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Research paper

Neurofeedback with low-cost, wearable electroencephalography (EEG) reduces symptoms in chronic Post-Traumatic Stress Disorder

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ABSTRACT

Background: The study examines the effectiveness of both neurofeedback and motor-imagery brain-computer interface (BCI) training, which promotes self-regulation of brain activity, using low-cost electroencephalography (EEG)-based wearable neurotechnology outside a clinical setting, as a potential treatment for post-traumatic stress disorder (PTSD) in Rwanda.

Methods: Participants received training/treatment sessions along with a pre- and post- intervention clinical assessment, ($N = 29$; control $n = 9$, neurofeedback (NF, 7 sessions) $n = 10$, and motor-imagery (MI, 6 sessions) $n = 10$). Feedback was presented visually via a videogame. Participants were asked to regulate (NF) or intentionally modulate (MI) brain activity to affect/control the game.

Results: The NF group demonstrated an increase in resting-state alpha 8–12 Hz bandpower following individual training sessions, termed alpha 'rebound' (Pz channel, $p = 0.025$, all channels, $p = 0.024$), consistent with previous research findings. This alpha 'rebound', unobserved in the MI group, produced a clinically relevant reduction in symptom severity in NF group, as revealed in three of seven clinical outcome measures: PCL-5 ($p = 0.005$), PTSD screen ($p = 0.005$), and HTQ ($p = 0.005$).

Limitations: Data collection took place in environments that posed difficulties in controlling environmental factors. Nevertheless, this limitation improves ecological validity, as neurotechnology treatments must be deployable outside controlled environments, to be a feasible technological treatment.

Conclusions: The study produced the first evidence to support a low-cost, neurotechnological solution for neurofeedback as an effective treatment of PTSD for victims of acute trauma in conflict zones in a developing country.

1. Introduction

Dependent on factors relating to individual vulnerabilities, post-traumatic stress disorder (PTSD) develops as a consequence of an emotional and neurobiological response induced by a psychosocial stressor; a traumatic experience characterised as an emotionally overwhelming event involving a threat to the persons physical being, or their personal integrity, i.e., experiencing danger of death, injury, or sexual violation. Prevalence statistics vary depending on time and geographic location. However, it is estimated that approximately one in ten people who experience such a trauma, develop symptoms of PTSD (Breslau et al., 1998; Kessler et al., 1995; Lewis et al., 2019; Menon, 2011; Olff et al., 2005; Resnick et al., 1993). Symptoms fall into four categories – re-experiencing, hyperarousal, cognitive and behavioural avoidance, and emotional numbing, resulting from an impaired ability to regulate processing of threat-related information (Kluetsch et al., 2014). In 1994, hundreds of thousands of Rwandese lost their lives in a genocide perpetrated against the Tutsi that lasted for one hundred days between April and June of that year (Des Forges, 1999; Schaal and Elbert, 2006). A survey by the Ministry of Local Administration, July 2000, stated the official number of victims stood at 1,074,017 (Bazivamo, 2004).

More than two decades on from this horrific event, PTSD prevalence among the Rwandan population of over sixteens was recorded as 26.1%, increasing to 41% when restricted to female survivors (Munyandamutsa

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et al., 2012; Rudahindwa et al., 2018). A recent meta-analysis finds PTSD prevalence of 15% in the general population, while PTSD pooled prevalence for genocide survivors is estimated at 37% (Musanabaganwa et al., 2020). Moreover, a review by Smigelsky et al. (2014) found entire communities in sub-Saharan Africa to be at risk for PTSD due to conflict (Smigelsky et al., 2014). The societal impact of PTSD is extremely heavy. The chronic nature of the disorder puts a strain on health care systems, household income, relationships, and parenting ability (Lambert et al., 2014; Sareen, 2014; Sherman et al., 2016). According to a report on a survey by the World Health Organisation (2011) conducted in 24 countries, two of which were South Africa and Nigeria, PTSD had the third largest impact on productivity due to missed workdays (Alonso et al., 2011; Smigelsky et al., 2014). Children with a parent suffering from PTSD are more likely to display conduct disorders, and poor attachment behaviours (Sherman et al., 2016). A meta-analysis conducted in 2014 found a medium effect size (r =0.35) for the relation between emotional distress in a child, behavioural problems, and parental PTSD (Lambert et al., 2014). Suicidal behaviour is high among PTSD patients compared to patients with other mental health diagnoses (Sareen, 2014). Thus, there is a clear and apparent necessity for research into solutions for PTSD treatment in Africa, that are affordable and easily accessible to people in remote communities.

Functional connectivity within large-scale neural networks in the brain precipitates and constrains cognitive processes. Hence, recent research has taken a network approach to the study of psychopathology, presenting a paradigm shift in the research methodologies employed. The findings that stem from this approach propose psychopathology, in general, arises from deficits in, or damage to, small-world networks (a cluster of nodes in the cortex connected either directly or via a small number of connections between other nodes within the cluster), cortical subsystems, or cortical hubs (information integration centres), leading to dysfunction within the local network and often propagating further to impact large-scale intrinsic networks (Alderson et al., 2018, 2020; Lanius et al., 2015; Menon, 2011). Higher cognitive function has been found to rely on the integrity of three core neurocognitive networks, i.e., having a distinct cognitive function; the default mode network (DMN), central executive network (CEN), and salience network (SN) (Greicius et al., 2003; Menon, 2011; Seeley et al., 2007). The DMN comprises an integrated system of brain areas, most notably (but not exclusively) the posterior cingulate cortex (PCC) and the medial/ventro-medial pre--frontal cortex (M/VMPFC) – involved in self-referential mental processes such as introspective, autobiographical, and social cognition. This large-scale network is necessarily deactivated to allow for the mental processing involved in most stimulus-driven cognitive tasks, which involve activation of the CEN – while the SN mediates the dynamic interactions between the DMN and the CEN through on-going monitoring of the internal and external environments. The central executive system is critically responsible for many higher-order functions such as maintenance and manipulation of information in working memory (WM), problem-solving, decision-making, and goal-directed behaviour – all of which require focused and selective attention. All three networks are referred to as intrinsic connectivity networks (ICN's) as they are part of a group of large-scale networks that connect interdependent brain regions even when the brain is effectively at rest (Lanius et al., 2015; Menon, 2011; Seeley et al., 2007). Dysfunction and /or disorganisation of these three ICN's has been associated with characteristic features of multiple psychiatric and neurological disorders (Menon, 2011). In particular, aberrant functioning within the SN hub located in the frontal insula cortex (FIC) plays an integral role in many psychopathologies through inappropriate tagging of stimuli as salient, leading to abnormal behavioural responses (Abdallah et al., 2019; Allman et al., 2005; Bonnelle et al., 2012; Goulden et al., 2014; Menon, 2011; Seeley et al., 2007). Predictably, PTSD is linked to a heightened stress response causing the sufferer to remain in a constant state of vigilance (Abdallah et al., 2019; Bell et al., 2019; Goulden et al., 2014). Brain connectivity and dynamics can be positively impacted by directed self-regulation or intentional modulation of brain activity which can be facilitated by neurofeedback (Lanius et al., 2015) and potentially, through a brain-computer interface (BCI) (Alimardani et al., 2014).

