Impact of virtual reality-based biofeedback on sleep quality among individuals with depression and anxiety: a 4-week randomized controlled study

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Submitted to: Journal of Medical Internet Research
on: August 26, 2024

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Hong Jin Jeon[1, 2, 3, 4]; Sisu Seong[1]; Hyewon Kim[2]; Yaehee Cho[2]; Min-Ji Kim[5]; Ka Ram Park[1]; Jooeun Choi[1]; Seonah Lee[2]; Dong Jun Kim[2]; Seog Ju Kim[2]

[1]Department of Medical Device Management and Research, Samsung Advanced Institute for Health Sciences & Technology (SAIHST) Sungkyunkwan University Seoul KR
[2]Department of Psychiatry, Depression Center, Samsung Medical Center Sungkyunkwan University School of Medicine Seoul KR
[3]Department of Health Sciences & Technology and Department of Clinical Research Design & Evaluation, Samsung Advanced Institute for Health Sciences & Technology (SAIHST) Sungkyunkwan University Seoul KR
[4]Meditrix Co., Ltd. Seoul KR
[5]Biomedical Statistics Center, Research Institute for Future Medicine Samsung Medical Center Seoul KR

Corresponding Author:
Hong Jin Jeon
Department of Medical Device Management and Research, Samsung Advanced Institute for Health Sciences & Technology (SAIHST)
Sungkyunkwan University
81 Irwon-Ro Gangnam-gu
Seoul
KR

Abstract

Background: Depressive disorders, projected by the WHO to rank third in global disease burden by 2030, significantly impair quality of life, with over 300 million affected worldwide. Sleep difficulties, particularly insomnia, are closely linked to depression, exacerbating its severity. Biofeedback (BF) therapy, specifically heart rate variability biofeedback (HRV-BF), shows promise in treating insomnia and associated depressive symptoms. Recent studies suggest that integrating virtual reality (VR) into BF therapy could enhance its efficacy by creating immersive, calming environments that improve sleep quality. This study explores the potential of VR-based BF to improve sleep in individuals with depression and anxiety.

Objective: To investigate impact of virtual reality-based biofeedback (VR-based BF) on sleep quality as measured by the Pittsburgh Sleep Quality Index (PSQI) of individuals with depressive or anxiety symptoms.

Methods: Between December 2019 and February 2022, 131 adult volunteers were recruited at Samsung Medical Center, Seoul, South Korea. Individuals with specific medical or psychiatric conditions were excluded. Those with depressive and anxiety symptoms (DAS) were randomized into VR (n = 40) and BF (n = 38) groups by computer-generated random number. A Healthy Control (HC, n = 40) cohort with sham intervention mirroring the DAS/VR group was also included. Over three visits, participants received VR-based BF or conventional BF with a therapist. Iterative baseline and 4-week follow-up PSQI assessments were performed. Following intervention, subcomponent scores of the PSQI decreased in both DAS/VR and DAS/BF groups.

Results: After 4-week intervention, a decrease in global PSQI scores was observed across all groups. For Global PSQI score, the DAS/VR group demonstrated a substantial reduction from 9.70 (±2.49) to 7.20 (±2.46) ($p<0.001$), and the HC/VR group from 5.85 (±2.39) to 4.90 (±2.11) ($p=0.007$). Notably, improvements in sleep quality, latency, disturbance, and day dysfunction were statistically significant in the DAS/VR groups but not in sleep duration, efficiency, and sleep medicine uses.

Conclusions: This study provides evidence that VR-based BF can serve as effective psychological intervention for enhancing sleep quality of individuals experiencing symptoms of depression and anxiety, and also effective in health subjects.

(JMIR Preprints 26/08/2024:65772)
DOI: https://doi.org/10.2196/preprints.65772

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Impact of virtual reality-based biofeedback on sleep quality among individuals with depression and anxiety: a 4-week randomized controlled study

Subtitle: Effect of VR-based BF on PSQI

Sisu Seong[1]; Hyewon Kim[2]; Yaehee Cho [2]; Min-Ji Kim[3]; Ka Ram Park[1]; Jooeun Choi[1]; Seonah Lee[2]; Dong Jun Kim[2]; Seog Ju Kim[2]; Hong Jin Jeon[1,2,4,5*]

[1]*Department of Medical Device Management and Research, Samsung Advanced Institute for Health Sciences & Technology (SAIHST), Sungkyunkwan University, Seoul, South Korea*

[2]*Department of Psychiatry, Depression Center, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea*

[3]*Biomedical Statistics Center, Research Institute for Future Medicine, Samsung Medical Center, Seoul, South Korea*

[4]*Department of Health Sciences & Technology and Department of Clinical Research Design & Evaluation, Samsung Advanced Institute for Health Sciences & Technology (SAIHST), Sungkyunkwan University, Seoul, South Korea*

[5]*Meditrix Co., Ltd., Seoul, South Korea*

†Correspondence: Hong Jin Jeon, MD, Ph.D.

Professor

Department of Psychiatry, Depression Center, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea

Vice dean of Research, Sungkyunkwan University School of Medicine, Seoul, Korea

Director of the Digital Therapeutics Research Center, Samsung Medical Center

Samsung Advanced Institute for Health Sciences & Technology (SAIHST)

CEO of Meditrix Co., Ltd.

