Population (P): All ages and genders of participants.

Intervention (I): Biofeedback-based virtual reality intervention (BF-VR). The most important was the existence of a closed-loop environment where the user physiological data will be recorded in real-time and utilized to modify the VR environment in real-time and dynamically.

Comparison (C): This can be either any form of control group, including a waitlist, treatment-as-usual or active control group or no control group (single-arm pilot studies, and technical validation studies).

Outcomes (O):

Primary Outcome: Change (pre-to post) in validated scales of anxiety symptoms (e.g., State-Trait Anxiety Inventory (STAI), Hamilton Anxiety Rating Scale (HAM-A)).

Secondary Outcomes: (a) physiological indicators of arousal and regulation (e.g., Heart Rate Variability (HRV), Electrodermal Activity (EDA), salivary cortisol); (b) neuroplasticity biomarkers (e.g., presence, comfort, preference, simulator sickness); (c) technical performance measures (e.g., system latency, signal processing accuracy, error rates); (d) user experience measures (e.g., presence, comfort, preference, simulator sickness).

Study Design (S): Non-randomized controlled trials, Case series, Pre-post design studies, technical validation study, studies that specifically evaluate the user experience of BF-VR system, and randomized controlled trials (RCT).

2.3. Study selection and data extraction process

The deduplication of all cites was done in EndNote 20 reference management software into which all of the records, which were retrieved in the database searches and unique citations, were imported. The studies were selected by an independent single reviewer and measures taken towards rigour. This was done in two phases: The first step involved screening of titles and abstracts on the basis of the set eligibility criteria. After this, there was a complete review of the potentially qualified studies. To reduce the error and bias, a second and independent review was simulated. This was done by re-screening a random 20% sample of the titles/ abstracts and full-text articles after a period of two weeks to ascertain consistency. The choice of the studies will be reported in a way that is supported by the Preferred Reporting Items of Systematic Reviews and Meta-Analyses (PRISMA) guidelines and will be exemplified with the help of a flow diagram (see Section 3.1).

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The information of the included studies were converted into an already pre-designed database. The information that was extracted included: (1) Study characteristics: authors, year of publication, country; (2) Methodology: study design, number of participants, descriptions of those participants (age, gender, specific anxiety condition), description of any control group; (3) Intervention details: description of the VR hardware/software, type of biofeedback signal used (e.g., EEG, HRV), description of the VR environment (including presence of biophilic elements), description of the intervention protocol (number of sessions, frequency and duration of sessions), loop-closing, (4) Outcome data: primary and secondary outcome measures, means and standard deviations of pre-post changes, between-group statistics (p-values, effect sizes), key findings related to mechanisms; (5)Key finding: authors' main finding.

2.4. Data synthesis

Since the study designs, intervention regimes, outcome measures, and outcome populations were expected to be heterogeneous, it was deemed unsuitable to conduct a meta-analysis [11]. Rather, a qualitative narrative synthesis that is led by PICOS framework and research objectives will be undertaken. Evidence synthesis will be organized into 4 thematic strands that will straightly deal with the objectives of the review:

(a) Clinical Efficacy: Summarizing evidence on the direction and the extent of reduced anxiety in a variety of disorders and BF-VR protocols.

(b) Mechanistic Evidence: The incorporation of results on the physiological alteration and neuroplasticity biomarkers as a way of investigating the suggested biophilic-neuroplasticity synergistic mechanism.

(c) Technical Implementation: Overview The various biofeedback modalities, closed-loop algorithms and system performance to exploit best practices and technical challenges.

(d) User Experience and Feasibility: Theming the data about acceptability, presence, immersion, and side effects in order to study the practical implementation of BF-VR.

The synthesis will be carried out in a structured approach of tabulation, thematic analysis and cross-study comparison to determine coherent results, conflicting results and gaps in the literature. The weight and consistency of the evidence in each thematic strand will be used to arrive at the conclusions that will be made.

3. Results

3.1. Study selection

The systematic literature search was performed and 133 records were retrieved using five electronic databases. After elimination of 57 duplicate records, 76 distinct records were screened under title and abstract. In the next step, rigorous eligibility evaluation of fifteen full-text articles was carried out. After an extensive search of available literature, 6 studies that fit the previously established inclusion criteria were chosen to be included in this systematic review. In addition, 14 articles were located in total by citation searching and 4 articles were excluded. The last systematic review had 16 studies. The PRISMA flow diagram represents the selection process of the studies. (Figure 1).