The term BCI describes a system that translates brain activity to send commands to computer systems for the purpose of control and communication and is often targeted at applications that support people with physical disabilities caused by disease or injury (Coyle et al., 2015; Prasad et al., 2010). Changes in the dynamics of brain rhythms (resulting from event related (de)synchronisation (ERS/ERD) of specific neuronal assemblies and networks (Pfurtscheller et al., 2006, 1997)) and brain potentials such as steady-state evoked potentials (SSEPs), evoked potentials (EPs) and event-related potentials (ERPs), are among the main brain signals used in an EEG-based BCI systems (non-invasive BCIs) (Millán et al., 2010; Pfurtscheller et al., 2010). The current research focuses on the use of BCI-based feedback training to improve alpha function, associated with a more relaxed state and reduced symptom severity (Kluetsch et al., 2014; Nicholson et al., 2016). Users of a BCI system intentionally modulate brain activity through mental tasks or focusing on stimuli to relay intent whilst machine learning is applied to maximise accuracy of detecting the user intent. Often more than one brain signal is employed in BCI. Motor-imagery is the mental execution of a movement without the actual movement of peripheral muscles, e.g., imaging a left/right arm movement (Emami and Chau, 2018; Mulder, 2007). Mental rehearsal of movement in this way, can be classified from an EEG recording of the sensorimotor rhythms (SMRs) which are normally associated with an 8-13 Hz oscillation (mu rhythm), which is associated with motor cortex at rest and beta activity (13-30 Hz) reflecting activated motor cortex. Typically, the lateralised pattern of activity differences due to mu ERD and beta ERS over the motor cortex contralateral to the imagined movement, is used to enable a user to communicate intention e.g., a binary response (Pfurtscheller et al., 2010). Mental-imagery paradigms are commonly used in BCI's and may also influence the regulation of brain networks that impact PTSD symptoms – a hypothesis that is tested in this paper.

Additionally, game-based neurofeedback to enable self-regulation of alpha bandpower (also 8-12 Hz and overlapping with mu) satisfies the definition of a BCI to a point (Pfurtscheller et al., 2010); the system records alpha activity directly from the brain, and the user can intentionally modulate their alpha to provide the necessary input for the BCI to process the signal in real-time to communicate with the system and provide feedback to the user regarding the effectiveness of their efforts to up or down regulate alpha bandpower. The alpha rhythm is associated with calmness, and hypoactive resting-state alpha is an EEG marker for PTSD arousal symptoms (Huang et al., 2014; Jokić-begić and Begić, 2003; Wahbeh and Oken, 2013). Normal alpha rhythms in the awake brain exhibit larger amplitudes over posterior regions (Nunez et al., 2001). Therefore, neurofeedback as a treatment for PTSD, focuses on increasing resting-state alpha (Bell et al., 2019; Gapen et al., 2016; Kluetsch et al., 2014; Nicholson et al., 2018; Van Der Kolk et al., 2016) – with feedback driven by real-time measurement of posterior alpha power (Deiber et al., 2020; Kluetsch et al., 2014; Laufs et al., 2006). Recently increased resting-state alpha has been achieved using neurofeedback to reward alpha suppression while on task, as reduced alpha activity while focusing on a task has been found to increase resting-state alpha following feedback, compared to the baseline measure taken prior to feedback – referred to as the alpha 'rebound' effect (Kluetsch et al., 2014; Lanius et al., 2015; Nicholson et al., 2016; Ros et al., 2014).

An important difference between neurofeedback and mental imagery based BCI is the input (derived from the brain signal) does not directly control the behaviour of the character in the game but instead influences the characters behaviour. For example, alpha bandpower is measured in real-time and the game functions correctly whilst the user regulates the alpha power (in this case) below a specified threshold. In contrast the input from the motor-imagery paradigm directly influences the behaviour of the game character, i.e., a specific pattern of mu desynchronization/beta synchronisation over the left motor cortex, predetermined

using machine learning methods, moves the character, for example, to the right. Therefore, for the purposes of the current study, we refer to the training as a BCI based intervention, with each condition named according to the level of control the particular brain signal exerts on the game behaviour: The neurofeedback (NF) condition uses alpha modulation to indirectly influence the game character, while the motor-imagery (MI) BCI uses SMR activity that is maximally separable for two classes of movement (left vs right) to directly control the movement of the game character left or right accordingly.

At present NF is recognised as an evidence-based treatment for PTSD in developed countries, supported by the findings of a substantial body of published research studies (Bell, 2018; Bell et al., 2019; Kluetsch et al., 2014; Lanius et al., 2015; Nicholson et al., 2016; Othmer and Othmer, 2009; Van Der Kolk et al., 2016). PTSD symptoms have been associated with the disruption of higher intrinsic brain function due to aberrant alpha oscillatory activity. The success of NF as a treatment for PTSD symptoms has thus been related to improving voluntary alpha regulation to restore efficient alpha synchronisation/desynchronisation within the ICN's involved in the maintenance of the disorder - impacting DMN functioning, and the SN which allows the brain to switch between the DMN and the CEN (Bell et al., 2019; Kluetsch et al., 2014; Lanius et al., 2015; Nicholson et al., 2018; Reiter et al., 2016; Rusiniak et al., 2014). Alpha and beta modulation over the sensorimotor cortex is associated with motor movement and motor imagery (Emami and Chau, 2020, 2018; McFarland et al., 2000; Yuan and He, 2014). Recent research has found that task-irrelevant distractors result in increases in the ratio of parietal theta power to parietal alpha power, using a BCI motor imagery (MI) task (Emami and Chau, 2020). Thus, improvements in the ability to switch between the DMN and CEN could be measured as a reduction in the ratio of parietal theta power to parietal alpha power. MI was thus chosen as an alternative feedback as both feedback types provided changes in cortical oscillatory activity as an outcome measure (alpha for the NF group and the parietal theta-parietal alpha ratio index for the MI group).