(06355) 115 Irwon-Ro, Gangnam-gu. Seoul, Korea

Phone: 010-3198-3586 TEL: +82-2-3410-3586 FAX: +82-2-3410-0050

Email: jeonhj@skku.edu, jhj001001@gmail.com

All authors agreed to this submission.

The material is original research. It has not been previously published or submitted for publication elsewhere while under consideration.

ABBREVIATIONS

ANOVA = analysis of variance

BF = biofeedback

CGI-S = clinical global impression-severity

CBT-I = cognitive behavioral therapy for insomnia

DAS = depressive and anxiety symptoms

DSM-IV = diagnostic and statistical manual of mental disorders, fourth edition

HC = healthy control

HMD = head-mounted display

HR/BP = heart rate/blood pressure

HRV-BF = heart rate variability biofeedback

MDD = major depressive disorder

MINI = mini-international neuropsychiatric interview

PDSS = panic disorder severity scale

PHQ-9 = patient health questionnaire-9

PSQI = Pittsburgh Sleep Quality Index

RCT = randomized controlled trial

SD = standard deviation

VR = virtual reality

Abstract

Background:

Objectives: To investigate impact of virtual reality-based biofeedback (VR-based BF) on sleep quality as measured by the Pittsburgh Sleep Quality Index (PSQI) of individuals with depressive or anxiety symptoms.

Methods: Between December 2019 and February 2022, 131 adult volunteers were recruited at Samsung Medical Center, Seoul, South Korea. Individuals with specific medical or psychiatric conditions were excluded. Those with depressive and anxiety symptoms (DAS) were randomized into VR (n=40) and BF (n=38) groups by computer-generated random number. A Healthy Control (HC, n=40) cohort with sham intervention mirroring the DAS/VR group was also included. Over three visits, participants received VR-based BF or conventional BF with a therapist. Iterative baseline and 4-week follow-up PSQI assessments were performed. Following intervention, subcomponent scores of the PSQI decreased in both DAS/VR and DAS/BF groups.

Results: After 4-week intervention, a decrease in global PSQI scores was observed across all groups. For Global PSQI score, the DAS/VR group demonstrated a substantial reduction from 9.70 (±2.49) to 7.20 (±2.46) ($p<0.001$), and the HC/VR group from 5.85 (±2.39) to 4.90 (±2.11) ($p=0.007$). Notably, improvements in sleep quality, latency, disturbance, and day dysfunction were statistically significant in the DAS/VR groups but not in sleep duration, efficiency, and sleep medicine uses.

Conclusion: This study provides evidence that VR-based BF can serve as effective psychological intervention for enhancing sleep quality of individuals experiencing symptoms of depression and anxiety, and also effective in health subjects.

Keywords: virtual reality, biofeedback, PSQI, sleep quality, depression

Introduction

According to the estimation by the World Health Organization (WHO), depressive disorders will become the third highest issue in the global burden of disease by 2030, accounting for 4.3% of the total burden [1]. With more than 300 million individuals affected worldwide, depressive disorders have substantial medical burdens and significant disability [2].

Individuals with major depressive disorder (MDD) in the United States, 84.7% of depressed respondents reported experiencing sleep difficulties, with a concurrent association noted between these difficulties and elevated severity scores of depression [3]. The existence of insomnia symptoms has demonstrated robust correlations with heightened severity of depressive symptoms, a decline in overall quality of life, and notable impairment in both psychological and physiological functioning [3]. In Korea, people with depression most frequently seek psychiatric care for insomnia [4]. A meta-analysis of 34 research articles with 172,077 individuals has found a correlation between insomnia and depression. It concluded that a lack of sleep could exacerbate depression and suggested that preventing the lack of sleep might minimize depression [5]. The relationship between sleep disorders and depression has been well-documented in existing literature [6]. A clear association between poor sleep status and psychological issues has also been established [7].

Biofeedback (BF) therapy involves guiding patients to recognize their capacity to regulate their physiological states by engaging them in therapy sessions that involve the use of BF equipment to practice technique. Ultimately, the efficacy of this intervention is evaluated based on the extent to which acquired skills could be generalized and integrated into a patient's daily life [8]. A frequently employed BF approach involves utilization of physiological connection between respiration and cardiac function [9]. This approach offers a comprehensive presentation of feedback parameters, utilizing numerical metrics and graphical representations or charts [10]. A systematic review of heart

rate variability biofeedback (HRV-BF) and the management of chronic diseases has suggested that it might be a useful therapy for several long-term illnesses (such as hypertension, anxiety, depression, asthma, and cardiovascular disease) and sleep disorders [11]. Research on the application of BF techniques as therapy for mental disorders has an extensive history [12]. BF is often discussed in the literature and commonly used in medical environments as an insomnia treatment [13]. HRV-BF is a comparatively recent BF method used for treating insomnia [14]. A previous study involving individuals with comorbid MDD and insomnia has found that a 6-week HRV-BF protocol can significantly improve insomnia symptoms, sleep quality, duration, and daytime dysfunction based on assessments encompassing psychological measures and physiological tests at various time points [15]. A pilot RCT has shown that a neurofeedback method and CBT-I are equally effective in decreasing symptoms of insomnia [16]. Other studies have shown that BF holds promise as a therapy for comorbid insomnia and other disorders [15,17].

