Novel VR-based Biofeedback systems: a comparison between heart rate variability- and electrodermal activity-driven approaches

Andrea Baldini, Elisabetta Patron, Claudio Gentili, Enzo Pasquale Scilingo, *Senior Member, IEEE*, Alberto Greco, *Senior Member, IEEE*

Abstract—Anxiety symptoms are important contributors to the global health-related burden. Low-intensity interventions have been proposed to reduce anxiety symptoms in the population. Among these, biofeedback (BF) offers an effective approach to reducing anxiety. In the present study, BF was integrated into a novel virtual reality (VR) architecture to enhance BF's effectiveness to i) evaluate the feasibility of a VR-based single-session BF in teaching participants to self-regulate; ii) compare the BF aiming at reducing sympathetic (measured though the tonic level of skin conductance, SCL) versus increasing cardiac vagal (i.e., normalized high frequency of heart rate variability, HFnu-HRV) activation, and iii) evaluate which of the two VR-BF single-sessions was most effective in reducing perceived state anxiety.

20 healthy participants underwent both SCL- and HFnu-based in a single session VR-BF. Results showed the feasibility of a short single-session VR-BF and the effectiveness of both VR-BF sessions in reducing perceived state anxiety. Moreover, SCL-based VR-BF determined a significant reduction in sympathetic activation and in sympathovagal balance as well as a greater reduction in perceived state anxiety compared to HFnu-based VR-BF. SCL-based VR-BF represents a safe and effective intervention in reducing anxiety while enhancing adaptive psychophysiological activation.

Index Terms—Biofeedback, Virtual Reality, Skin Conductance, Heart rate variability

✦

1 INTRODUCTION

In the general population, anxiety disorders are considered the most common mental disorders [1] and are among the leading causes of the global health-related burden [2]. Despite the fact that subclinical anxiety is often non-treated, anxiety symptoms that do not reach the diagnostic criteria have been linked to a higher risk to develop an anxiety disorder such as generalized anxiety disorder or panic disorder [3]. Moreover, during the COVID-19 pandemic, there has been an exacerbation of poor mental health conditions, including increased clinical and subclinical anxiety [4].

Given the large prevalence of anxiety, its impact on the population, and the fact that it is largely left untreated, there is an urgent need for high and low-intensity interventions to reduce anxiety. It's essential to address both the psychological and physiological aspects of this condition [5]. At physiological level, both clinical and subclinical anxiety, as well other mental health problems, have been often associated with alterations in the autonomic nervous system (ANS) balance, which manifest as elevated sympathetic activation and reduced parasympathetic activity. Low-intensity interventions have been found to be effective in reducing anxiety and its physiological manifestations [6]. They include computerized cognitive behavioral therapies, virtual reality (VR) exposure, behavioral activation, psychoeducation groups, and relaxation training. Among these, biofeedback (BF) is a non-invasive and non-pharmacologic biobehavioral technique effective in improving the ANS balance, through a reduction in sympathetic over-reactivity to stress and increased parasympathetic activation, which in turn has been linked with the reduction of symptoms in several medical conditions [7] and also psychiatric disorders [8] among which the most commonly treated are anxiety disorders [9], [10]. BF mechanisms are mostly grounded in operant learning principles (for an insight see [10]). These principles employ positive reinforcement to modify an individual's behavior through the use of rewards (e.g., positive feedback), making the desired behavior more likely to occur. In 1978 Miller's work demonstrated that operant learning principles could be extended to regulate ANS functions, allowing individuals to consciously influence otherwise involuntary bodily processes, like heart rate, skin conductance (SC), or bowel movements through training [11].

In a typical BF paradigm, information is provided by converting one physiological signal, of which the individual is usually not aware (e.g., heart rate or sweat glands activity), into meaningful visual or auditory representations, referred to as the feedback (e.g., a light on the screen that changes color in response to alterations in the physiological signal [10], [12]. When a desired physiological change occurs (e.g., reduced heart rate or lower SC level)

- *A. Baldini, E. P. Scilingo and A. Greco are with the Department of Information Engineering, and Research Center "E. Piaggio", University of Pisa, Italy, 56122.*
  E-mail: alberto.greco@unipi.it
- *E. Patron and C. Gentili are with the Department of General Psychology, University of Padua, Padua, Italy, 35131.*
- *C. Gentili is with Padova Neuroscience Center (PNC), University of Padua, Padua, Italy*

The research leading to these results has received partial funding from the Italian Ministry of Education and Research (MIUR) in the framework of the FoReLab project (Departments of Excellence) and from European Union Horizon 2020 Programme under grant agreement n 824153 of the project "POTION-Promoting Social Interaction through Emotional Body Odours".

the individual is rewarded with positive feedback (e.g., the light that was red turns green). Driven by positive reinforcement mechanisms, individuals learn to voluntarily control and modify the physiological processes underlying potential symptomatology of pathological conditions. For example, it has been shown that patients with generalized anxiety disorder were able to learn to reduce sympathetic ANS hyperactivation through BF, leading to reduced anxiety symptoms [13]. In addition, a meta-analysis demonstrated the effectiveness of BF in improving heart rate variability (HRV), thereby enhancing parasympathetic ANS activity and reducing anxiety symptoms [9]. Recent literature reviews support the common applications of BF to reduce stress and anxiety in clinical and nonclinical populations by improving control over bodily functions regulated by the ANS. Two prominent approaches include BF to regulate SC [14] and HRV [10], [15]. Regarding the first, since secretory channels of eccrine sweat glands are specifically innervated by sudomotor sympathetic nerves, measures derived from SC (also called electrodermal activity) reflects the activity of the sympathetic nervous branch innervating sweat glands in the deep layers of the skin [16]. BF of SC targets the reduction of sympathetic hyperactivity by providing feedback to reduce SC and has been applied effectively in clinical samples [17], [18] to reduce physiological arousal driven by the sympathetic nervous system and to reduce anxiety [19]. Regarding cardiac BF, HRV can be analyzed to extract reliable measures of the parasympathetic activity on the heart (i.e., cardiac vagal activity). HRV-derived cardiac vagal activity can be quantified through the application of spectral analysis of the beat-to-beat intervals obtaining the power in the high-frequency band (HF; [20]). BF of HF targets the increase in cardiac vagal activity by providing feedback to increase HF.

Several studies have empirically demonstrated the effectiveness of HRV BF in reducing ANS dysregulation in psychiatric samples and individuals with anxiety disorders [9]. It is important to note that the most common HRV BF protocols involve slow-paced breathing exercises guided by feedback, utilizing two physiological processes: synchronous variations in heart rate and respiration. While this protocol is highly effective in increasing HRV, but its effects largely rely on voluntary control of respiration. This factor could introduce confounding variables when comparing the effectiveness of different BF protocols, as most BF interventions target involuntary functions (e.g., SC BF). Therefore, in the present study, we introduced a short single-session HRV BF approach in which participants received feedback based on their level of cardiac vagal activity, independent of respiration.

Despite the clear potential of BF applications, some factors can impact the learning process and outcomes. For example, it has been reported that visual feedback is often too abstract or lacks meaningful engagement for the user, potentially leading to boredom [14], [21], [22]. This lack of engaging feedback can affect the participant's attention and motivation, as low levels of engagement have been shown to hinder self-regulation learning in game-based systems [23]. Therefore, for participants to effectively learn self-regulation, they need to maintain sustained focus on the feedback. However, uninteresting feedback, disruptive thoughts, and environmental distractions can hinder this focus.