This study investigates whether multiple sessions of NF training (alpha down regulation to promote post-session alpha 'rebound') or MI training (to modulate mu and beta and associated brain networks) could impact PTSD symptom severity in a population within a developing country that has very little experience with neurotechnology in general, suffers from high PTSD prevalence rates, and where neither NF nor MI based treatment have been previously investigated for treatment of PTSD. To ensure the ecological validity of both BCI-based feedback interventions as a viable treatment strategy in the context of a developing country such as Rwanda, low-cost wearable EEG is adopted, and the study was conducted in community settings with mobile experimental setups.

2. Methods

2.1. Procedure

To examine the effect of neurofeedback training on PTSD symptom severity, the study design included three groups: Control (no training), NF (neurofeedback training – seven sessions), and MI (motor-imagery BCI training – six sessions). There were three project phases: phase 1 to evaluate symptom severity prior to BCI-based feedback training intervention; phase 2 to deliver interventions; and phase 3 to evaluate changes in brain oscillatory patterns and/or symptom severity that could be attributed to the NF and/or MI training. The control group completed the clinical interview assessment in the same weeks as the NF and MI groups, before and after the training phase of the study. However, they did not undergo any experimental manipulation in between these interview dates.

2.2. Participant selection

Approval for the current study was granted by the Ulster University (UU) Research Governance Committee and by the University of Rwanda - College of Medicine and Health Sciences (UR-CMHS) Institutional Review Board. PTSD patients who had scored at the higher end of the spectrum for PTSD in a previous UR led study were invited to take part in this study, resulting in the recruitment of 29 participants, in three different localities: Kigali, Rwamagana, and Huye. All participants provided written informed consent. For practical reasons, participants were assigned to groups through a process of quasi-randomisation. To minimise logistical challenges associated with trialling the intervention over multiple session all seven participants in the Huye district were asked to participate in the control group, as it is a three-hour drive from Kigali. The Rwamagana group comprised fourteen participants, while the Kigali group formed the final eight participants. Given the larger size of the Rwamagana group, two were randomly assigned to the control group, and two were randomly assigned to the MI training group. The remaining ten participants were assigned to the NF group. All eight participants in the Kigali group were assigned to the MI group. The final groupings were as follows; control $n = 9$, NF $n = 10$, and MI $n = 10$, ($N = 29$, all female). Table 1 provides demographic and baseline psychological assessment information.

2.3. Clinical Interviews and subjective measures (pre- post- training questionnaires)

Clinical interviews: To assess an effect of NF training and/or MI training on symptom severity, an interviewer recorded participant responses to the following series of standardised psychological assessment tests both prior to, and following, the NF and MI training phase of the study:

1 PTSD Diagnostic and statistical manual of mental disorders (5th edition - DSM-5) check list (PCL-5, 20-item self-report measure, Blevins et al., 2015); to determine clinically relevant improvement due to treatment, a minimum threshold of a reduction in post treatment scores by 10 points is recommended.
2 Harvard Trauma Questionnaire (HTQ, 40-item self-report measure, Tay et al., 2017)), found to have an optimally sensitive cut-off score of 2.2.
3 Primary care PTSD screen for DSM-5 (5-item self-report PTSD Screen, (Prins et al., 2016)), which has an optimally sensitive cut-off score of 3, within the US population.
4 Warwick-Edinburgh Mental Well-being Scale (WEMWBS, 14-item self-report measure, Tennant et al., 2007), which has an average population mean of 51 (Stewart-Brown and Janmohamed, 2008).

Table 1
Demographic and initial psychological assessment data.

Measure	Participants (PTSD Patients, $N = 29$), $M \pm SD$
Sex	All female
Age	53.72 ± 6.094
PCL-5	37.62 ± 17.346
HTQ	86.66 ± 20.801
PC-PTSD	2.72 ± 1.509
WEMWBS	42.28 ± 7.837
CD-RISC	16.59 ± 5.877
BRS	16.38 ± 5.913
GSE	22.24 ± 4.976

Abbreviations: PCL-5 = PTSD Diagnostic and statistical manual of mental disorders (5th edition - DSM-5) check list, HTQ = Harvard Trauma Questionnaire, PC-PTSD = Primary care PTSD screen for DSM-5, WEMWBS = Warwick-Edinburgh Mental Well-being Scale, CD-RISC = Connor-Davidson Resilience Scale, BRS = Resilience Scales, GSE = General Self-Efficacy Scale, N = number of participants, M = mean, and SD = standard deviation.

5 Connor-Davidson Resilience Scale (CD-RISC, 10-item self-report measure, Connor and Davidson, 2003) – scores range from 0 to 40, and higher scores imply higher resilience.
6 Brief Resilience Scales (BRS, 6-item self-report measure, Smith et al., 2008) – scores range from 1 to 5, and higher scores imply higher resilience.
7 General Self-Efficacy Scale (GSE, 10-item self-report measure, Schwarzer and Jerusalem, 1995) – scores range from 10 to 40, and higher scores imply higher self-efficacy.

The psychological assessment data is presented in Table 2. Given the small sample size, the Mann-Whitney U test was performed on the baseline measures for each questionnaire, to compare groups prior to intervention and the Wilcoxon signed-rank test (2-tailed) was conducted on the pre- post intervention measures for each questionnaire, dependent on group assignment, i.e., control, NF, or MI groups.

Subjective measure of mood and stress: To assess whether participants perceived a difference in their mood and/or their level of stress, either from one training session to the next or directly following a training session compared to just before that session, all participants completed a pre- and post- self-report evaluation of both their perceived mood and stress level. Due to the small sample size of each group, and some missing values in the data, a Friedman test was conducted on pre-training self-report measures to evaluate changes in perceived mood and stress levels from one session to the next, followed by the Wilcoxon signed-rank test (2-tailed) on each combination. To evaluate perceived changes in both mood and stress levels following each training session, the Wilcoxon signed-rank test (2-tailed) was applied to each pre- post-dataset combination, for each group.

2.4. FlexEEG headset

On the first day of training, EEG was recorded from 32 channels using one g.Nautilus Pro and one g.Nautilus Ladybird, 32 channel active electrode wearable headset system (g.NAUTILUS RESEARCH | Wearable EEG Headset, 2020), for high-resolution EEG. The reference electrode was fixed on the right earlobe and the ground electrode was positioned over the AFz electrode location according to the international 10/20 EEG standard. This setup was used for all training sessions for one participant in the NF group due to an incompatible fit with the FlexEEG headset. For all other participants, EEG was recorded using the low-cost FlexEEG 8-channel passive electrode EEG headset (NeuroCONCISE, 2021), which has 3 bipolar channels and 5 unipolar channels – for montage see Fig. 1.