HRV-BF, the most prevalent form of BF, posits several potential benefits. However, there are several obstacles that could inhibit its positive therapy outcomes. To overcome these limitations, a setting that fosters prolonged attention, gives immersive feedback components, and creates a cozy and comfortable atmosphere needs to be implemented [18]. One study has demonstrated the effectiveness of virtual reality natural environments in the context of stress reduction and relaxation, underscoring their viability as therapeutic tools [19]. Benefits of interaction with nature are influenced by the Attention Restoration Theory [20]. VR technologies can give users the capacity to create and manage virtual interactive environments that can be utilized to alter their physiological and emotional responses [21]. Consequently, virtual natural environments appear to constitute a suitable backdrop for the application of BF as they can effectively redirect attentional resources in a calming and tranquil manner while affording numerous possibilities for immersive and contextually pertinent feedback elements [18]. VR operates by deflecting attention and submerging users in soothing

simulations designed to activate and regulate different physiological and mental functions that may induce sleep [21]. One study has shown that putting on VR headsets before bedtime can lower PSQI value at post-treatment assessment, supporting the ability of VR intervention to enhance sleeping quality [22].

Our hypothesis was that virtual reality-based biofeedback (VR-based BF) could enhance sleep quality among individuals exhibiting symptoms of depression and anxiety. The primary objective of this study was to examine alterations in sleep quality at 4-week follow-up assessment after implementing VR-based BF intervention compared to the sleep quality at baseline.

Methods

Participants

Between December 2019 and February 2022, a total of 131 adults were enrolled in this study through advertising in Samsung Medical Center in Seoul, South Korea. Participants were disqualified if they had a history of, or were presently experiencing mental health issues, including substance abuse, intellectual disability, degenerative neuropsychiatric illnesses, neurological disorders, serious medical illnesses, or brain damage. All participants were previously not exposed to psychiatric medication. The screening process involved the use of the Korean version of the Mini International Neuropsychiatric Interview (MINI) [23] to comply with the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV). This study had two cohorts: 1) a depressive or anxiety symptom (DAS) cohort, and 2) a healthy control (HC) cohort. Inclusion criteria for the DAS cohort were as follows: self-reported subjective anxiety or depression, no psychiatric treatment within the past six months, and scored ≥ 10 on the Patient Health Questionnaire-9 (PHQ-9) [24] or ≥ 9 on the Panic Disorder Severity Scale (PDSS) [25].

The HC cohort was comprised of individuals who did not meet the established diagnostic criteria for

MDD and/or anxiety-related disorders as outlined in the DSM-IV. Additionally, these individuals demonstrated normal results in both medical and neurological screening tests. All eligible participants provided written informed consent prior to their inclusion in this study. This study received approval from the Institutional Review Board of Samsung Medical Center (No. SMC 2019-07-039-010).

Study Designs and Procedures

Primary study was focused on using VR-based BF therapy to reduce depressive and anxiety symptoms. This study was formulated to evaluate the efficacy of VR-based BF therapy in improving sleep quality using a pre-post comparative approach of PSQI.

This study was conducted as a 4-week randomized controlled study at a single medical center, in which the effectiveness of VR-based BF was compared to that of conventional BF with a therapist. Participants in the DAS cohort were allocated to either a VR-based BF (DAS/VR) or a conventional BF (DAS/BF) intervention group using randomized allocation. They were assigned at a 1:1 ratio based on computer-generated randomized numbers. In order to evaluate the effect of VR-based BF on healthy subjects, the HC cohort received VR-based BF intervention (HC/VR).

All participants were asked to visit the Clinical Study Center at Samsung Medical Center three times (at weeks 0, 2, 4) and receive the allocated intervention followed by interviews after each session. During the VR session, a Samsung Odyssey plus (Samsung Electronics Co., Ltd., Suwon, South Korea) was used with peripheral devices, including the head-mounted display (HMD) with head tracking and stereo earphones, connected. Each participant sat in the motion chair and wore the HMD.

Participants watched and listened to VR relaxation training video comprised of four natural scenes for five minutes. A psychiatrist (HJJ) led participants through a breathing exercise during the VR session. After an ancient bell rang, participants started to slowly wander through nature in virtual reality while listening to classically soothing background music and digital nature sounds that were specifically designed to go with VR images, such as sounds of birds chirping, wind, water flowing, and so on. At the same time, guided relaxation therapy was performed (such as, "Relax your muscles. Breathe in slowly while your stomach expands, then exhale one, two, three times. Exhale gradually as your abdomen expands"). While practicing relaxation techniques, participants were permitted to slowly cross a river, soar to skies, and stroll through a tranquil meadow in the VR.

Regarding conventional BF, a computerized biofeedback device ProComp Infiniti (Thought Technology, Ltd., Montreal, Canada) was used. Participants were instructed about relaxation techniques while observing physiological parameter signals, which encompassed heart rate/blood pressure (HR/BP), skin conductance, respiration, and skin temperature displayed on the screen with a therapist. During the BF session, the researcher provided feedback to subjects when physiological markers changed by 15%. Five minutes were spent carrying out the BF intervention.

Outcome Measures

Participants were requested to recollect and report their sleep patterns from the preceding month, responding to a set of 19 distinct inquiries related to seven primary components of sleep, including overall sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disturbance, sleep medicine uses, and day dysfunction due to sleepiness using the Pittsburgh Sleep Quality Index (PSQI) [26].