Recently, the great commercial diffusion of advanced hardware systems has introduced virtual reality (VR) as an innovative interface for BF applications [24], [25], [26]. Integrating BF into a VR environment offers a promising solution. VR is an advanced human-computer interface that immerses individuals in a simulated environment, providing a highly engaging and interactive experience [27]. Using VR in these treatments can enhance the sense of presence and engagement, which are crucial for effective BF interventions [28]. The immersive nature of VR technology, facilitated by head-mounted displays that cover the users' full field of view [29], can enhance sustained attention. Previous studies have also suggested that immersive and interactive virtual environments depicting natural settings, such as beaches and mountain scenery, can be effective in promoting relaxation and reducing stress levels [30], [31]. BF of physiological parameters like the skin conductance level (SCL) has been implemented in serious games to enhance human-computer interaction [32], mitigate eating disorder symptoms [19], and alleviate anxiety-related symptoms [33]. Similarly, heart HRV BF has been tested to reduce pain, stress, or anxiety [34] While both VR exposure training and BF training have shown effectiveness in reducing anxiety symptoms, to the best of our knowledge, no study has investigated the feasibility and effects of combined VR technology and BF training on anxiety symptoms. Furthermore, there is a lack of research comparing the effects of BF aimed at reducing sympathetic activity (targeting SCL) with BF designed to increase parasympathetic activity (targeting HRV) in reducing anxiety symptoms.

For these reasons, in the present study, an innovative VR-BF control algorithm was applied to SC- and HRV-derived measures to improve participants' autonomic balance by either reducing sympathetic activity or improving parasympathetic activity with the ultimate scope of reducing anxiety symptoms.

The objectives of the study were i) to evaluate the feasibility of a VR-based BF single-session in teaching healthy participants to modulate their level of autonomic activation; ii) to compare the VR-BF sessions aiming at reducing sympathetic (as measured by SC derived indexes) versus increasing cardiac vagal (as measured by HRV indexes) activation, and iii) to evaluate which of the two VR-BF single-sessions (i.e., SC-based or HRV-based) was most effective in reducing perceived state anxiety.

2 MATERIALS & METHODS

2.1 Participants

20 healthy volunteers (9 female) with a mean (standard deviation (SD)) age of 27.44 (4.28) range (19-57 years) were included in the study. Subjects suffering from acrophobia (i.e., phobia of height) and who experienced cybersickness during the experiment were excluded.

The present study was conducted in accordance with the Declaration of Helsinki, and all procedures were performed with an adequate understanding and written consent of the participants. The experiments were conducted at the

University of Pisa under the approval of the local ethics committee (prot. No. 14/2019).

2.2 Procedure

After enrollment and sensor placement, each participant underwent both VR-BF sessions (i.e., SC-based VR-BF, HRV-based VR-BF). The order of the VR-BF sessions was randomized across the participants to avoid an order effect in the experimental design. Each VR-BF session lasted 5 minutes, and a recovery period of 10 minutes was set up between them. Participants were requested to fill out the State and Trait Anxiety Inventory Y1 (STAI-Y1; [35]) to evaluate their level of state anxiety four times, that is immediately before and after each VR-BF session. The STAI-Y1 form is a 20-item questionnaire measuring state or current anxiety. Scores range from 20 to 80, and higher scores reflect greater anxiety levels. Before starting each VR sessions, physiological signals (i.e., SC and HRV) were recorded at rest for 30 seconds 1.

During each VR-BF session, participants were seated within the virtual hot air balloon (VHAB) and could observe the VHAB's ascent and descent in real-time. When participants were able to effectively reduce their level of activation, they noticed the VHAB rising higher, while when they were unable to reduce the level of activation, thus arousal increased, this led to a descent in the VHAB within the virtual environment. This direct correlation between the level of physiological activation and the height and direction of movement of the VHAB acted as a visual cue. Modification of VHAB movements in response to participants' physiological changes created a dynamic and immersive experience that encouraged participants to modulate autonomic responses. A video demonstration is available in the supplementary materials of this article.

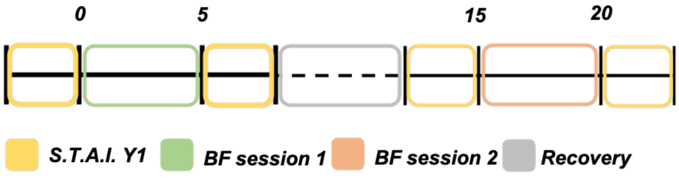

Figure 1. The scheme represents the experimental protocol: the study staretd with the assessment of state anxiety level (the participants filled the STAI-Y1 questionnaire) which was repeated four times, before and after each biofeedback (BF) session. The two 5-min BF sessions (that is, SC-based and HRV-based VR-BF) were separated by a 10-minute interval. The order of the BF sessions (that is, VR-BF based on SC and HRV) was counterbalanced between the participants..

2.3 Virtual reality biofeedback systems

In this section, we describe the main components of both VR-BF systems, i.e., i) the virtual environment design, ii) the physiological signal processing to extract sympathetic and parasympathetic correlates, and iii) the mapping algorithm for converting the physiological signal into feedback.

2.3.1 Virtual environment design

A VR environment was designed to provide a meaningful and intuitive representation of the ANS-related physiological changes to improve the subject's control over it and consequently foster relaxation.

In this context, the intuitiveness of the feedback virtual representation is a crucial developing aspect. Indeed, an unintuitive representation of the ANS-correlate (i.e., SC or HRV) parameter makes the VR-BF session a multi-tasking exercise that could force subjects to divide the efforts among different tasks turn would decrease the BF effectiveness [36]. In this study, participants were "virtually" placed in a virtual hot air balloon (Figure 2), whose height was directly related to the physiological parameter value. Such VR representation required the participants to focus only on the VHAB height. In addition, the design of the VR scenario was optimized to facilitate participants' understanding of the biofeedback practice of relaxation. According to the Stress Recovery Theory [37], which suggests that time spent in a natural environment can promote stress reduction, VHAB was placed in an immersive naturalistic virtual environment designed to maximize its realism. Specifically, the VR scenario included 3D geometries of grasses, plants, flowers, and moving clouds. In addition, the light and color schemes were set to evoke a pleasant and calming environment. Finally, to avoid distraction of the participants from the learning task, no task-relevant stimuli were included [38]. The design of each virtual element was developed using the well-known Unity3D platform (Unity3D 2019.4.8f1, Unity Technologies, USA) applying geometrical models from open-source repositories to take advantage of design flexibility and facilitate the integration with the Oculus Rift S.

The VR contents were displayed exploiting the Oculus Rift S (Lenovo Technologies and Facebook Technologies, USA). Such a headset is a commercially available device with a 2560x1440 LCD and a refresh rate of up to 80 Hz. A PC was used to support this head-mounted display in rendering and updating the VR environment.

Figure 2. The virtual hot air balloon whose flight was used to map the subject's physiological processes of interest.

2.3.2 Physiological measures

Online Skin Conductance (SC) processing: Skin conductance was acquired through the Shimmer 3 GSR+ unit (Shimmer, MA, USA), with a sampling rate of 100 Hz. Electrodes were placed on the palmar surface of the first phalanges of the index and middle fingers of the non-dominant hand. Before starting the recording, signal quality was checked by stimulating electrodermal responses (e.g., by clapping or asking participants to take a few deep breaths). Every recording started at least 15 min after the sensor placement.

A *pseudo-real-time* processing was performed to estimate the

SC-derived physiological parameter for the VR-BF session. First, the slow-varying component of the SC, i.e, SCL, was estimated by applying a 4th-order low-pass filter with a cut-off frequency of 0.05 Hz [39]. Then, to evaluate the SCL variations over time, the derivative of the SCL signal was estimated and its mean value was computed within consecutive time windows of 1 second (SCLd) [$SCLd = \frac{1}{\Delta T}\sum_{i=1}^{N}\frac{dSCL_i}{dt}$ where ΔT is a 1 sec time window and N the number of samples in the time window]. SCLd was adopted as the feedback during the SC-based VR-BF session with a time sampling of 1 sec. Note that SCLd can be considered an effective correlate of the arousal state variation [16].

Online photoplethysmography (PPG) processing : The PPG signal was acquired through the Shimmer 3 GSR+ unit (Shimmer, MA, USA) with a sampling rate of 100 Hz. The PPG optical probe was positioned on the ring finger in the distal position.