For data acquisition, the reference electrode was fixed on the right earlobe and the ground electrode was positioned at the AFz electrode location, according to the international 10/20 EEG standard. A user datagram protocol (UDP) based communication was used to manage the communication between a Simulink (Mathworks, 2015) module, used for EEG data acquisition and online signal processing, and the experimental protocol controller application developed in the Unity 3D Game Engine (Unity Technologies, 2020).

2.5. Design of the BCI based feedback training intervention

Neurofeedback paradigm: The neurofeedback paradigm was designed to train participants to down regulate their alpha brain rhythm (8-12 Hz) while on task, using the NeuroSensi games platform to cue the task (Bigirimana et al., 2020). The alpha signal used to modulate the feedback was measured from the Pz (located over the midline parietal cortex), in line with Kluetsch et al., (2014), as this area covers the PCC which is the main hub for the DMN (Kluetsch et al., 2014; Sridharan et al., 2008). Furthermore, measuring from one electrode, rather than the alpha signal averaged over multiple electrodes, avoids a mixing of local cortical dynamics in the signal (Kluetsch et al., 2014; Nicholson et al., 2016; Ros et al., 2013).

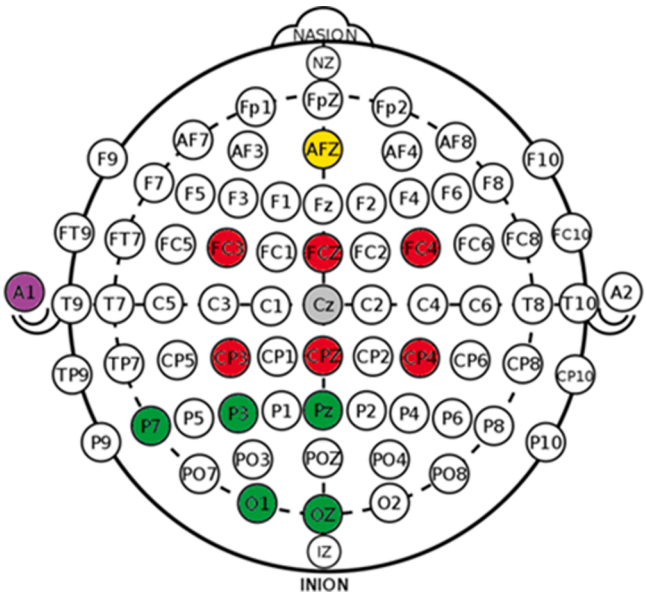

Fig. 1. FlexEEG 8-channel montage: Illustration of the positions of EEG and ground electrodes for the FlexEEG 8-channel setup. Yellow: BIAS electrode (zero volt driven), Red: 3-channel Motor Imagery electrodes (Bi-polar, each pair (FC3-CP3, FCZ-CPZ, and FC4-CP4) referenced from each other), Green: 5-channel Visual area electrodes (uni-polar, each electrode referenced from the left earlobe), Purple: Ear reference for visual electrodes (ear clip).

The aim of the game was to keep an astronaut character on track, collecting rewards and avoiding hazards (Fig. 2). One session comprised a baseline relax period of 134 seconds (s) duration followed by 10 feedback runs (games – each of ~134 s duration), with 9 breaks (up to 15 s in duration while the next run loaded), finishing with a second 134 s relax period. The participants baseline (resting-state) alpha amplitude was computed from the Pz channel data during the 134 s relax period immediately before the feedback session – using a 500 ms sliding window, the EEG signal was band-pass filtered to extract alpha from each 500 ms epoch. The mean alpha band power from the first relax period was then used as the initial threshold for the subsequent run in the feedback session (see section 0 for more details). The task required participants to supress real-time alpha (8-12 Hz), and the game character was correctly positioned on the track if the measured alpha level was below the threshold and deviated from the correct position otherwise. The threshold was updated for the next game by setting it to the value smaller than approximately 60% of the alpha levels measured from the preceding game i.e., periodically adapting the threshold setting. It was anticipated that alpha suppression during the NF training session would result in increased resting-state alpha following the session – termed alpha 'rebound', and that this improved alpha state would be supported by a reduction in symptom severity post intervention.

Motor Imagery paradigm: The motor-imagery paradigm was designed to train participants to consciously activate areas of their cortex that are unconsciously activated during movement preparation and execution (Lotze and Cohen, 2006; Mulder, 2007), using the NeuroSensi games platform to cue the task (Bigirimana et al., 2020). The game display has a representation of an axon on both sides of the interface (see Fig. 3). One trial is 8 s in duration. Three seconds from the beginning of a trial, a light (representing an action potential, or neural spike) appears at the far end of one of the axons to cue the participant to begin the motor-imagery task for the corresponding hand. The light takes 5 s to travel down the 'axon'. At the beginning of the first feedback session, the task was explained to the participant – they were instructed to avoid eye-blinks and other movements during the task, and to imagine lifting a mug (without tensing muscles) using the hand indicated by