The PSQI is a robust and widely acknowledged instrument for evaluating self-reported adult sleep quality. The PSQI effectively gauges seven key components, allowing for discernment between

"poor" and "good" sleep experiences. These essential parameters encompass subjective sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disruptions, sleep medicine uses, and day dysfunction due to sleepiness over the preceding month. Importantly, each of these seven facets can be systematically assessed by participants, contributing to a comprehensive and nuanced understanding of an individual's sleep habits and their implications. These seven components were scored on a Likert scale from 0 to 3, with a score of 0 representing the positive extreme ("not during the past month") and a score of 3 representing the negative extreme. Each participant received a global PSQI score after adding up scores for the seven factors (all equally weighted on a 0–3 scale), with a final range of 0–21. A higher score indicated a poorer sleep quality. In comparison with clinical and laboratory measurements, a global PSQI score > 5 was indicative of poor sleep quality [26].

The test-retest reliability analysis revealed a notable overall correlation coefficient of 0.87 for a PSQI global score among patients afflicted with primary insomnia. Notably, as an indicator of sleep disruptions within the context of insomnia patients compared to control groups, a PSQI global score exceeding 5 demonstrated a remarkable sensitivity of 98.7% and a specificity of 84.4%. This underscores the practical utility of the PSQI as a diagnostic tool in distinguishing sleep disturbances among individuals with insomnia, confirming its practical significance within clinical and research settings [27].

Statistical Analyses

To analyze each group's distribution of clinical and demographic characteristics (DAS/VR, DAS/BF, HC/VR), descriptive statistics are presented as mean with standard deviation (SD) and frequency with percentage for continuous and categorical variables, respectively. Group comparisons among three groups were conducted using the chi-square test or Fisher’s exact test for categorical variables.

For continuous variables, they were compared using one-way analysis of variance (ANOVA) or Kruskal-Wallis test according to satisfaction of normality assumption. Changes in outcome measurements between baseline (0 week) and 4-week follow-up visit were examined via paired t-test or Wilcoxon signed rank test in each group. For changes in outcome measurements, Wilcoxon rank sum test or t-test were used for two pairwise comparisons between VR and BF in DAS and between DAS/VR and HC/VR. After adjusting for sex and age, we additionally performed linear regression analysis to compare between groups. Statistical significance was declared when p-value was less than 0.05. All statistical analyses were done with SAS version 9.4 (SAS Institute, Cary, NC, USA).

Results

Baseline Characteristics of Participants

A total of 131 participants self-referred to this research. The screening process resulted in exclusion of 13 volunteers due to psychiatric diagnoses, including 9 major depressive disorders, 3 comorbid phobic disorders, and 1 antisocial personality disorder. Finally, 120 participants were enrolled for this study, including 80 participants in the DAS cohort and 40 participants in the HC cohort. Those in the DAS cohort were allocated into the VR intervention group (n=41) and the BF intervention group (n=39) at random. After the first visit, one person in the VR group and one person in the BF group withdrew. Finally, a total of 118 participants were subjected to comprehensive analysis. These participants' demographic details and initial clinical measurements are shown in **Table 1**. To reduce the impact of potential confounding factors, a propensity-matched analysis was conducted, taking into account demographic variables such as age, sex, and education level. Each of the three groups was characterized by a mean age within the 40s of demographic range. Differences in age, sex, education, drinking frequency, and smoking were not significant between groups. However, the mean global PSQI score at baseline of participants was 9.7 (SD = 2.5) for the DAS/VR group, 10.8 (SD = 2.8) for the DAS/BF group, and 5.9 (SD = 2.4) for the HC/VR group, showing a significant

($p<0.001$) difference.

Table 1. Baseline characteristics of participants.

	Depression and anxiety		Healthy control	p-value
	DAS[a]/VR[c] group (n=40)	DAS[a]/BF[d] group (n=38)	HC[b]/VR[c] group (n=40)	
	N (%)	N (%)	N (%)	
Age	45.1 (10.2)	42.9 (10.6)	40.3 (12.0)	0.152
Sex				0.078
Male	8 (20.0)	8 (21.1)	16 (40.0)	
Female	32 (80.0)	30 (79.0)	24 (60.0)	
Education [28]	14.8 (2.1)	14.8 (1.8)	15.3 (2.1)	0.308
Marriage status				0.020
Single	7 (17.5)	6 (15.8)	16 (40.0)	
Married/Divorced	33 (82.5)	32 (84.2)	24 (60.0)	
Drinking frequency				
No	11 (27.5)	15 (39.5)	12 (30)	
Yes	29 (72.5)	23 (60.5)	28 (70)	
Smoking				0.156
Never	36 (90.0)	28 (73.7)	30 (76.9)	
Current	4 (10.0)	10 (26.3)	9 (23.1)	
	Mean [29]	Mean [29]	Mean [29]	
BIS-11[e]	63.2 (10.1)	68.9 (7.9)	57.4 (7.8)	<0.001
CGI-S[f]				<0.001*
not ill	23 (57.5)	18 (47.4)	37 (92.5)	
minimally ill	15 (37.5)	16 (42.1)	3 (7.5)	
mildly ill	2 (5.0)	4 (10.5)	0 (0.0)	
Global PSQI[g] Score at baseline	9.7 (2.5)	10.76 (2.8)	5.85 (2.4)	<0.001†

[a]DAS = Group with Depressive or Anxiety Symptoms.

[b]HC = Healthy Control.

[c]VR = Virtual reality.

[d]BF = Biofeedback.

[e]BIS-11 = Barratt Impulsiveness Scale-11.