Similarly to the approach applied to the SC a *pseudo-real-time* processing with a sampling time of 1 sec was performed to estimate the PPG-derived physiological parameter for the VR-BF session. More specifically, interbeat Intervals (IBIs) were derived by detecting the peak of each pulse and calculating the pulse intervals (i.e., the distances between pulse wave foot points). First, the PPG signal was band-pass filtered (0.05 - 4 Hz) on an online sliding window of 30 sec with a time step of 1 sec to remove high-frequency noise. Then, an online peak detection was applied by comparing neighbouring samples to identify all local maxima. Spurious peaks were discarded by imposing an adaptive amplitude threshold and a minimum distance between consecutive peaks [25]. HRV signals were then obtained by an online cubic-spline interpolation of the IBIs series at 4 Hz. Finally, the power spectrum was estimated from the HRV series through the autoregressive model method (16th order) to avoid poor spectral resolution. Power in the low-frequency (LF; 0.04-0.15 Hz), and high-frequency (HF; 0.15-0.40 Hz) bands were extracted. In this way, it was possible to have a pseudo-real-time measurement of normalized HF power (HFnu) obtained through the ratio between HF and the sum between HF and LF [i.e., $HFnu = HF/(HF + LF)$]. According to studies on animal models [40] and pharmacological studies in humans [41] HFnu of HRV power is a reliable index of modulation of the ANS parasympathetic branch mediated by the vagus nerve over the cardiac muscle [40], [41], [42], [43], [44], [45], [46], [47]. Higher HRV HF power reflect higher parasympathetic activation that has been linked with better cardiovascular health [43], [48]. [42], [44], [45], [47]. HFnu has been reported to correlate with the level of perceived relaxation [49], [50], and is inversely associated with perceived stress, arousal and anxiety [51], [52]. Therefore, HFnu was adopted as the physiological parameter linked to the feedback in the HRV-based VR-BF session [53].

Off-line post-processing: In the off-line post-processing phase, for each BF session, we calculated a validated index of sympathetic activity [54], i.e., the spectral power in the range of 0.045-0.25 Hz in the SC signal (EDAsymp). In addition, we calculated a validated multimodal index estimating the sympathovagal balance, combining SC sympathetic activity and cardiac vagal control, as the ratio between EDAsymp and HFnu [55].

2.3.3 *Adaptive update of the virtual environment*

The VR environment was appropriately coded to support TCP-IP communication (see supplementary material file) and constantly and fastly adapt the VHAB height as a function of the physiological signal according to two ad-hoc mapping algorithms integrating SCLd and HFnu. The VHAB translations across the time steps were smoothed to limit motion sickness and unrealistic movements (Unity Vector3.Lerp function). The mapping strategy, which allowed describing the VHAB height as a function of the physiological signal (i.e., SCLd and HF), was different depending on the physiological signal:

- for the HRV-based VR-BF, VHAB height was expressed as a linear function of HFnu [53], [56] The following mathematical formula was used to represent the cardiac dynamics in the VR environment:

  $$Height(i) = mHeight \cdot HFnu(i) \tag{1}$$

  Where $Height(i)$ represents the height of the VHAB at the i^{th} time step, $mHeight$ is the maximum height the subjects could reach (set at 30 meters), and $HFnu(i)$ describes the estimate of HFnu at thei^{th} time step.
- for the SC-based VR-BF, since SCLd was not a normalized measure (from 0 to 1) as HFnu, linear mapping of the VHAB height was not feasible. Accordingly, a novel mapping function based on the normalized speed of SCL variation (expressed in radians $SCLd_{rad}(i)$) was developed. Specifically, the following function was applied to estimate the VHAB height over time (which could vary from $0m$ to $30m$ as for HRV-based BF):

  $$Height(i) = -\beta \cdot SCLd_{rad}(i) \tag{2}$$

  Where $Height(i)$ represents the VHAB height at the i^{th} time step, $SCLd_{rad}(i)$ represents the SCLd measured at the i^{th} time step expressed in radians, and β is an empirically estimated constant so that $mHeight$ (i.e., 30m) could be reached in case of constant SCLd maximum speed of decrease equals to -80 degrees (MaxVelocity) for 2 minutes $\beta = \frac{mHeight[m]}{(MaxVelocity[rad/s]\cdot 120[s])} = 0.003125m$. In case the $Height(i) > mHeight$ $Height(i) = mHeight$.

2.4 Learning measure

To devise a quantitative measure of the participant's ability to learn the control the modification in physiological activation, the VHAB height time series was analyzed during the different VR-BF sessions (i.e., SCLd- and HFnu-driven). Four different parameters for each subject were computed:

- the height over time experienced by the subject during the SC-based VR-BF session according to the eq. 2 ($Height_{SC-SCLd}$);
- the height over time experienced by the subject during the HFV-based VR-BF session according to the eq. 1 ($Height_{HRV-HFnu}$);

- the height over time estimated in post-processing by considering the HFnu signal collected during the SC-based VR-BF session and applying the eq. 1 ($Height_{SC-HFnu}$);
- the height over time estimated in post-processing by considering the SCLd collected during HRV-based VR-BF session and applying the eq. 2 ($Height_{HRV-SCLd}$);

From each extracted time series, we fitted a linear model explaining the height values as a function of the time:

$$Height(t) = \lambda + \gamma \cdot t \tag{3}$$

Where $Height(t)$ represents VHAB height over time (t), λ is the model intercept and γ defines the model slope.

The height of the VHAB reflects the physiological signal modification, and the slopes of the models (i.e. the coefficient of the time, $\gamma_{SC-SCLd}$, $\gamma_{SC-HFnu}$, $\gamma_{HRV-HFnu}$, $\gamma_{HRV-SCLd}$) reflects the average speed at which the VHAB moves over time, while the sign indicates the direction. Therefore, the models' slope can be considered as a measure of the speed (i.e, ability) in learning the modulation of physiological arousal/relaxation. The higher the average speed the participant flew during the session, the faster the participant learned to control the physiological mechanism (for a graphical example see Figure 3).

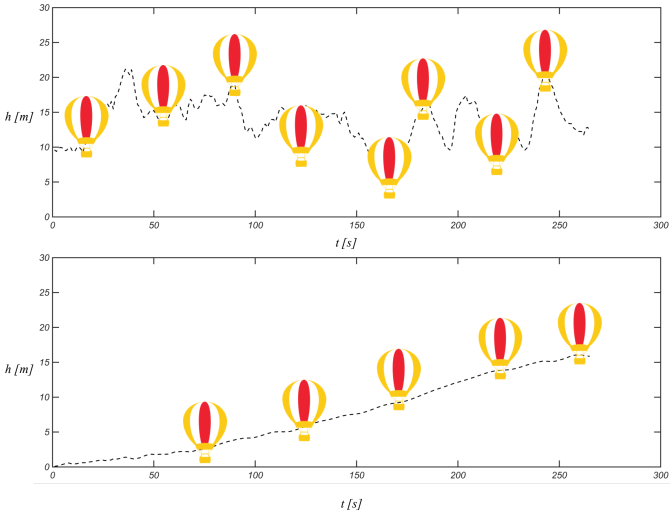

Figure 3. A comparison between the two mapping algorithms. Top: VHAB height over time during the HFnu-driven session. Bottom: VHAB height over time during the SCLd-driven session.

2.5 Statistical analysis

To compare the SC-based and HRV-based VR-BF effectiveness in inducing relaxation, we considered three aspects:

i) the effectiveness of the two VR-BF sessions in reducing the physiological arousal by modulation of the sympathovagal dynamics (i.e., EDAsymp, HFnu and EDAsymp/HFnu);
ii) the effectiveness of the VR-BF sessions on the perceived level of anxiety (i.e., STAI-Y1 scores);
iii) the participant's ease in learning the two different control mechanisms.

To this aim, we performed three different corresponding statistical comparisons, as it follows:
i) To study changes in the physiological arousal during both SC-based and HRV-based BF, three specific features able to quantify the ANS dynamics and more specifically the parasympathetic and sympathetic nervous system dynamics, i.e., EDAsymp, HFnu, and EDAsymp/HFnu were analized. A time series has been built for each feature by computing it in consecutive time windows of 30 sec with an overlap of 29 sec. Afterwards, the dynamics of each feature time series was characterized by computing the corresponding area under the curves (AUC). For each AUC, statistical differences between the resting baseline (30 sec before the first movement of the VHAB) and VR-BF sessions was tested through a non-parametric Wilcoxon sign-rank tests under different null hypotheses:

- during SC-based VR-BF, compared to baseline, a reduction in EDAsymp and EDAsymp/HFnu;
- during HRV-based VR-BF, compared to the baseline, an increased in HF and reduction in EDAsymp/HFnu.