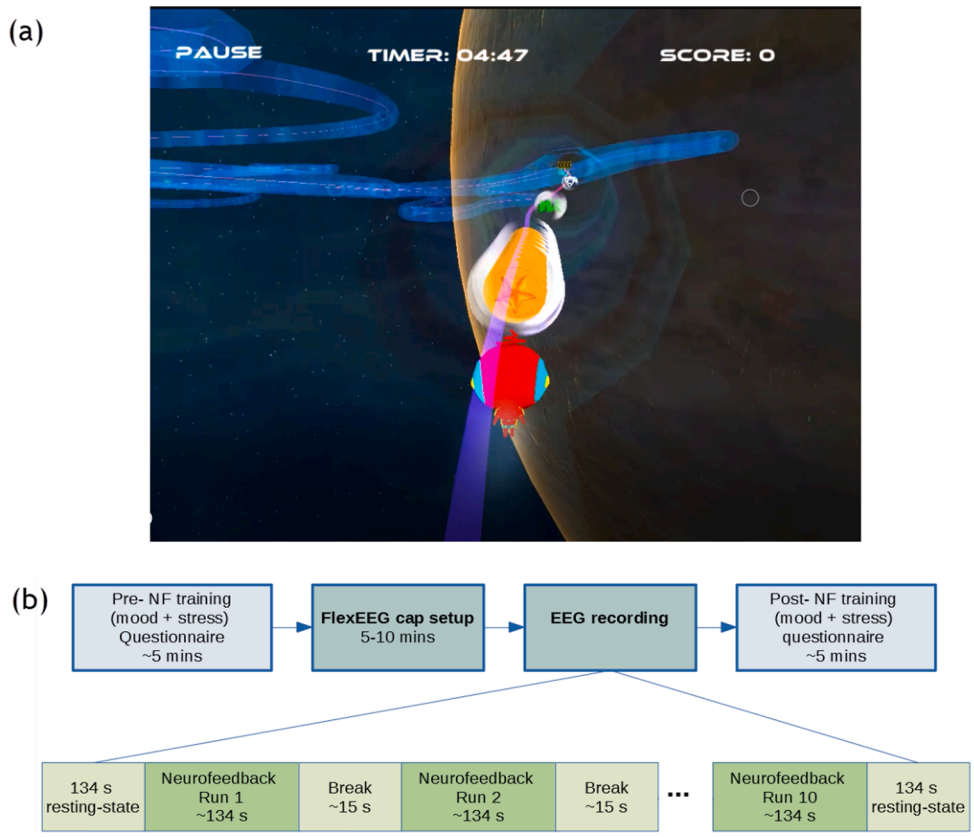

Fig. 2. **(a)** The game display for the neurofeedback brain-computer interface (BCI) using the NeuroSensi games platform (Bigirimana et al., 2020). **(b)** Breakdown of the NF training session.

the cue. During the task period, continuous feedback is given to the participant in the form of a horizontally moving neuron (cell body and dendrites) character. The neuron character moves left or right based on the trained classifier model output (see section 2.7 for details) and the aim of the game is to collect as many spikes traversing the axons as possible (points are given for proximity to spike when each reaches the end of the axon and when the neuron character is moving in the correct direction towards the axon containing the spike).

The MI participant group were all BCI novices – a term used to categorise people who have not had any previous experience with BCI systems. Furthermore, as with the NF participants, the MI participant group similarly did not have any experience of current western technologies in their daily lives. Given this low-level of tech-engagement coupled with the substantial number of BCI users reported to be unable to successfully modulate the sensory motor rhythms (SMR's) necessary to control a motor imagery BCI (Ahn et al., 2013; Sannelli et al., 2019), participants were allowed to practice before the first session, until they were happy to begin. It was hypothesised that participants would show a reduction in the ratio of parietal theta power to parietal alpha power across feedback sessions, as they learned to regulate their SMR activity, thus stabilising the functional brain rhythms sub serving the CEN, DMN, and SN, resulting in a reduction of symptom severity.

2.6. Neurofeedback EEG: Signal processing and data analysis methods

EEG channel selection: The quality of the eight acquired EEG channels was inspected manually offline after each session, and EEG channels with high-level noise (>200 μV) were removed from further processing. **Frequency filtering:** Alpha (8-12 Hz) was extracted from the recorded signals by band-pass filtering with Simulink (Mathworks, 2015) using high-pass and low-pass FIR filter modules (band-pass attenuation 0dB, band-stop attenuation 60 dB). The preprocessed EEG dataset was downsampled from 250Hz to 125Hz to reduce the size of the EEG dataset. **Epochs:** The frequency filtered EEG data for baseline resting-state and resting-state following the training session were epoched separately, applying an interval of 134 s to each epoch. Furthermore, EEG data for each run of the game were epoched using intervals of 134 s per epoch. **Bandpower calculation:** The bandpower within an epoch was calculated by averaging the square values of the band-pass filtered EEG potentials recoded within the epoch as described in Eq. (1) (Korik et al., 2019).

$$B_n = \frac{\sum_{m=1}^{M} (P(m)_n)^2}{M} \quad (1)$$

where B_n is the bandpower value calculated from EEG channel n, within an epoch. M is the number of samples within the epoch and $P(m)_n$ is the m^{th} band-pass filtered sample within the epoch.

Neurofeedback data analysis methods: An initial assessment of the data found the distribution to have a significant positive skew (>0.5). The results of a Shapiro-Wilk test found the distribution to be significantly non-normal (global (all channels): baseline resting-state; $W(53) = 0.887$, $p < 0.01$, NF session data; $W(53) = 0.848$, $p < 0.01$, and resting-state following the NF session; $W(53) = 0.855$, $p < 0.01$, and Local (Pz electrode only): baseline resting-state; $W(53) = 0.903$, $p < 0.01$, NF session data; $W(53) = 0.898$, $p < 0.01$, and resting-state following NF session; $W(53) = 0.847$, $p < 0.01$). Therefore, data for the baseline period before training (resting-state, RS 1), the training period, and the relax period following training (RS 2) were normalised for the statistical analyses, using a $\log_{10}$ transform in the Statistical Package for Social Sciences (IBM SPSS statistics 25). To determine whether participants had significantly suppressed their absolute alpha amplitude during neurofeedback training, the alpha amplitude values averaged over a neurofeedback session (all runs) were compared to resting-state alpha