[f]CGI-S = Clinical Global Impression-Severity, Chi-square test (* Fisher's exact test) for categorical variable.

[g]PSQI = Pittsburgh Sleep Quality Index, One-way ANOVA († Kruskal-Wallis test) for continuous variable.

Significance of Change in PSQI in Each Aroup (0 week and 4 weeks)

Pre- and post-intervention mean (SD) scores in the PSQI at 0 week and 4 weeks for the three groups (DAS/VR, DAS/BF, and HC/VR) are shown in **Table 2**. In terms of sleep quality, the DAS/VR group showed a noteworthy enhancement from pre-intervention (1.90 ± 0.44) to post-intervention (1.50 ± 0.64, p=0.001), as did the DAS/BF group, improving from 2.08 ± 0.36 to 1.45 ± 0.60 (p<0.001). However, HC/VR group observed from pre-intervention (1.30 ± 0.65) to post-intervention (1.13 ± 0.52), did not reach statistical significance (p=0.192). Sleep latency reductions were significant in both DAS/VR (2.10 ± 0.71 to 1.60 ± 0.74, p<0.001) and DAS/BF (2.24 ± 0.75 to 1.47 ± 0.80, p<0.001) groups, while the HC/VR group exhibited a decrease (1.25 ± 0.84 to 1.00 ± 0.82) without statistical significance (p=0.063). Similarly, both DAS/VR and DAS/BF groups displayed significant improvements in sleep disturbance, with respective p-values of <0.001, whereas the HC/VR group's change pre-intervention (1.05 ± 0.50) to post-intervention (0.98 ± 0.42) was not statistically significant (p=0.549). Daytime dysfunction significantly improved in DAS/VR (2.08 ± 0.73 to 1.23 ± 0.86, p<0.001) and DAS/BF (2.08 ± 0.78 to 1.24 ± 0.71, p<0.001) groups, and the HC/VR group exhibited a substantial improvement pre-intervention (1.15 ± 0.80) to post-intervention (0.63 ± 0.74) with a significant p-value of less than 0.001. For Global PSQI score, the DAS/VR group demonstrated a substantial reduction from 9.70 (±2.49) to 7.20 (±2.46) with a p-value of less than 0.001. Similarly, the DAS/BF group showed a significant improvement from 10.76 (±2.76) to 7.37 (±2.28) with a p-value of less than 0.001. The HC/VR group also experienced a noteworthy decrease from 5.85 (±2.39) to 4.90 (±2.11) with a p-value of 0.007 (See Figure 1).

Figure 1. Changes in global PSQI scores over 4 weeks. The mean (SD) Global PSQI score significantly decreased from baseline (9.70, 2.49) to 4 weeks (7.20, 2.46) in the DAS/VR group (p<0.001). Similarly, the DAS/BF group showed a significant decrease from baseline (10.76, 2.76) to

4 weeks (7.37, 2.28) in the Global PSQI score ($p<0.001$). In the HC group, the Global PSQI score changed from 5.85 (2.39) at baseline to 4.90 (2.11) at 4 weeks, with a statistically significant reduction ($p=0.007$). DAS = Depressive and Anxiety Symptoms; BF = biofeedback; VR = virtual reality; HC = Healthy Control.

The HC/VR group also showed statistically significant improvements in their daytime dysfunction and global PSQI score from baseline to at 4 weeks after intervention. However, there were no statistically significant changes in sleep duration, sleep efficiency, sleep medicine use, or sleep disturbance for the HC/VR group. Overall, both DAS/VR and DAS/BF groups demonstrated significant improvements in sleep quality, sleep latency, sleep disturbance, and daytime dysfunction (all $p<0.05$) (See Figure 2).

Figure 2. Significant Improvements in Sleep Quality Measures. (**A**) Sleep Quality. The DAS/VR Group exhibited a substantial enhancement from pre-intervention (1.90 ± 0.44) to post-intervention (1.50 ± 0.64) with a significant p-value of 0.001. Similarly, the DAS/BF Group demonstrated a significant improvement from 2.08 ± 0.36 to 1.45 ± 0.6 ($p<0.001$). However, the HC Group, while showing positive changes from pre-intervention (1.30 ± 0.65) to post-intervention (1.13 ± 0.52), did not reach statistical significance ($p=0.192$). (**B**) Sleep Latency. Both the DAS/VR and DAS/BF Groups experienced substantial reductions in sleep latency ($p<0.001$), with DAS/VR decreasing from 2.10 ± 0.71 to 1.60 ± 0.74 and DAS/BF from 2.24 ± 0.75 to 1.47 ± 0.80. The HC Group also saw a decrease from 1.25 ± 0.84 to 1.00 ± 0.82, though not statistically significant ($p=0.063$). (**C**) Sleep Disturbance. Significant improvements were observed in sleep disturbance for both the DAS/VR (pre: 1.78 ± 0.62, post: 1.20 ± 0.46, $p<0.001$) and DAS/BF (pre: 1.89 ± 0.61, post: 1.24 ± 0.54, $p<0.001$) Groups. The HC Group also showed a decrease from pre-intervention (1.05 ± 0.50) to post-intervention (0.98 ± 0.42), but the change was not statistically significant ($p=0.549$). (**D**) Daytime

Dysfunction. Both DAS/VR and DAS/BF Groups demonstrated significant improvements in daytime dysfunction ($p<0.001$), with DAS/VR decreasing from 2.08 ± 0.73 to 1.23 ± 0.86 and DAS/BF from 2.08 ± 0.78 to 1.24 ± 0.71. The HC Group exhibited a substantial improvement from pre-intervention (1.15 ± 0.80) to post-intervention (0.63 ± 0.74) with a significant p-value of less than 0.001. DAS = Depressive and Anxiety Symptoms; BF = biofeedback; VR = virtual reality; HC = Healthy Control.