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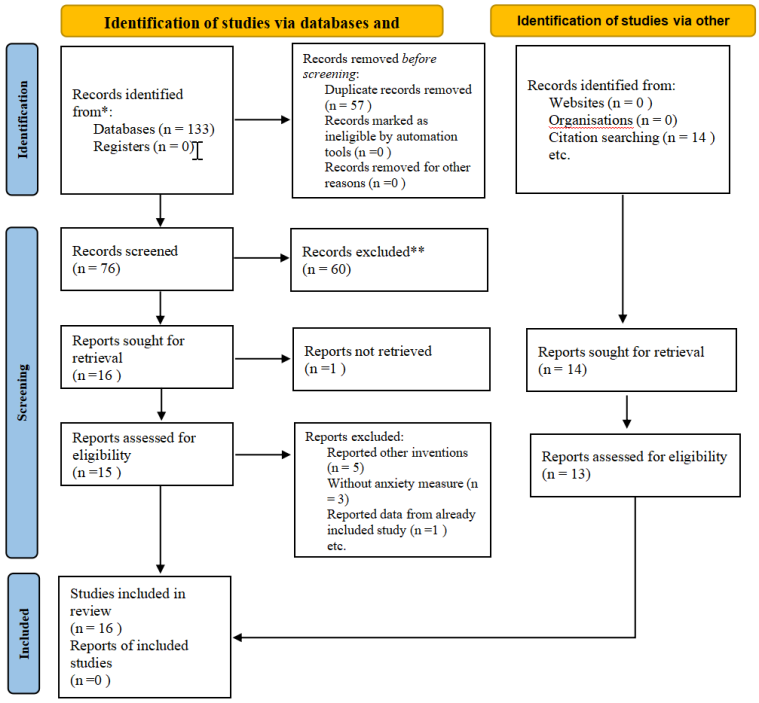

Figure 1. PRISMA chart of screening, exclusion and inclusion criteria

3.2. Characteristics of included studies

Sixteen articles found in this review were between 2013 and 2025, and they involved 555 participants. The intervention arms (sample sizes) varied between 5 and 38. There was a wide heterogeneity in the study designs which included randomised controlled studies (RCTs, n=7), crossover designs (n=1), non-randomized experimental (n=4) studies and pilot/feasibility studies (n=4). The groups involved healthy volunteers (n=8 studies), clinical or subclinical disorder (i.e., Generalized Anxiety Disorder (GAD), social anxiety, and ailurophobia) participants (n=5 studies), and those with medical conditions (n=3 studies). The key characteristics of each included study are summarised in Table 1.

Table 1. Characteristics of included studies investigating biofeedback-integrated virtual reality (BF-VR) for anxiety

#	Source	Country	Study Design	Total N (TG, CG)	Population & Anxiety Type	VR Hardware	Biofeedback Modality	VR Environment Description
1	[12]	Italy	Crossover RCT	20 (20, N/A)	Healthy volunteers	Oculus Rift S; Unity3D	HRV (HFnu), SCL	Naturalistic environment (plants, clouds); balloon height linked to physiology
2	[13]	Germany	RCT	60 (31, 29)	Healthy volunteers	Oculus Rift CV1; Custom	HRV	Virtual beach at sunset (palms, ocean, campfire)
3	[14]	Germany	RCT	36 (36, N/A)[4]	Healthy volunteers	Oculus Rift CV1; Custom	Respiration (Abdominal)	Stylized natural landscape (hills, trees, flowers)
4	[15]	China	Experimental	40 (30, 10)[5]	Healthy adults	Oculus Quest 2; Unity3D	EEG, HRV	Daytime beach & Nighttime starry sky with campfire
5	[16]	USA	Experimental	33 (33, N/A)[4]	University students	Large Screen; Vicon; Unity3D	EEG, GSR, PPG	Two architectural VEs (stress-reducing vs. stress-inducing)
6	[17]	Iran	Pilot RCT	10 (5, 5)	Ailurophobia patients	Smartphone VR; Unity	Heart Rate (HR)	Park with trees; various cat types (exposure therapy)

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Table 1. (continued)