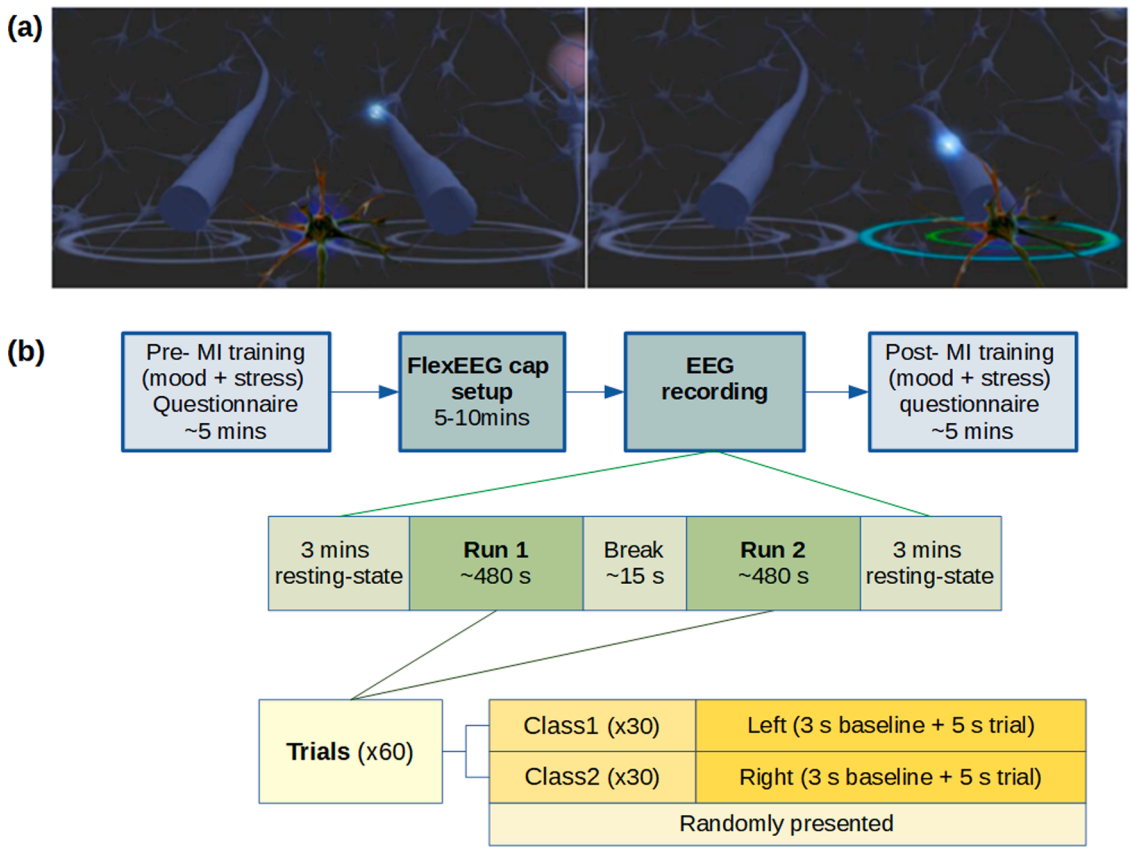

Fig. 3. **(a)** Illustration of a cue (left) and feedback (right) presentation for the motor-imagery BCI using the NeuroSensi games platform (Bigirimana et al., 2020). **(b)** Breakdown of the MI training session.

amplitude values, averaged over the baseline period, using a two-tailed Wilcoxon signed-ranked tests (the non-parametric related samples comparison test was chosen in place of paired t-tests due to the small sample size). Moreover, to evaluate plastic changes in absolute alpha amplitude as a consequence of neurofeedback training, absolute alpha amplitude values averaged over the baseline resting-state period for each session were compared to the averaged values over the resting-state period following the neurofeedback period, again using Wilcoxon signed-rank tests. The methodology employed in previous neurofeedback research using this neurofeedback approach normalised alpha desynchronisation values against the baseline resting-state alpha power, to provide an estimate of the percentage signal change between conditions (for details, see Kluetsch et al., 2014; Nicholson et al., 2016). However, as the present data were normalised prior to making the estimated percentage signal change calculations, this technique was not necessary. The estimated percentage signal change between baseline resting-state alpha amplitude and alpha amplitude under feedback conditions, is referred to as 'training alpha change', calculated by subtracting the averaged baseline resting-state alpha from the alpha amplitude averaged across feedback runs for each session. Similarly, the difference between baseline and post-neurofeedback resting-state alpha amplitude is referred to as 'resting alpha change' and is calculated by subtracting the averaged resting-state alpha following a neurofeedback session from the corresponding averaged baseline resting-state alpha (Kluetsch et al., 2014). Thus, both are normalised alpha amplitude values that represent change scores. Importantly, a relative percent increase in alpha amplitude is represented by alpha amplitude values $>$ 0 and conversely, values $<$ 0 denote a relative percent decrease in alpha amplitude, i.e., a negative training alpha change value indicates successful alpha amplitude suppression during the run under feedback conditions, while a positive resting alpha amplitude value signifies an increase in absolute resting-state alpha amplitude following feedback – termed alpha 'rebound' (Kluetsch et al., 2014; Nicholson et al., 2016). A Pearson product moment correlation was computed between the training alpha change scores and the baseline resting-state alpha amplitude values, and also between the resting alpha change scores and the baseline resting-state alpha amplitude values, to examine the influence of baseline resting-state alpha on subsequent alpha change. Furthermore, to ascertain whether training alpha change predicted resting alpha change, a partial correlation was assessed between these change scores while controlling for baseline resting-state alpha amplitude. The alpha amplitude values were derived separately from both the EEG data recorded from the Pz electrode, used to modulate the feedback, and also the recorded EEG from all channels, to assess whether qualitative differences existed between the local (Pz) measure and the global (all channels) measure.

2.7. *Motor Imagery EEG: Signal processing and data analysis methods*

Offline signal processing: The signal processing framework involved filter-bank common spatial patterns (Ang et al., 2012) and mutual information (FBCSP-MI) –based features selection (Pohjalainen et al., 2015). This framework was calibrated on the no-feedback EEG data on the first occasion, and on the final feedback run of the previous session for subsequent MI training sessions. FBCSP applied along with an Linear discriminant analysis (LDA) classifier is a commonly used EEG classification framework for discriminating imagined movements (Korik et al., 2019).

EEG channel selection: The quality of the eight acquired EEG channels was inspected manually, and EEG channels with high-level noise ($>$200 μV) were removed from further processing. **Frequency filtering:** Band-pass filters in four non-overlapped standard EEG's

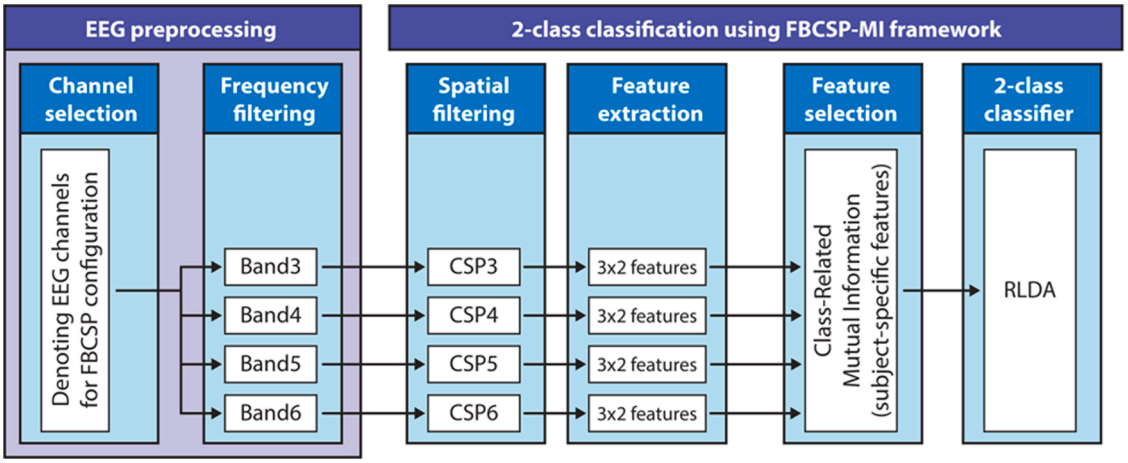

Fig. 4. Illustration of the FBCSP based multi-class classification method using mutual information selection (FBCSP-MI) and the regularized linear discriminant analysis (RLDA) based 2-class classifier. For the main analysis, four standard EEG bands were applied (i.e., bands 3-6: alpha, low-beta, high-beta, low-gamma).