To test which VR-BF was more effective in inducing a reduction in physiological activation (i.e., lower sympathetic, higher parasympathetic and lower sympathovagal balance) statistical differences between the two VR-BF sessions were compared through a two-tail non-parametric Wilcoxon sign-rank tests.
ii) On the STAI-Y1 scores a one-tailed nonparametric Wilcoxon sign-rank test comparing the self-assessed anxiety level collected before (PRE) and after (POST) each VR-BF session, under the null hypothesis of higher anxiety perceived in the PRE VR-BF session than in the POST VR-BF session. Also differences in the effectiveness of the two VR-BF sessions were tested through a mixed-effects model explaining the STAI-Y1 scores at POST conditions ($STAI_{POST_i}$) as a function of the VR-BF session (BF_{param}). The model was controlled for STAI-Y1 scores at PRE condition ($STAI_{PRE_i}$)and a random effect accounting for variability among subjects:

$$\begin{cases} STAI_{POST_i} = \beta_{0i} + \beta_1 \cdot BF_{param} + \beta_2 \cdot STAI_{PRE_i} \\ \beta_{0i} = \beta_{00} + b_{0i}, b_{0i} \sim N(0, \sigma^2) \end{cases} \tag{4}$$

Where i represents an index for the subjects, β_{00} can be interpreted as $STAI_{POST_i}$ grand mean, b_{0i} is a value sampled from a Gaussian distribution with 0 mean and σ^2 variance, while β_1 and β_2 are the coefficients for BF_{param} and $STAI_{PRE_i}$ respectively. Finally, β_{0i} which is obtained by adding β_{00} and b_{0i} describes the subject-varying intercept accounting for the within-subject design of the experimental timeline.
iii) To evaluate differences in the learning ability to modulate physiological arousal, the models' slope (i.e., the γ coefficients) were statistically compared by applying three non-parametric Wilcoxon signed-rank tests:

- $\gamma_{HRV-HFnu}$ Vs. $\gamma_{SC-HFnu}$
- $\gamma_{HRV-SCLd}$ Vs. $\gamma_{SC-SCLd}$
- $\gamma_{HRV-HFnu}$ Vs. $\gamma_{SC-SCLd}$

3 RESULTS

3.1 Physiological measures response

Wilcoxon sign-rank test comparing the AUC of the physiological time series compared to the baseline revealed that SC-based VR-BF was effective in reducing EDAsymp (p = 0.041) and reducing EDAsymp/HF (p = 0.048) while no significant modification emerged in HF (p = 0.093). During HRV-based VR-BF no significant modification in HF emerged (p = 0.406) while a significant reduction in EDAsymp (p = 0.002) and EDAsymp/HF (p = 0.002) emerged.

Moreover, the comparison between the two VR-BF (i.e., SC- and HRV-based) showed lower values of EDAsymp/HF during the SC-based session than in the HRV-based one (p = 0.04). Concerning the AUC of the other physiological features, the statistical analysis did not show significant differences.

3.2 Perceived state anxiety

The Wilcoxon signed-rank test on the psychometric assessment of anxiety levels (STAI-Y1) collected before (median = 36, mad = 6) and after (median = 32.5, mad = 4.5) the SC-based BF session revealed a significant decrease (p = 0.001). A statistically significant decrease (p = 0.036) was found also between the STAI-Y1 scores measured before (median = 34, mad = 3) and after (median = 33, mad = 3.5) the HRV-based session. Summary statistics and results of this analysis are shown in Figure 4.

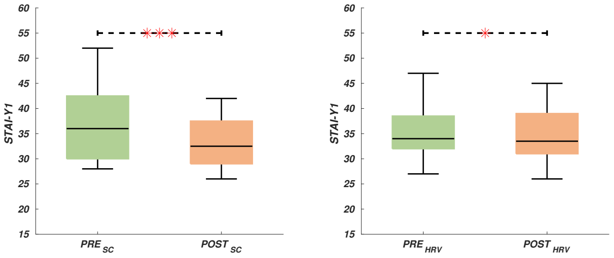

Figure 4. Results of the Wilcoxon sign-rank test on the psychometric scores collected before and after each BF session. Statistically, significant comparisons are marked with "*". On the left side: comparison between the STAI-Y1 scores collected before and after the SC-based BF session; On the right side: comparison between the STAI-Y1 scores collected before and after the HRV-based BF session.

3.2.1 *Learning ability*

Statistical results on the learning ability revealed significant differences between the two VR-BF sessions. During the SC-based VR-BF session compared to the HRV-based one, participants showed a better ability to increase the VHAB height. This was assessed by the comparison between the two slope coefficients, i.e., $\gamma_{SC-SCLd}$ and $\gamma_{HRV-HFnu}$; p = 0.0028; see Figure 5.a). As expected, the comparisons between $\gamma_{SC-SCLd}$ and $\gamma_{HRV-SCLd}$ showed a greater coefficient of the SC-based VR-BF,i.e., $\gamma_{SC-SCLd}$ (p = 0.0192; see Figure 5.b) meaning that participants were able to reach higher heights and a faster increase in SC during the SC-based compared to the HRV-based VR-BF session occurred. In addition, the comparison between $\gamma_{SC-HFnu}$ and $\gamma_{HRV-HFnu}$ (p = 0.074; see Figure 5.c) did not show a significant difference, although, on average, the participants were able to reach a faster increase in HF during the SC-based VR-BF session than during the HRV-based one.

4 DISCUSSION

In the present study, a novel virtual reality architecture was implemented to embed and compare a short single biofeedback session based on two different autonomic parameters to improve participants' autonomic balance by either reducing sympathetic or improving cardiac vagal activity, with the ultimate scope of reducing state anxiety symptoms. The objectives of the study were first to evaluate the feasibility of a VR-based BF session in teaching healthy participants to modulate their level of autonomic activation; second to compare the VR-BF sessions aiming at reducing sympathetic (i.e., SCLd) and increasing cardiac vagal (i.e., HFnu) activation and finally compare the two VR-BF sessions in reducing perceived state anxiety (i.e., STAI-Y1 scores).

Regarding the first objective, results showed that during the SC-based VR-BF session participants were able to modulate the targeted physiological activation. Specifically, participants significantly reduced sympathetic activation as well as sympathovagal balance compared to baseline. Therefore, during a short SC-based VR-BF a specific response of reduced sympathetic activation was achieved. During the HRV-based VR-BF session, participants were unable to modify the targeted physiological parameter compared to baseline (i.e., no significant increase in cardiac vagal control emerged). Nonetheless, during HRV-based VR-BF a pattern of physiological modification similar to the one displayed during SC-based VR-BF emerged. Specifically, a significant reduction in sympathetic activation as well as lower sympathovagal balance emerged. It could be speculated that during HRV-based VR-BF participants were able to reach a general relaxation state characterized by reduced sympathetic activation, but in the short single session, they were unable to specifically modify parasympathetic activity on the heart.