Table 2. Significance of the change in the PSQI score in each group (baseline and 4 weeks)

	Depression and anxiety						Healthy control		
	DAS[a]/VR[c] group (n=40)			DAS[a]/BF[d] group (n=38)			HC[b]/VR[c] group (n=40)		
	Pre at 0 week	Post at 4 weeks	p-value	Pre at 0 week	Post at 4 weeks	p-value	Pre at 0 week	Post at 4 weeks	p-value
PSQI[e] Components Scores	Mean [29]	Mean [29]		Mean [29]	Mean [29]		Mean [29]	Mean [29]	
Sleep Quality	1.90 (0.44)	1.50 (0.64)	0.001	2.08 (0.36)	1.45 (0.60)	<0.001	1.30 (0.65)	1.13 (0.52)	0.192
Sleep Latency	2.10 (0.71)	1.60 (0.74)	<0.001	2.24 (0.75)	1.47 (0.80)	<0.001	1.25 (0.84)	1.0 (0.82)	0.063
Sleep Duration	1.40 (0.84)	1.25 (0.87)	0.300	1.66 (0.81)	1.42 (0.86)	0.175	0.88 (0.72)	0.98 (0.70)	0.424
Sleep Efficiency	0.40 (0.74)	0.43 (0.87)	1.000	0.79 (1.04)	0.55 (0.8)	0.248	0.23 (0.66)	0.20 (0.46)	0.945
Sleep Disturbance	1.78 (0.62)	1.20 (0.46)	<0.001	1.89 (0.61)	1.24 (0.54)	<0.001	1.05 (0.50)	0.98 (0.42)	0.549
Sleep medicine Uses	0.05 (0.22)	0.00 (0.00)	0.500	0.03 (0.16)	0.00 (0.00)	1.000	0.00 (0.00)	0.00 (0.00)	NA
Daytime Dysfunction	2.08 (0.73)	1.23 (0.86)	<0.001	2.08 (0.78)	1.24 (0.71)	<0.001	1.15 (0.80)	0.63 (0.74)	<0.001
Global PSQI Score	9.70 (2.49)	7.20 (2.46)	<0.001	10.76 (2.76)	7.37 (2.28)	<0.001	5.85 (2.39)	4.90 (2.11)	0.007

[a]DAS = Group with Depressive or Anxiety Symptoms.

[b]HC = Healthy Control.

[c]VR = Virtual reality.

[d]BF = Biofeedback.

[e]PSQI = Pittsburgh Sleep Quality Index, p-value by paired t-test or Wilcoxon signed rank test according to the normality assumption.

Comparison of PSQI Score Between Pairwise and Adjusted Pairwise Comparisons

Table 3 presents mean (SD) changes at the last session (post-intervention at week 4) compared to baseline (pre-intervention at week 0) analyzed by Wilcoxon rank sum test or t-test for two pairwise comparisons between VR and BF in DAS and between DAS/VR and HC/VR in each group. Further analysis was also performed for adjusted pairwise comparisons of the PSQI score between different groups. According to linear regression analysis that was adjusted for age and sex, there was no significant difference in improvement of the PSQI score following VR or BF intervention between DAS/VR and DAS/BF groups. In contrast, there were significant differences in components of sleep disturbance and global PSQI score when results of DAS/VR and HC/VR groups were compared (all $p<0.05$).

Both the DAS/VR and DAS/BF groups demonstrated notable improvements in sleep disturbance, reflecting reductions of -0.58 (SD: 0.75) and -0.66 (SD: 0.75), respectively. However, the difference in the reduction of sleep disturbance between the two groups was not statistically significant ($p=0.487$). When comparing the DAS/VR group to the HC/VR group, the DAS/VR group exhibited a marked and statistically significant improvement in sleep disturbance ($p=0.001$). The Global PSQI Score showed notable improvements for both the DAS/VR and DAS/BF groups, with decreases of -2.5 (SD: 2.89) and -3.39 (SD: 2.80), respectively. Nevertheless, the Global PSQI Score decrease did not differ statistically significantly between the DAS/VR and DAS/BF groups ($p=0.136$).