frequency bands (8-12Hz (alpha), 12-18Hz (low beta), 18-28Hz (high beta), and 28-40Hz (low gamma)) were applied to the EEG signals in Simulink (Mathworks, 2015) using high-pass and low-pass FIR filter modules (band-pass attenuation 0dB, band-stop attenuation 60 dB). Using these four bands (alpha, low beta, high beta, and low gamma) in the FBCSP-MI framework has been shown to result in a more stable and higher decoding accuracy (DA) rate in the classification of imagined movement performed with the left versus right hands (Korik et al., 2019). Therefore, the delta and theta bands were not applied to the main analysis. The pre-processed EEG dataset was downsampled from 250Hz to 125Hz to reduce the size of the EEG dataset. **Trials:** The filtered dataset was epoched for each EEG channel separately, to include task-relevant time intervals (between 3s prior to, and 5s after, the onset of the motor imagery task). There were 30 trials per class in a run (60 trials in total per run). Maximum of three runs per participant in all the MI sessions were removed from further analyses due to noise, mostly resulting from movement of participant's or poor electrode connectivity due to hair density. **Spatial filtering:** In each frequency band, common spatial patterns (CSP) filter was applied to maximise the discriminability of two classes by learning spatial filters that maximise the variance of band-pass filtered EEG signals from one class while minimising the variance of signals in the other classes (Lotte and Guan, 2011). Transformation values in a CSP filter are weights of the linear transformation matrix that convert the pre-processed EEG signals into a new vector space defined by the CSP filters. The number of selected CSP filter pairs for each frequency band was set to three. **Feature extraction:** The analysis was performed using the time-varying log-variance of the CSP filtered EEG – calculated using a 1s sliding window, with 200 ms gap between two consecutive windows. In each window, six features were extracted for every frequency band resulting in 24 features for all the frequency bands. **Feature selection:** The mutual information between features and associated target class using a quantised feature space, was estimated to identify a subset of features that optimise the decoding accuracy (Pohjalainen et al., 2015). The number of the features selected by the mutual information module was set in a range from four to fourteen. For each participant in the analysed run, the peak decoding accuracy (DA) values resulting from using different feature number options were compared to find the optimal mutual information module configuration for the dataset acquired for that participant in the analysed run. **Two-class classification:** Linear discriminant analysis (LDA) uses a hyperplane to separate features obtained from two classes where the class assigned to an unseen feature vector depends on the polarity of the classifier output, determined by position with respect to the hyperplane (Lotte et al., 2007). A regularised LDA (RLDA) algorithm (from the RCSP toolbox (Lotte and Guan, 2011)) was applied to classify the extracted features i.e., either the left or right hand movement imagery. The time-varying DA was calculated using the time-varying average and standard deviation of participant-specific DA obtained using a six-fold cross-validation (CV) setup.

The offline FBCSP-MI configuration was repeated for a 2 s sliding window (instead of the 1 s) to find the optimum participant-specific classification window. The configuration that yielded a higher DA peak in the task period was selected for the online analysis setup. The task period was marked as 0 ms to 5000 ms post task-cue onset while the reference (baseline) period was marked as -1000 ms to 0 ms pre-task cue onset.

Online signal processing: Optimised configuration from the offline analysis of the motor imagery training run, through the FBCSP-MI framework, was deployed in a MATLAB© Simulink learning model for online processing. This learning model implements the FBCSP-MI online setup to decode (or classify) the SMR activations and drive the feedback. During the online processing, the classifier's output is translated into the game character's movement presented to the participant in the feedback run. At each sample point, the classifier's output is a distance computed from the classifier's learned weights vector; this distance is often referred to as time-varying signed distance (TSD) (Pfurtscheller et al., 2000; Schlögl et al., 2002). The TSD's sign indicates the classifier's output label (left or right) and its magnitude measures the classification confidence. The magnitude of the TSD indicates how far the character moves, and the sign indicates the direction of the character's movement (moving to the right or to the left).

Offline Motor Imagery data analysis methods: To determine whether DA peaks obtained in the task periods were significantly higher ($p < 0.05$) than DA peaks obtained in the corresponding reference baseline periods, calculated in test folds of the six-fold CV for the corresponding run, one-tailed Wilcoxon's signed-rank test was performed on these data. According to Emami and Chau (2020), parietal theta power to parietal alpha power ratios provide an index by which objective cognitive load can be measured, particularly in relation to interference control. Thus, it was anticipated that MI training would improve spontaneous alpha oscillatory activity, resulting in a reduction of these index values across training sessions. Therefore, to examine whether MI resulted in reduced parietal theta power to parietal alpha power ratios, the ratios were determined as follows. The time-varying bandpower of the theta (4-8Hz) and alpha (8-12Hz) EEG oscillations were calculated by averaging the square values of the band-pass filtered EEG potentials as described in Eq. (1) (see Korik et al., 2018, for details). Next, for each frequency band, the bandpower for the task period was normalised

against the bandpower of the corresponding baseline period and then the ratio of parietal theta to parietal alpha was computed for each run. A Friedman test was performed to examine whether there was an overall reduction in parietal theta to parietal alpha ratios across runs, followed by Wilcoxon signed-rank tests to look at paired comparisons.

3. Results

3.1. Clinical Interviews and pre- post- training questionnaires

At the time of testing for the current study, 79% of the total patient group had scores above the threshold on at least two of the measures of trauma (PCL-5, PC-PTSD, and HTQ). With reference to the DSM-IV PTSD measures, i.e., the PCL-5 and the PC-PTSD, a breakdown of the group percentages above the recommended thresholds at baseline, is as follows; control group = 66%, MI group = 80%, and NF group = 90%. The diagnostic rule for the PCL-5 requires a score for at least one question from category B items (questions 1-5), one from category C item (questions 6-7), two from category D items (questions 8-14), and two from category E items (questions 15-20) – and the typical cut-off score is 30.

Baseline group comparison: Analysis of the clinical interview data at baseline found a significant difference between the MI and NF groups on WEMWBS scores, due to a higher score for the NF group ($U = 22.5$, $p = 0.037$, $d = -0.956$).