Regarding the second objective, the comparison between the two VR-BFs showed no differences in sympathetic and cardiac vagal activity, while a greater reduction in the sympathovagal balance index (i.e., EDAsymp/HF) during SC-based compared to HRV-based VR-BF emerged. The present results showed that a short single-session SC-based VR-BF was effective in leading to a specific modulation in the physiological system selected, that is sympathetic activation, which in turn was also reflected in a lower sympathovagal balance. This is of relevance considering that an imbalance in the autonomic nervous system activity characterized by a sympathetic dominance driven by cholinergic neurotransmission has been suggested to be a hallmark of both medical and psychological conditions, such as fibromyalgia, cardiovascular diseases, chronic pain, anxiety disorders, and major depression [57], [58], [59], [60], [61], [62]. Training based on the SC-based VR-BF used in the present study could help reduce sympathetic activation and therefore improve the balance between sympathetic and parasympathetic activity with positive effects on risk

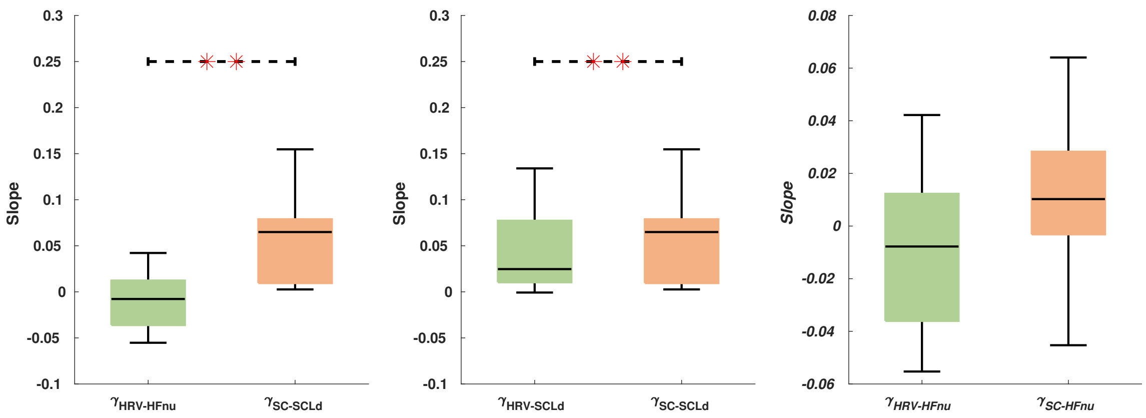

Figure 5. Results of the Wilcoxon sign-rank test on the slopes (γ) of the linear model fitted on positions over time. Statistically, significant comparisons are marked with "*". On the left side: comparison between $\gamma_{SC-HFnu}$ and $\gamma_{HRV-HFnu}$; in the middle: comparison between $\gamma_{HRV-SCLd}$ and $\gamma_{SC-SCLd}$; On the right side: comparison between $\gamma_{SC-SCLd}$ and $\gamma_{HRV-HFnu}$.

factors for several conditions. Interestingly, a clinical application of SC-based BF has demonstrated that voluntary regulation of peripheral activation can enhance functional connectivity between cortical and subcortical brain regions, specifically the orbitofrontal cortex and amygdala, leading to suppression of seizures in patients with drug resistant epilepsy [63]. Furthermore, an increasing body of literature supports the effectiveness of SC-based BF in modulating the activity of both cortical and subcortical brain regions. Previous studies have shown that this training results in reduced amygdala activation and increased activation in prefrontal areas, including the anterior cingulate cortex and insular cortex [64], [65], [66]. t's worth noting that anxiety disorders have been associated with increased amygdala activity [67] and disruptions in functional connectivity between prefrontal areas and the amygdala [51]. Therefore, it could be speculated that long-term SC-based BF could lead to stable modifications in the activation of specific brain areas and the functional connectivity between cortical and subcortical regions. These modifications could potentially have a positive impact on patients with anxiety and stress disorders.

At a speculative level, we can assume that over time, BF of EDA might bring about stable changes in brain activity, which could potentially result in reduced sympathetic activity and fewer symptoms in patients with anxiety and stress disorders. However, it's essential to note that our study did not directly examine these alterations in brain activity. Further neuroimaging research is required to validate these hypotheses.

Concerning perceived state anxiety, although our study recruited subjects from a healthy population with an initially low anxiety level on average (i.e., median STAI-Y1 score below 38, with only some subjects with moderate level (38-44) [68]), results displayed a significant decrease in anxiety levels from pre- to post-training for both the VR-BF sessions (i.e., SC- and HRV-based). Moreover, after SC-based BF participants reported a greater reduction compared to the HRV-based one in perceived state anxiety, independent of the order of VR-BF sessions. Such a greater reduction in perceived state anxiety could be determined by two factors: first, from a physiological perspective participants showed a greater reduction in sympathetic and sympathovagal balance, which have been linked with higher anxiety levels [69]; second, in the SC-based VR-BF session participants were more effective in learning to control the height of the hot air balloon, and therefore to modulate the feedbacked physiological parameter (i.e., SC). This result is also supported by the fact that the index reflecting the ability to learn to control the feedbacked physiological parameter showed that participants were able to learn to control SC-based feedback faster and more effectively compared to HRV-based VR-BF. This could be determined by the fact that SC-based feedback was devised to prevent the occurrence of abrupt altitude variations (both positive and negative) in the hot air balloon. In this way, participants can better focus and engage in the task, leading to a better-learned control of the physiological parameter, which in turn might have an impact on the levels of anxiety and worry about their performance [70]

Taken together, the present results suggest that both the short single-session of SC-based and HRV-based VR-BF were feasible and effective in reducing perceived state anxiety. Nonetheless, SC-based VR-BF resulted superior to HRV-based VR-BF in improving the sympathovagal balance through a reduction in sympathetic activity that led to a greater reduction in perceived state anxiety.

An important characteristic to be considered in the evaluation of BF applications concerns learning to control the physiological parameter. In fact, it provides information on the effectiveness of biofeedback training within the VR environment. Although the measure of learning ability was influenced by the design of the VR scenario, which was optimized to facilitate the practice of relaxation by participants, it is important to note that our analysis compared learning ability between the two control mechanisms considered. Therefore, our results are not biased by the specific characteristics of the VR scenario, as these characteristics remained consistent between the two biofeedback systems. In this context, our novel control algorithm developed to map the variations in SCLd on the virtual scenario allows facilitating the participant's ability to gain control of the physiological parameter. Moreover, it seems to provide a more substantial effect in reducing physiological arousal (inducing a state of relaxation) as well as perceived anxiety. Most importantly, this effect was obtained in a short single-session training, suggesting that the novel control algorithm could support faster learning that in turn could be crucial to reduce the number of patient-clinician contacts designed for patient training. Indeed, BF protocols usually include 10 to 15 sessions and electroencephalographic BF (also called neurofeedback) could require up to more than 40 sessions which have been linked to increased treatment noncompliance and financial burden on patients, limiting clinical utility [10]. The combination of VR-BF technicalities and interpolated smooth changes of the feedback (i.e., hot air balloon height) provided the subjects with a fluid experience characterized by high rendering resolution and no lags between frames. This is a relevant factor when evaluating VR-based training to induce a reduction in physiological activation and perceived anxiety, in fact, low rendering resolution, lags between frames, and an excessive speed of the virtual movements could induce negative side effects (i.e., cybersickness; [71]). It is important to note that in the present study, no participant reported experiencing cybersickness symptoms during the two VR-BF sessions.

The current findings should be interpreted in light of a number of possible methodological issues. First, this study used a relatively small sample size; therefore, the present findings need to be replicated to better understand the effectiveness of SC-based and HRV-based VR-BF training to allow a more robust generalization of the results. However, it is crucial to emphasize that the primary objective of this study was to introduce and assess the feasibility and effects of these two combined VR-BF systems. Despite the limitation of the sample size, we achieved statistically significant results and demonstrated the expected physiological and psychological responses. These results underscore the potential effectiveness of these combined VR-BF systems and provide a promising starting point for future investigations involving a larger and more diverse participant pool, including individuals with clinically relevant anxiety disorders (e.g., specific phobias such as acrophobia, generalized anxiety disorder or panic disorder). Second, in the present study photoplethysmography instead of the electrocardiogram, which is considered the gold-standard method to measure cardiac activity and HRV, was used. Nonetheless, several studies have reported that the parameters of photoplethysmographic variability are highly correlated with HRV extracted from electrocardiograms [72]. Moreover, the photoplethysmographic sensor is portable and non-invasive, widening the possible applications of BF training in clinical samples as well as in ecological settings. Third, the present study included a short single-session SC-based and HRV-based VR-BF. Usually, BF training includes multiple sessions (range 5 to 15) and the duration of each session is between 20 and 45 minutes. The present study had the objective to evaluate the feasibility of a short single-session VR-BF and also the effectiveness in learning to modulate sympathetic (i.e., SCLd) and cardiac vagal (i.e., HFnu) activity. Despite the short duration, the present results showed that a sample of healthy participants was able to learn to reduce sympathetic activation parameters (i.e., SC) and sympathovagal balance in such a short time. Future studies should test the possibility to integrate this VR-BF into a standard BF protocol in patients with anxiety disorders. Another potentially significant clinical application lies in the treatment of specific phobias, such as acrophobia. This approach allows patients to confront their feared stimuli (e.g., heights) while either maintaining or even reducing their physiological arousal. Indeed, VR technology has previously demonstrated its effectiveness in treating height-based fears, specifically acrophobia [73]. However, the potential effects of combining VR technology with BF training in patients with acrophobia is still unexplored. Future works are needed to determine the feasibility and effectiveness of this approach in acrophobia patients.