7	[18]	China	Feasibility	20 (10, 10)	University students	HTC Vive; Unity3D	Respiration, EEG, Tactile	Virtual avatar with "fire channel" color feedback
8	[19]	Singapore	Pilot RCT	50 (25, 25)	Adults with social anxiety	Custom Headband; Laptop	EEG, HR, HRV	Virtual audience with varying expressions
9	[20]	USA	RCT	27 (18, 9)[6]	TKA patients (Older adults)	HTC Vive Pro; Unity	HRV, Respiration	Beach environment (sun, waves, palms) with visual guidance
10	[21]	France	Experimental	36 (36, N/A)[4]	Healthy sport students	HTC Vive Pro; Unity	HRV	Floating island in a sea of clouds (restorative)
11	[22]	UK	RCT	73 (38, 35)	High social anxiety	Samsung Gear VR; Unity3D	HR, FAA (EEG)	Virtual lecture hall for speech exposure
12	[23]	Italy	RCT	24 (7, 17)[7]	GAD patients	Vuzix iWear; 3DVIA	HR, GSR	Tropical island (campfire, beach, waterfall)
13	[24]	Germany	RCT	68 (24, 44)[8]	Healthy volunteers	Oculus Rift CV1; Unity3D	HRV (Coherence)	Virtual beach at sunset (ocean, palms, campfire, boat)
14	[25]	USA	Feasibility Pilot	15 (15, N/A)	Cancer patients	Oculus Go; Healium™	EEG (Relaxation)	Nature scenes (waterfall, beach, snow) with meditation
15	[26]	USA	Pilot Study	26 (14, 12)	High GAD-7 scores	Samsung Gear VR; StoryUp	None (EEG recorded)	360° nature scene (mountains, mist) with mindfulness audio
16	[27]	USA	Pilot Study	17 (17, N/A)[4]	Rheumatology patients	Samsung Gear VR; AppliedVR	Respiration (Pace)	Natural environment for Guided Meditation & Biofeedback

Note: TG = Treatment Group; CG = Control Group; N/A = Not Applicable (single-arm or within-subject design); HRV = Heart Rate Variability; SCL = Skin Conductance Level; EEG = Electroencephalography; GSR = Galvanic Skin Response; PPG = Photoplethysmography; FAA = Frontal Alpha Asymmetry.

[4] Within-subject design, no separate CG. [2] TG split into Day VR (n=30) and Night VR (n=10) groups, CG (n=10). [3] CG (n=30) is a no-intervention control; study also had a 2D Video group. [2] CG includes VRM (n=7), no BF (n=5) and WL (n=10). [3] CG includes 2D-BF (n=22) and non-treated CG (n=22).

3.3. Efficacy of biofeedback-integrated VR on anxiety symptoms

A narrative synthesis has been performed to examine the effectiveness of BF-VR interventions in anxiety symptoms. Measuring of these symptoms was done by standardised self-reported or clinician-administered scales (e.g. STAI, BAI, HAM-A). Summary of findings tabulated according to the type of control group used in the studies is provided in Table 2.

Table 2. Summary of efficacy findings on anxiety by control group type

Control Group Type	Study	Population	Key Efficacy Finding	Conclusion
Waitlist/No Intervention	[23]	GAD patients	Sig. reduction in BAI and STAI-Y2 only in BF-VR group.	Superiority. BF-VR is more effective than no treatment.
	[20]	TKA patients (Anxiety)	Sig. reduction in STAI and VAS Anxiety in BF-VR vs. control.	
Active Control (2D Biofeedback)	[13]	Healthy volunteers	Similar improvement in cardiac coherence. VR-BF superior in self-efficacy, focus, and stress buffering.	Non-inferiority & Enhanced UX. Physiologically comparable, but BF-VR offers superior psychological benefits and user experience.
	[24]	Healthy volunteers	No sig. difference in HRV parameters or mood improvement. VR-BF superior in motivation, concentration, and time perception.	

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Table 2. (continued)

VR without Biofeedback	[23]	GAD patients	Greater reduction in BAI/STAI in BF-VR group compared to VR-only group.	Added Value of Biofeedback. Integrating biofeedback enhances the anxiolytic effect of VR.
	[18]	University students	Improved breathing control and reduced sleepiness in BF-VR group vs. VR control.	
Within-Subject (Different BF/VE)	[12]	Healthy volunteers	STAI-Y1 sig. decreased in both conditions. SCLd-based BF more effective than HFnu.	Efficacious. Different BF protocols and environments can be effective, with some nuances in efficacy.
	[15]	Healthy adults	Nighttime (Starry) VR most effective for relaxation and sleepiness. Daytime VR increased stress response.	