Table 3. Changes between pre and post intervention in the PSQI score

	Mean (SD) of the change in the PSQI score			Pairwise comparison		Adjusted pairwise comparison	
	DAS[a]/VR[c] group (n=40)	DAS[a]/BF[d] group (n=38)	HC[b]/VR[c] group (n=40)	DAS[a]/VR[c] vs DAS[a]/BF[d]	DAS[a]/VR[c] vs HC[b]/VR[c]	DAS[a]/VR[c] vs DAS[a]/BF[d]	DAS[a]/VR[c] vs HC[b]/VR[c]
PSQI[e] Components Scores	**Mean** [29]			**p-value***		**p-value****	
Sleep Quality	-0.4 (0.67)	-0.63 (0.67)	-0.18 (0.71)	0.151	0.179	0.151	0.206
Sleep Latency	-0.5 (0.72)	-0.76 (0.79)	-0.25 (0.74)	0.101	0.143	0.131	0.141
Sleep Duration	-0.15 (0.80)	-0.24 (0.94)	0.1 (0.59)	0.543	0.127	0.570	0.095
Sleep Efficiency	0.03 (1.05)	-0.24 (1.10)	-0.03 (0.80)	0.457	0.667	0.237	0.812
Sleep Disturbance	-0.58 (0.75)	-0.66 (0.75)	-0.08 (0.53)	0.782	0.001	0.487	0.001
Sleep medicine Uses	-0.05 (0.22)	-0.03 (0.16)	0.00 (0.00)	0.600	0.160	0.581	0.097
Daytime Dysfunction	-0.85 (1.19)	-0.84 (0.68)	-0.53 (0.78)	0.839	0.139	0.968	0.238
Global PSQI Score	-2.5 (2.89)	-3.39 (2.80)	-0.95 (2.09)	0.199	0.010	0.136	0.012

[a]DAS = Group with Depressive or Anxiety Symptoms.

[b]HC = Healthy Control.

[c]VR = Virtual reality.

[d]BF = Biofeedback.

[e]PSQI = Pittsburgh Sleep Quality Index,*t-test or Wilcoxon rank sum test according to the normality assumption, **Linear regression analysis adjusted with age and sex, change = post-pre.

Discussion

In this study, we employed a randomized controlled study design to assess the effectiveness of VR-based BF in comparison with conventional BF in improving sleep quality of individuals experiencing symptoms of depression and anxiety. Our results demonstrated significant improvements in sleep quality, sleep latency, sleep disturbance, daytime dysfunction, and global PSQI score in intervention groups (DAS/VR and DAS/BF). This underscored the effectiveness of VR-based BF as a valuable psychosocial intervention for enhancing sleep quality of individuals with symptoms of depression and anxiety.

Findings of this study suggest that VR-based BF which is a new technology added to conventional therapy can be used to improve sleep quality of adults with depressive and anxiety symptoms according to pre- and post-intervention mean scores of the PSQI. In this study, three distinct groups (DAS/VR, DAS/BF, and HC/VR) underwent a 4-week intervention. Both DAS/VR and DAS/BF groups displayed notable enhancements in sleep quality, sleep latency, sleep disturbance, daytime dysfunction, and global PSQI score. The HC/VR group also exhibited improvements in daytime dysfunction and global PSQI score, although there were no significant changes in sleep duration, efficiency, medication use, or disturbances. These findings emphasize the effectiveness of such interventions in addressing sleep-related issues among respective groups. However, when comparing DAS/VR with HC/VR, significant differences were observed in components of sleep disturbance and global PSQI score. Notably, the DAS cohorts exhibited similar substantial improvements in these parameters, while the HC/VR group showed smaller changes, highlighting the distinctive impact of these interventions in addressing sleep-related issues.

Several components of PSQI, including sleep quality, sleep latency, sleep disturbance, daytime dysfunction, and global PSQI score, were improved after receiving VR-based BF. Improvements of components of PSQI were observed for both DAS/VR and DAS/BF groups in this study. A previous study based on HRV-BF was equally effective in improving those components. It found that HRV-BF could improve insomnia symptoms and decrease the incidence of anxiety and depression [15]. Mobile HRV-BF intervention can also effectively improve insomnia symptoms, reduce anxiety and depression, and enhance subjective sleep quality in healthy young adults [30].

Despite the extensive 36-year history of utilizing BF as a therapy modality for insomnia, there remains a scarcity of comprehensive investigations and rigorously designed experimental studies in this field [31]. This study addressed limitations of a previous study by conducting a comprehensive comparison of DAS/VR, DAS/BF, and HC/VR groups. Through this comparison, this study not only contrasted them with conventional BF, but also examined differences between the DAS/VR group and the HC/VR group. This study suggests that VR-based BF has potential to enhance sleep quality, demonstrating comparable effectiveness to conventional BF. These findings indicate a compelling opportunity to implement this innovative technology into BF therapy for patients.

This study has a number of limitations. First, this study was performed in a single center only, which could limit its generalizability. A future study should be conducted for different locations to avoid geographical constraint. Second, maintenance effects were not evaluated. It has been shown that insomnia can be worsened by depression [32]. In addition, co-occurrence of insomnia symptoms in those who also have mental illnesses could seriously

hinder results from being improved [33]. The poor quality of sleep does not appear immediately. It may occur after a period of time. Thus, patients with depression need to progress a cautious monitor. Depression is treated through medication and psychotherapy. While these interventions can be effective in alleviating depressive symptoms, such symptoms often remain inadequately addressed [34]. Insomnia is a common comorbid symptom. The use of hypnotic medications to manage sleep disturbances has been associated with a significantly elevated risk of mortality from various causes [35]. There is a need for alternative approaches to address sleep disorders in depressive patients. This study could not find difference between existence and nonexistence of the intervention due to limitation of the study design. In this study, we did not explore the optimal duration or intensity of VR-based BF to achieve the maximum potential benefits. Different treatment durations or frequencies of sessions may yield different results. We used self-report only for the outcome measure. The reliance of self-report inventories might have introduced reporting bias. Subsequent research should incorporate objective measures of sleep quality such as actigraphy or polysomnography to mitigate this potential bias.