The current study, to our knowledge, is the first to investigate, the feasibility and compare the effectiveness of short single-session SC-based and HRV-based VR-BF in reducing perceived state anxiety in healthy participants. The findings of the present study, even though based on a small group of participants, provide preliminary evidence on the feasibility of a short single-session VR-BF, in reducing perceived state anxiety. Moreover, it shows how SC-based VR-BF was effective in improving the sympathovagal balance and further reducing state anxiety. Overall, the proposed multithreading system represented a new tool for implementing BF sessions in clinical samples that are capable of taking advantage of many benefits offered by VR without being heavily affected by possible drawbacks of this technology.

5 CONCLUSION

In conclusion, our study introduced and assessed the feasibility and effects of two combined VR-BF systems targeting ANS-related physiological changes. The present results suggest that both the SC-based and HRV-based VR-BF systems were effective in reducing physiological arousal and perceived state anxiety. SC-based VR-BF showed better results in reducing sympathetic activation, leading to enhanced sympatovagal balance. Furthermore, during SC-based VR-BF healthy participants showed a higher ability to learn to control physiological parameters in a short single-session training. In addition, the design of VR environments plays a crucial role in facilitating participants' understanding of the biofeedback practice. Developers should aim to create immersive and intuitive environments that improve the learning process.

Future works will further investigate the long-term effectiveness of such interventions and their applicability to clinical populations, particularly individuals with anxiety-related disorders (e.g., specific phobias such as acrophobia, generalized anxiety disorder, or panic disorder). Furthermore, to promote the widespread adoption of such systems, we have openly shared the source codes to implement these solutions on a public repository (see the supplementary materials).

ACKNOWLEDGMENTS

The research leading to these results has received partial funding from the Italian Ministry of Education and Research

(MIUR) in the framework of the ForeLab project (Departments of Excellence), from European Union Horizon 2020 Programme under grant agreement n 824153 of the project ”POTION-Promoting Social Interaction through Emotional Body Odours”, and from PNRR-M4C2-Investimento 1.3, Partenariato Esteso PE00000013-“FAIR- Future Artificial Intelligence Research”-Spoke 1 “Human-centered AI”, funded by the European Commission under the NextGeneration EU programme. Elisabetta Patron’s work was supported by the University of Padua under the 2021 STARS Grants programme (Acronym and title of the project: Brain-beat - From the brain to the heart and back: an integrated psychophysiological approach to the brain-heart interplay). The authors declare no competing interests.

REFERENCES

[1] R. C. Kessler, W. T. Chiu, O. Demler, and E. E. Walters, “Prevalence, severity, and comorbidity of 12-month dsm-iv disorders in the national comorbidity survey replication,” *Archives of general psychiatry*, vol. 62, no. 6, pp. 617–627, 2005.

[2] G. . M. D. Collaborators *et al.*, “Global, regional, and national burden of 12 mental disorders in 204 countries and territories, 1990–2019: a systematic analysis for the global burden of disease study 2019,” *The Lancet Psychiatry*, vol. 9, no. 2, pp. 137–150, 2022.

[3] R. Hoehn-Saric, R. L. Hazlett, and D. R. McLeod, “Generalized anxiety disorder with early and late onset of anxiety symptoms,” *Comprehensive Psychiatry*, vol. 34, no. 5, pp. 291–298, 1993.

[4] D. F. Santomauro, A. M. M. Herrera, J. Shadid, P. Zheng, C. Ashbaugh, D. M. Pigott, C. Abbafati, C. Adolph, J. O. Amlag, A. Y. Aravkin *et al.*, “Global prevalence and burden of depressive and anxiety disorders in 204 countries and territories in 2020 due to the covid-19 pandemic,” *The Lancet*, vol. 398, no. 10312, pp. 1700–1712, 2021.

[5] S. W. Chan and M. Adams, “Service use, drop-out rate and clinical outcomes: a comparison between high and low intensity treatments in an iapt service,” *Behavioural and cognitive psychotherapy*, vol. 42, no. 6, pp. 747–759, 2014.

[6] J. Palacios, A. Adegoke, R. Wogan, D. Duffy, C. Earley, N. Eilert, A. Enrique, S. Sollesse, J. Chapman, and D. Richards, “Comparison of outcomes across low-intensity psychological interventions for depression and anxiety within a stepped-care setting: A naturalistic cohort study using propensity score modelling,” *British Journal of Psychology*, 2022.

[7] K. Kondo, K. M. Noonan, M. Freeman, C. Ayers, B. J. Morasco, and D. Kansagara, “Efficacy of biofeedback for medical conditions: an evidence map,” *Journal of general internal medicine*, vol. 34, pp. 2883–2893, 2019.

[8] P. L. Schoenberg and A. S. David, “Biofeedback for psychiatric disorders: a systematic review,” *Applied psychophysiology and biofeedback*, vol. 39, pp. 109–135, 2014.

[9] V. C. Goessl, J. E. Curtiss, and S. G. Hofmann, “The effect of heart rate variability biofeedback training on stress and anxiety: a meta-analysis,” *Psychological medicine*, vol. 47, no. 15, pp. 2578–2586, 2017.

[10] M. S. Schwartz and F. Andrasik, *Biofeedback: A practitioner’s guide*. Guilford Publications, 2017.

[11] N. E. Miller, “Biofeedback and visceral learning,” *Annual review of psychology*, vol. 29, no. 1, pp. 373–404, 1978.

[12] J. Weerdmeester, M. M. van Rooij, R. C. Engels, and I. Granic, “An integrative model for the effectiveness of biofeedback interventions for anxiety regulation,” *Journal of medical Internet research*, vol. 22, no. 7, p. e14958, 2020.

[13] A. Biswas, D. Biswas, and P. Chattopadhyay, “Cognitive behaviour therapy in generalised anxiety disorder.” *Indian Journal of Clinical Psychology*, 1995.

[14] B. Yu, M. Funk, J. Hu, Q. Wang, and L. Feijs, “Biofeedback for everyday stress management: A systematic review,” *Frontiers in ICT*, vol. 5, p. 23, 2018.

[15] R. Gevirtz, “The promise of heart rate variability biofeedback: evidence-based applications.” *Biofeedback*, vol. 41, no. 3, 2013.

[16] W. Boucsein, *Electrodermal activity*. Springer Science & Business Media, 2012.

[17] A. Khanna, M. Paul, and J. S. Sandhu, “A study to compare the effectiveness of gsr biofeedback training and progressive muscle relaxation training in reducing blood pressure and respiratory rate among highly stressed individuals.” *Indian J Physiol Pharmacol*, 2007.

[18] H. Ferdowsian and D. Merskin, “Parallels in sources of trauma, pain, distress, and suffering in humans and nonhuman animals,” *Journal of Trauma & Dissociation*, vol. 13, no. 4, pp. 448–468, 2012.

[19] N. Pop-Jordanova, “Psychological characteristics and biofeedback mitigation in preadolescents with eating disorders,” *Pediatrics international*, vol. 42, no. 1, pp. 76–81, 2000.

[20] S. W. Porges, “A phylogenetic journey through the vague and ambiguous xth cranial nerve: A commentary on contemporary heart rate variability research,” *Biological psychology*, vol. 74, no. 2, pp. 301–307, 2007.