As compared to Waitlist or No-Intervention Controls: The effectiveness of BF-VR was shown in a clear and significant manner. BF-VR groups have statistically significant lower anxiety scores than their passive control groups [23,20]. The finding is used to prove that BF-VR is an effective and active intervention.

In comparison to Active Controls: Compared to the existing non-VR biofeedback techniques, BF-VR has a strong efficacy. BF-VR was equally effective, at least, as compared to the conventional 2D biofeedback, i.e., core physiological outcomes, e.g. HRV coherence. Above all, these research works shared the opinion that BF-VR was the most efficient method of enhancing the psychological variables, user experience measures, including relaxation, self-efficacy, attentional focus, motivation, and enjoyment [13,24].

VR with biofeedback and without biofeedback: The available studies provide a solid argument that biofeedback additively affects VR interventions. The anxiety levels (BAI, STAI-Y2) of the BF-VR group reduced more than the levels of anxiety of the group that received VR without biofeedback [23]. Therefore, it can be concluded that the active mechanisms that make the observed effectiveness more than that one of an immersion can be the physiological feedback in real-time and the closed-loop adaptation.

Within-Subject Comparisons: A number of experiments have been conducted, which have involved the various BF-VR protocols subject to comparison. The findings of those studies have proven the effectiveness of the intervention and began to give the insight into the parameters of the best ones. As an example, Feedback using SCLd and HFnu could reduce state anxiety, although the former was stronger [12]. Similarly, even the design of the virtual reality environment is a crucial determinant of the anxiolytic result [15].

In conclusion, a meta-synthesis of the results based on a variety of study designs and groups has always shown that BF-VR is a useful intervention to decrease the level of anxiety symptoms. It was already proven that this practice is more effective than the use of the inert controls, as well as it is not physiologically inferior to the conventional form of biofeedback, whereas it has a better user experience. Moreover, it offers the value addition, as compared to VR interventions, which are not integrated with biofeedback.

3.4. Mechanisms of action: physiological and environmental mediators

To explore the proposed biophilic-neuroplasticity synergistic mechanism, data on physiological outcomes and environmental design were synthesized. The findings are presented in Table 3.

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Table 3. Evidence for proposed mechanisms of action

Study	Physiological Changes (Neuroplastic Proxy)	Biophilic Elements in VR Environment	Key Findings Related to Mechanisms
[12]	↑ HFnu (Parasympathetic activity); ↓ SCLd (Sympathetic activity)	Naturalistic environment with plants, grasses, flowers, moving clouds	SCLd-based feedback, coupled with the natural environment, was more effective in reducing sympathetic arousal and perceived anxiety.
[13]	↑ HRV Coherence (Cardiac Vagal Tone)	Beach at sunset with palms, rocks, campfire, ocean	VR-based biofeedback enhanced relaxation self-efficacy and present-moment focus, buffering the impact of stress beyond physiological changes alone.
[15]	↓ Heart Rate (most in Night VR); Altered EEG (Theta/Beta ratio)	Daytime beach; Nighttime starry sky with campfire	The nighttime environment (starry sky, campfire) was most effective for relaxation and sleepiness, suggesting a strong interaction between environment and physiological state.
[16]	↑ EEG oscillations (Theta, Alpha, Beta in VE1); ↓ GSR peaks in VE1	VE1: Sufficient daylight, bright colors, visible landmarks	Architectural design features mimicking beneficial natural environments (daylight, bright colors) directly influenced physiological stress markers.
[20]	↓ LF/HF ratio (indicating ↑ Parasympathetic activity)	Beach environment with sky, waves, sun, palm trees, grass	VR was more effective than 2D video in enhancing parasympathetic activity, potentially due to greater immersion in the restorative environment.
[24]	↑ SDNN, ↑ Coherence Ratio (during manipulation)	Beach with ocean, sand, palm trees, campfire	While physiological gains were equal to 2D-BF, the VR environment led to significantly higher motivation and concentration, facilitating engagement and learning.
[25]	EEG-based relaxation state feedback	Nature scenes: waterfall, beach, snow	The integration of EEG neurofeedback within nature scenes was feasible and associated with significant reductions in pain and tiredness.
[26]	↓ High-Beta EEG, ↑ Low-Beta/High-Beta ratio	360∘ nature scene with mountains, rocks, mist	VR mindfulness in a natural setting reduced physiological arousal (EEG) even without real-time biofeedback, highlighting the standalone impact of a restorative environment.