Depression is treated through medication and psychotherapy. While these interventions can be effective in alleviating depressive symptoms, symptoms often remain inadequately addressed [34]. Sleep-promoting agents, especially in older adults, may result in adverse effects such as drowsiness, concentration difficulties, headaches, nausea, dry mouth, oversleeping, nightmares, and memory impairment including short-term memory deficits and occasional amnesia that can significantly impact quality of life [36-39]. There is a need for alternative approaches to address sleep disorders in depressive patients. Several studies have explored innovative interventions to tackle this issue, such as using cognitive behavioral therapy of insomnia (CBT-I) [40] and timed bright light treatment [41]. Previous studies have

shown the promising effectiveness of those interventions in improving insomnia symptoms. However, it is crucial to continue exploring complementary approaches to maximize treatment options available for this population.

Regrettably, a limited number of studies have investigated effects of HRV-BF in the context of adults presenting comorbid depressive symptoms and insomnia [42], although around a third of depressive patients experience insomnia symptoms and about 40% of young patients and 10% of older patients experience hypersomnia [34]. Our study contributes to efforts by exploring the potential of VR-based BF as an alternative for treating insomnia symptoms in patients with depression. VR-based BF could offer a safe and effective means of addressing sleep disturbances without causing apparent serious side effects. The flexibility of VR-based BF in delivering therapeutic content and monitoring progress adds on a valuable adjunct to conventional BF approaches. VR-based Biofeedback (BF) offers a distinct advantage of not necessitating the physical presence of highly trained medical professionals alongside the patient, thereby facilitating therapy delivery through guided VR sessions. This characteristic renders it a versatile modality applicable across diverse healthcare institutions, presenting an approach with heightened accessibility relative to alternative therapeutic methodologies. Moreover, it has the capacity for patients to engage in repetitive therapeutic sessions at a location of their choosing under the guidance of a physician's prescription.

This study adds to the existing body of research by examining the potential of VR-based BF as an alternative therapeutic approach for addressing insomnia symptoms in individuals concurrently experiencing depression and anxiety. VR-based BF offers a safe and effective means to improve sleep quality with minimal apparent side effects. Its flexibility in delivering therapeutic content and monitoring progress enhances its value as an adjunct to conventional

BF approaches. Moreover, the utilization of VR technology in this context aligns with the growing trend in the medical field, positioning VR-based BF as a promising medical technology and treatment modality in the future.

Acknowledgments

This research was supported by the Bio & Medical Technology Development Program of the NRF funded by the Korean government, MSIP (No. NRF-2017M3A9F1027323; PI HJJ), by the Bio & Medical Technology Development Program of the National Research Foundation (NRF) funded by the Ministry of Science & ICT (No. 2021M3A9E4080784), and by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (HR21C0885).

Conflicts of Interest

This was not an industry supported study. The authors have indicated no financial conflicts of interest.

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Supplementary Files

Figures

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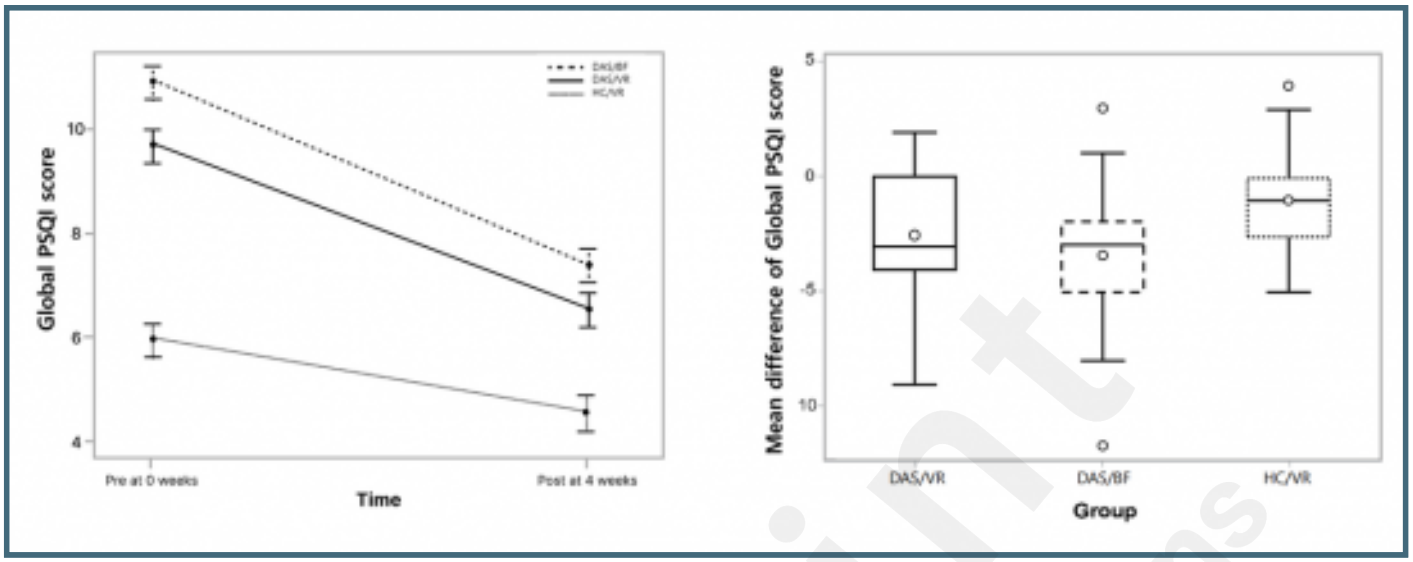

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