[21] J. Blum, C. Rockstroh, and A. S. Göritz, “Heart rate variability biofeedback based on slow-paced breathing with immersive virtual reality nature scenery,” *Frontiers in Psychology*, vol. 10, p. 2172, 2019.

[22] A. Gaume, A. Vialatte, A. Mora-Sánchez, C. Ramdani, and F.-B. Vialatte, “A psychoengineering paradigm for the neurocognitive mechanisms of biofeedback and neurofeedback,” *Neuroscience & Biobehavioral Reviews*, vol. 68, pp. 891–910, 2016.

[23] J. L. Sabourin and J. C. Lester, “Affect and engagement in game-basedlearning environments,” *IEEE transactions on affective computing*, vol. 5, no. 1, pp. 45–56, 2013.

[24] O. D. Kothgassner, A. Goreis, I. Bauda, A. Ziegenaus, L. M. Glenk, and A. Felnhofer, “Virtual reality biofeedback interventions for treating anxiety: A systematic review, meta-analysis and future perspective,” *Wiener klinische Wochenschrift*, pp. 1–11, 2022.

[25] C. Rockstroh, J. Blum, and A. S. Göritz, “Virtual reality in the application of heart rate variability biofeedback,” *International Journal of Human-Computer Studies*, vol. 130, pp. 209–220, 2019.

[26] M. Van Rooij, A. Lobel, O. Harris, N. Smit, and I. Granic, “Deep: A biofeedback virtual reality game for children at-risk for anxiety,” in *Proceedings of the 2016 CHI conference extended abstracts on human factors in computing systems*, 2016, pp. 1989–1997.

[27] J. N. Latta and D. J. Oberg, “A conceptual virtual reality model,” *IEEE Computer Graphics and Applications*, vol. 14, no. 1, pp. 23–29, 1994.

[28] A. Gorini, F. Pallavicini, D. Algeri, C. Repetto, A. Gaggioli, and G. Riva, “Virtual reality in the treatment of generalized anxiety disorders,” *Annual Review of Cybertherapy and Telemedicine 2010*, pp. 39–43, 2010.

[29] M. Slater and S. Wilbur, “A framework for immersive virtual environments (five): Speculations on the role of presence in virtual environments,” *Presence: Teleoperators & Virtual Environments*, vol. 6, no. 6, pp. 603–616, 1997.

[30] M. Annerstedt, P. Jönsson, M. Wallergård, G. Johansson, B. Karlson, P. Grahn, Å. M. Hansen, and P. Währborg, “Inducing physiological stress recovery with sounds of nature in a virtual reality forest—results from a pilot study,” *Physiology & behavior*, vol. 118, pp. 240–250, 2013.

[31] S. Liszio, L. Graf, and M. Masuch, “The relaxing effect of virtual nature: immersive technology provides relief in acute stress situations,” *Annu. Rev. Cyberther. Telemed*, vol. 16, pp. 87–93, 2018.

[32] K. Kuikkaniemi, T. Laitinen, M. Turpeinen, T. Saari, I. Kosunen, and N. Ravaja, “The influence of implicit and explicit biofeedback in first-person shooter games,” in *Proceedings of the SIGCHI conference on human factors in computing systems*, 2010, pp. 859–868.

[33] A. Khanna, M. Paul, and J. S. Sandhu, “Efficacy of two relaxation techniques in reducing pulse rate among highly stressed females,” *Calicut Medical Journal*, vol. 5, no. 2, pp. 23–25, 2007.

[34] R. Lüddecke and A. Felnhofer, “Virtual reality biofeedback in health: a scoping review,” *Applied Psychophysiology and Biofeedback*, vol. 47, no. 1, pp. 1–15, 2022.

[35] C. D. Spielberger, F. Gonzalez-Reigosa, A. Martinez-Urrutia, L. F. Natalicio, and D. S. Natalicio, “The state-trait anxiety inventory,” *Revista Interamericana de Psicologia/Interamerican journal of psychology*, vol. 5, no. 3 & 4, 1971.

[36] C. D. Wickens, J. Goh, J. Helleberg, W. J. Horrey, and D. A. Talleur, “Attentional models of multitask pilot performance using advanced display technology,” in *Human Error in Aviation*. Routledge, 2017, pp. 155–175.

[37] R. S. Ulrich, R. F. Simons, B. D. Losito, E. Fiorito, M. A. Miles, and M. Zelson, “Stress recovery during exposure to natural and urban

environments," *Journal of environmental psychology*, vol. 11, no. 3, pp. 201–230, 1991.

[38] G. Makransky, S. Borre-Gude, and R. E. Mayer, "Motivational and cognitive benefits of training in immersive virtual reality based on multiple assessments," *Journal of Computer Assisted Learning*, vol. 35, no. 6, pp. 691–707, 2019.

[39] D. R. Bach, K. J. Friston, and R. J. Dolan, "An improved algorithm for model-based analysis of evoked skin conductance responses," *Biological psychology*, vol. 94, no. 3, pp. 490–497, 2013.

[40] T. B. Kuo, C. J. Lai, Y.-T. HUANG, and C. C. Yang, "Regression analysis between heart rate variability and baroreflex-related vagus nerve activity in rats," *Journal of cardiovascular electrophysiology*, vol. 16, no. 8, pp. 864–869, 2005.

[41] M. V. Kamath and E. L. Fallen, "Power spectral analysis of heart rate variability: a noninvasive signature of cardiac autonomic function." *Critical reviews in biomedical engineering*, vol. 21, no. 3, pp. 245–311, 1993.

[42] D. L. Eckberg and M. J. Eckberg, "Human sinus node responses to repetitive, ramped carotid baroreceptor stimuli," *American Journal of Physiology-Heart and Circulatory Physiology*, vol. 242, no. 4, pp. H638–H644, 1982.

[43] M. Malik, "Heart rate variability," *Annals of Noninvasive Electrocardiology*, vol. 1, no. 2, pp. 151–181, 1996.

[44] R. E. Kleiger, P. K. Stein, and J. T. Bigger Jr, "Heart rate variability: measurement and clinical utility," *Annals of Noninvasive Electrocardiology*, vol. 10, no. 1, pp. 88–101, 2005.

[45] J. F. Thayer, S. S. Yamamoto, and J. F. Brosschot, "The relationship of autonomic imbalance, heart rate variability and cardiovascular disease risk factors," *International journal of cardiology*, vol. 141, no. 2, pp. 122–131, 2010.

[46] J.-A. Palma and E. E. Benarroch, "Neural control of the heart: recent concepts and clinical correlations," *Neurology*, vol. 83, no. 3, pp. 261–271, 2014.

[47] F. Shaffer and J. P. Ginsberg, "An overview of heart rate variability metrics and norms," *Frontiers in public health*, p. 258, 2017.

[48] V. N. Patel, B. R. Pierce, R. K. Bodapati, D. L. Brown, D. G. Ives, and P. K. Stein, "Association of holter-derived heart rate variability parameters with the development of congestive heart failure in the cardiovascular health study," *JACC: Heart failure*, vol. 5, no. 6, pp. 423–431, 2017.

[49] N. Markil, M. Whitehurst, P. L. Jacobs, and R. F. Zoeller, "Yoga nidra relaxation increases heart rate variability and is unaffected by a prior bout of hatha yoga," *The Journal of Alternative and Complementary Medicine*, vol. 18, no. 10, pp. 953–958, 2012.

[50] K. Bin Waleed, I. Lakhani, M. Gong, T. Liu, L. Roever, K. Christien Li, R. Rajan, M. Qasim Ibrahimi, Y. Xia, G. Tse *et al.*, "Heart rate variability and meditation: a meta-analysis," *Europace*, vol. 24, no. Supplement_1, pp. euac053–053, 2022.

[51] H.-G. Kim, E.-J. Cheon, D.-S. Bai, Y. H. Lee, and B.-H. Koo, "Stress and heart rate variability: a meta-analysis and review of the literature," *Psychiatry investigation*, vol. 15, no. 3, p. 235, 2018.

[52] J. A. Chalmers, D. S. Quintana, M. J.-A. Abbott, and A. H. Kemp, "Anxiety disorders are associated with reduced heart rate variability: a meta-analysis," *Frontiers in psychiatry*, vol. 5, p. 80, 2014.