Physiological Mechanisms (Neuroplasticity Proxies): Most of the studies demonstrated significant and positive changes in physiological measures of the relaxation response and possible neuroplastic changes. Heart Rate Variability (HRV) increase and associated parameters (e.g., HFnu, RMSSD, Coherence Ratio) were the most consistent results that showed an improvement in parasympathetic (vagal) tone [13,20,21]. At the same time, the sympathetic arousal decreases were also confirmed by lower Skin Conductance Levels (SCL) [12,23] and lower respiration rates [14,18]. Two studies have directly tested EEG relaxation correlates, with all of them finding a decrease in high-beta power (anxiety) and an increase in theta activity (calm states) [26,15]. Although the changes in BDNF or neural connectivity were not directly measured in studies, these physiologic advances are defined as proxies of an otherwise neuroplastically conducive state.

The Role of Biophilic Design: It is interesting to note that all the 16 studies employed VR environments which are highly endowed with biophilic features. The natural environments, the subjects of the researches were beaches (n=7 studies), forests/gardens/parks (n=5 studies), mountains/sky (n=3 studies), and water-based settings (n=1 study). What is available thus indicates that these settings are not just a background, but a working therapeutic component. The environments with biophilic design principles (i.e. daylight, bright colours, landmarks) provoked much lower physiological stress reactions than those ones lacked the design elements [16]. A nocturnal scenery that included a camp fire was found to be more effective in inducing relaxation than a diurnal beach environment. The implication of this finding is that biophilic qualities can be optimised to increase well-being [15].

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Interaction and Synergy: BF-VR is closed-loop, which creates synergistic interaction between the user and the environment physiologically. As an example, the HRV coherence improvements directly correlated with the VR environment (e.g., clearer sky, brighter fire) [24,13]. Such contingent feedback can potentially provide better learning and create a better reinforcement of the physiological response than when there is no contingent exposure, and in doing so could potentially strengthen neural pathways as a result of rewarded self-regulation.

4. Discussion

Using a broad literature search, one can conclude that biofeedback (BF-VR) combined with virtual reality (VR) can engage fewer of the symptoms of anxiety among various population domains and diverse study designs. Biofeedback in these methods was found to produce much more when contrasting with passive control groups, however, physiologically it also could not be compared with other traditional means of delivering biofeedback. In addition to this, BF-VR was also reported to be better regarding the user engagement and experience. It should be stressed that biofeedback performance in providing the anxiety relief was an improvement over VR interventions, which is an essential part of the closed-loop component.

4.1. The synergistic mechanism: a proposed framework

The current results clearly lead to conclude that the Biophilic-Neuroplasticity Synergistic Mechanism (BNSM) is the most likely one. According to this new mechanism, the beneficial effects of BF-VR are due to the interference of the bottom-up and top-down processes that are multiplied in a closed-loop mechanism. The proposed model is illustrated in Figure 2.

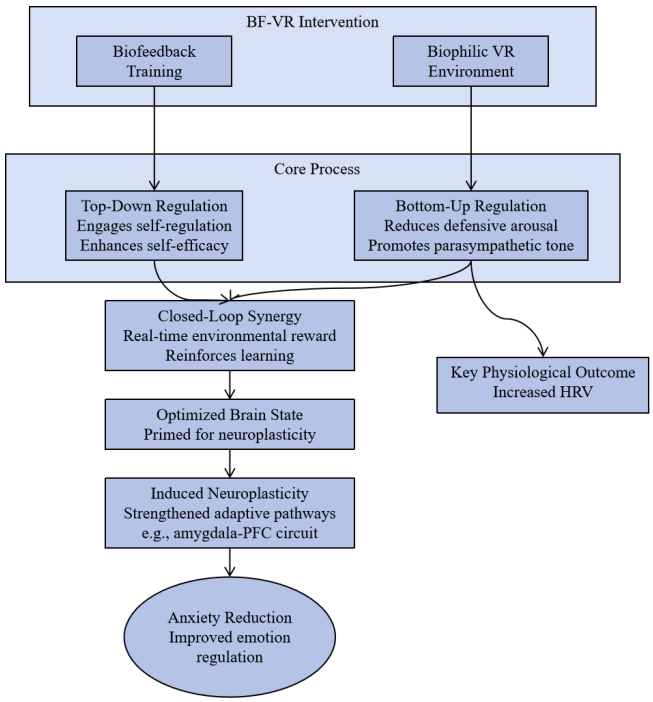

Figure 2. The proposed biophilic-neuroplasticity synergistic mechanism (BNSM) of biofeedback-integrated virtual reality (BF-VR) for anxiety

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Top-down regulation operations are on the stage due to the introduction of biofeedback to the ensemble. The visualization and manipulation of physiological states (e.g. heart rate, arousal) has been found to enhance the self-efficacy and the deliberate self-regulation [23,13] cascade of reactions that relies on the prefrontal cortex as the central anatomic foundation. It is also revealed that in this brain reorganisation (neuroplasticity) one of the primary origins of this reorganisation is the repeated practice of volitional control [9].