[53] B. Bornemann, P. Kovacs, and T. Singer, "Voluntary upregulation of heart rate variability through biofeedback is improved by mental contemplative training," *Scientific Reports*, vol. 9, no. 1, p. 7860, 2019.

[54] H. F. Posada-Quintero, J. P. Florian, A. D. Orjuela-Cañón, T. Aljama-Corrales, S. Charleston-Villalobos, and K. H. Chon, "Power spectral density analysis of electrodermal activity for sympathetic function assessment," *Annals of biomedical engineering*, vol. 44, no. 10, pp. 3124–3135, 2016.

[55] S. Ghiasi, A. Greco, R. Barbieri, E. P. Scilingo, and G. Valenza, "Assessing autonomic function from electrodermal activity and heart rate variability during cold-pressor test and emotional challenge," *Scientific reports*, vol. 10, no. 1, pp. 1–13, 2020.

[56] M. Siepmann, V. Aykac, J. Unterdörfer, K. Petrowski, and M. Mueck-Weymann, "A pilot study on the effects of heart rate variability biofeedback in patients with depression and in healthy subjects," *Applied psychophysiology and biofeedback*, vol. 33, pp. 195–201, 2008.

[57] H. Cohen, L. Neumann, A. Alhosshle, M. Kotler, M. Abu-Shakra, and D. Buskila, "Abnormal sympathovagal balance in men with fibromyalgia." *The Journal of rheumatology*, vol. 28, no. 3, pp. 581–589, 2001.

[58] J. Indumathy, G. K. Pal, P. Pal, P. H. Ananthanarayanan, S. C. Parija, J. Balachander, and T. K. Dutta, "Decreased baroreflex sensitivity is linked to sympathovagal imbalance, body fat mass and altered cardiometabolic profile in pre-obesity and obesity," *Metabolism*, vol. 64, no. 12, pp. 1704–1714, 2015.

[59] C. R. Jahan, S. Begum, S. Ferousi, and M. M. Uddin, "Impaired cardiac vagal tone in patients with major depressive disorder," *Journal of Bangladesh Society of Physiologist*, vol. 10, no. 2, pp. 41–45, 2015.

[60] G. K. Pal, P. Pal, N. Nanda, D. Amudharaj, and C. Adithan, "Cardiovascular dysfunctions and sympathovagal imbalance in hypertension and prehypertension: physiological perspectives," *Future cardiology*, vol. 9, no. 1, pp. 53–69, 2013.

[61] A. Steptoe, M. Cropley, and K. Joekes, "Job strain, blood pressure and response to uncontrollable stress," *Journal of hypertension*, vol. 17, no. 2, pp. 193–200, 1999.

[62] L. B. Stone, C. C. McCormack, and L. M. Bylsma, "Cross system autonomic balance and regulation: Associations with depression and anxiety symptoms," *Psychophysiology*, vol. 57, no. 10, p. e13636, 2020.

[63] Y. Nagai, J. Aram, M. Koepp, L. Lemieux, M. Mula, H. Critchley, S. Sisodiya, and M. Cercignani, "Epileptic seizures are reduced by autonomic biofeedback therapy through enhancement of fronto-limbic connectivity: a controlled trial and neuroimaging study," *EBioMedicine*, vol. 27, pp. 112–122, 2018.

[64] H. Critchley, R. Melmed, E. Featherstone, C. Mathias, and R. J. Dolan, "Brain activity during biofeedback relaxation: a functional neuroimaging investigation," *Brain*, vol. 124, no. 5, pp. 1003–1012, 2001.

[65] H. D. Critchley, R. N. Melmed, E. Featherstone, C. J. Mathias, and R. J. Dolan, "Volitional control of autonomic arousal: a functional magnetic resonance study," *Neuroimage*, vol. 16, no. 4, pp. 909–919, 2002.

[66] Y. Nagai, H. D. Critchley, E. Featherstone, M. R. Trimble, and R. J. Dolan, "Activity in ventromedial prefrontal cortex covaries with sympathetic skin conductance level: a physiological account of a "default mode" of brain function," *Neuroimage*, vol. 22, no. 1, pp. 243–251, 2004.

[67] S. L. Rauch, L. M. Shin, and C. I. Wright, "Neuroimaging studies of amygdala function in anxiety disorders," *Annals of the New York Academy of Sciences*, vol. 985, no. 1, pp. 389–410, 2003.

[68] O. Kayikcioglu, S. Bilgin, G. Seymenoglu, and A. Deveci, "State and trait anxiety scores of patients receiving intravitreal injections," *Biomedicine hub*, vol. 2, no. 2, pp. 1–5, 2017.

[69] G. A. Reyes del Paso and P. de la Coba, "Reduced activity, reactivity and functionality of the sympathetic nervous system in fibromyalgia: An electrodermal study," *PLoS One*, vol. 15, no. 10, p. e0241154, 2020.

[70] D. L. Heinrich and C. D. Spielberger, "Anxiety and complex learning." *Series in Clinical & Community Psychology: Achievement, Stress, & Anxiety*, 1982.

[71] A. Agić, E. Murseli, L. Mandić, and L. Skorin-Kapov, "The impact of different navigation speeds on cybersickness and stress level in vr," *Journal of Graphic Engineering and Design*, vol. 11, no. 1, p. 5, 2020.

[72] S. Lu, H. Zhao, K. Ju, K. Shin, M. Lee, K. Shelley, and K. H. Chon, "Can photoplethysmography variability serve as an alternative approach to obtain heart rate variability information?" *Journal of clinical monitoring and computing*, vol. 22, pp. 23–29, 2008.

[73] C. M. Coelho, A. M. Waters, T. J. Hine, and G. Wallis, "The use of virtual reality in acrophobia research and treatment," *Journal of Anxiety disorders*, vol. 23, no. 5, pp. 563–574, 2009.

Andrea Baldini received the M.S. degree in biomedical engineering from the University of Pisa in 2019. He is currently a Ph.D. student in Smart Industry at the University of Pisa. His current research mainly involves virtual reality design, statistical learning, and physiological signal modeling and processing.

Elisabetta Patron Ph.D., received her PhD degree in Psychological Sciences from the University of Padova in 2014. She is currently an assistant professor at the Department of General Psychology, University of Padova. Her main research interests are psychophysiological mechanisms underlying the interaction between the brain cortex and the heart, and psychophysiological correlates of emotion regulation in clinical and healthy individuals. Applications include biofeedback and neurofeedback in chronic disorders and stress related conditions. She is author of several international scientific contributions in these fields.

Claudio Gentili Ph.D., is Full Professor of Clinical Psychology at University of Padova. He has been involved as local PI of two European Project and National PI of Italian Ministry of University National Grant. He has several teaching activities and he is supervisor of several PhD students. His main research interest are in psychophysiological and neurobiological correlates of mental disorders and psychological and biological mechanism of treatment efficacy in psychology. He is author of more than 200 papers on peer-review journals, contributions to international conferences and chapters in international books. He is also serving as director of the Center for Clinical Services at the University of Padova.

Enzo Pasquale Scilingo (M10), PhD, is a Full Professor in Electronic and Information Bioengineering at the University of Pisa. He has several teaching activities and he is supervisor of several PhD students. He coordinated the European project “PSYCHE”, and he is currently coordinating the H2020 European projects “NEVERMIND” and “POTION”. His main research interests are in wearable monitoring systems, human-computer interfaces, biomedical and biomechanical signal processing, modeling, control and instrumentation. He is author of more than 200 papers on peer-review journals, contributions to international conferences and chapters in international books.

Alberto Greco (M16-SM12), Ph.D., received his PhD degree in Automatics, Robotics and Bioengineering from University of Pisa in 2015. He is currently an assistant professor at Research Center “E. Piaggio”, University of Pisa. His main research interests are physiological modeling, wearable monitoring system, and biomedical signal processing. Applications include affective computing and the assessment of mood and consciousness disorders. He is author of several international scientific contributions, in these fields. He is co-coordinator of the European research project POTION.