The VR aspect, on the other hand, and primarily the settings where nature-loving features are predominant (e.g., woods, seashores, starry sky), alters the mood of an individual because it regulates the bottom-up fashion. Such conditions will automatically involve concentration in the mind of an individual and a decrease in the stimulation of a defensive mechanism, thereby leading to parasympathetic hegemony- it is possible to observe it in terms of the increase in HRV observed in all the studies [13,20,21]. It leads to low threat, safe window, which is biologically ready to be plastic [8].

The synergy is based on the fact that they are combined in a closed-loop, as shown in Figure 2. To begin with, the relaxing VR setting reduces the first obstacle to entering the biofeedback training, thus, it becomes simpler to reach the self-regulatory success [24]. Secondly, the objective validation of the relaxing effect of the VR environment (e.g., reduction of HR correlates with the clarity of the virtual sky) by the real-time biofeedback data creates a strong positive feedback mechanism that strengthens the learning [15]. Thirdly, such an experience of successful, highly rewarding self-regulation, in which deliberate effort is immediately rewarded by environmental condition, is probably reinforcing a novel, adaptive neural network, with the potential to result in neuroplastic alterations in anxiety networks in the long run.

4.2. Dialogue with existing evidence

Even though neuroplasticity markers, like BDNF, were not directly measured in any of the included studies, the uniformity of its outcomes (enhanced physiological regulation (HRV and SCL) and the durability of effects in some of the follow-up studies) [16] is solid indirect evidence in favor of the BNSM. Moreover, certain biophilic design features are actively involved in the regulation of physiological stress responses, which proves that they are not just backdrops [15].

4.3. Limitations

This review has a number of limitations. To begin with, the study designs, populations, and intervention protocols were heterogeneous, which could not allow a meta-analysis. Second, most of the encompassed studies possessed limited sample sizes and a limited follow-up regarding the follow-up period, which restricted the generalizability and efficacy evaluation of the studies over time. Third, since none of the studies directly determined the markers of neuroplasticity (e.g., BDNF, fMRI), the hypothesized BNSM is still just a hypothesis that has not been directly proved yet. Lastly, the omnipresence of biophilic settings, which is supporting our hypothesis, does not allow separating its impact on VR immersion in the existing literature.

4.4. Clinical implications and future directions

The results of the review have a direct implication on the dynamic nature of digital mental health. BF-VR is a scalable, interactive, and possibly effective intervention that may supplement the

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conventional treatment, especially in patients that are resistant to treatment or those that have low access to care.

The future studies should focus on:

a) Mechanistic Validation: Welle powered RCTs of the BNSM with direct assessments of neuroplasticity (e.g. peripheral BDNF, resting-state fMRI/EEG connectivity).

b) Component testing: The use of factorial designs to separate the distinct effects of biophilic design and biofeedback and their interaction.

c) Personalization: Exploring the most effective BF-VR protocols to use with regard to different anxiety manifestations (e.g., GAD and social anxiety) and patient-specific features.

5. Conclusion

This review makes BF-VR a powerful and immersive intervention that can be used to alleviate anxiety. In addition to the efficacy consolidation, the current research suggests the Biophilic-Neuroplasticity Synergistic Mechanism as a new theoretical framework that would describe its inner mechanisms. The hypothesis in the mechanism is that when biophilic VR environments suggests the brain to the change, it causes less stress, whereas, biofeedback positively trains and strengthens new neural pathways with rewarded self-regulation. The combination of these aspects in a closed-loop creates a strong and interactive therapeutic experience, which is in favor of neuroplastic adaptation in the long run. Although initial physiological data is encouraging, more studies are needed in order to directly test this hypothesis in mechanistic studies. Finally, ongoing improvement of BF-VR under this mechanistic knowledge proposal has a great potential on the creation of more specific and efficient digital therapeutic interventions of anxiety.

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