Pre- Post- measures comparison for each group: Analysis of the pre- and post- training clinical interview data revealed a reduction in symptom severity post training for the NF group only, on four out of seven measures (see Table 2); the PCL-5 ($Z = -2.81$, $p = 0.005$, $d = 2.24$), the PC-PTSD for DSM-5 ($Z = -2.83$, $p = 0.005$, $d = 3.1$), the Harvard Trauma questionnaire ($Z = -2.8$, $p = 0.005$, $d = 2.41$), and the 10-item CD-RISC ($Z = -2.04$, $p = 0.041$, $d = -0.4$). The effect size for the increase in the score for resilience, on the CD-RISC scale was medium ($d = -0.4$), with 70% of participants demonstrating an increase in scores on the post-intervention CD-RISC measure. While there was a significant reduction in post-intervention HTQ scores for the NF group, with a large effect size ($d = 2.41$), only two participants had met the > 3-point cut-off on the pre-intervention measure. However, the reduction in symptom severity scores for the majority of the NF group following the intervention period, on both DSM-IV measures of trauma, i.e., the PCL-5, the PC-PTSD for DSM-5, was evidenced by large effect sizes ($d = 2.24$ and $d = 3.1$, respectively). Notably, the NF group's post-training scores indicate clinically meaningful reductions in PTSD symptom severity. Sixty percent had scores equal to or above the cut-off of 30 points on the pre-intervention PCL-5 measure, all of whom met the ≥ 10-point reduction threshold on the post-intervention PCL-5 measure ($M = 11$, $SD = 5.52$). Furthermore, all participants in the NF group demonstrated a reduction in symptom severity scores on the post-intervention measure, 90% of whom had scores which were reduced by ≥ 10 points. Seventy percent of the NF group participants had scores equal to or above the cut-off of 3 on the pre-intervention PC-PTSD for DSM-5 measure, all of whom had scores below this cut-off on the post-intervention measure ($M = 0.3$, $SD = 0.67$), with all NF group participants showing a reduction in symptom

Table 2
Pre- post- psychological assessment data per group.

Group	Measure	Pre-training score		Post-training score	
		M±*SD*	Range	*M*±*SD*	Range
	PCL-5	34.44±23.84	5-71	28.66±20.08	2-53
	PC-PTSD	3±1.73	1-5	2.44±2.01	0-5
Control	HTQ	2.07±0.71	1.2-3.33	1.86±0.61	1.1-2.7
n = 9	WEMWBS	38.89±9.61	30-57	37±10.7	23-56
	CD-RISC	17.56±9.26	4-35	16.33±5.83	8-27
	BRS	2.65±1.28	1-4.83	2.63±1.23	1-4.33
	GSE	20.33±6.29	10-30	20.33±6.23	12-30
	PCL-5	39.2±11.71	17-55	35.3±14.45	7-54
	PC-PTSD	2±1.49	0-4	1.1±1.2	0-3
MI	HTQ	2.24±0.38	1.65-2.85	2.03±0.43	1.2-2.78
n = 10	WEMWBS	40.9±4.77	31-46	37.4±5.74	31-49
	CD-RISC	15.6±3.03	12-28	15.9±4.04	7-21
	BRS	2.68±0.63	2-3.67	2.8±1.01	1.83-4
	GSE	23.9±4.99	17-32	23.3±5.23	15-32
	PCL-5	38.9±16.7	9-61	11±5.52+**	4-22
	PC-PTSD	3.2± 1.14	1-4	0.3±0.68^**	0-2
NF	HTQ	2.18±0.48	1.55-3.05	1.28±0.21+**	1-1.8
n = 10	WEMWBS	46.7±7.13+	33-56	42.6±6.99	25-50
	CD-RISC	16.7±4.47	7-22	18.3±3.13*	10-20
	BRS	2.85±1.07	1.33-4	3.4±0.97	2-4
	GSE	22.3±3.2	17-28	24.3±5.23	12-30

Abbreviations: PCL-5 = PTSD Diagnostic and statistical manual of mental disorders (5th edition - DSM-5) check list, PC-PTSD = Primary care PTSD screen for DSM-5, HTQ = Harvard Trauma Questionnaire, WEMWBS = Warwick-Edinburgh Mental Well-being Scale, CD-RISC = Connor-Davidson Resilience Scale, BRS = Brief Resilience Scales, GSE = General Self-Efficacy Scale, *n* = number of participants in the corresponding group, *M* = mean, and *SD* = standard deviation. All participants were female. * = *p* value <0.05, ** = *p* value less than 0.01, ^ = significant difference between NF group compared to control group, and + = significant difference between NF group compared to MI group. **Note:** A reduced score on the PCL-5, PC-PTSD, and HTQ measures post- training indicates reduced symptom severity (better outcome), while an increased score on the WEMWBS, CD-RISC, BRS, and GSE measures post- training indicates a better outcome for these variables.

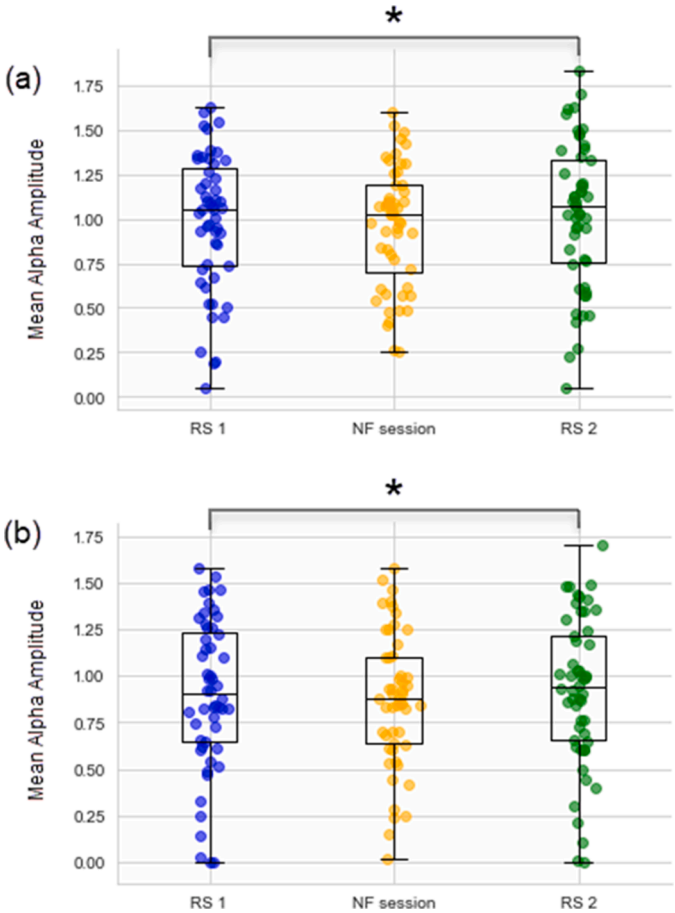

Fig. 5. Representation of the alpha 'rebound' effect (a term coined by Kluetsch et al., 2014), as computed **(a)** from the local Pz electrode channel data and **(b)** from the global all channels data. The $\log_{10}$ normalised mean alpha band (8-12 Hz) amplitude is presented on the y-axis. The boxplots present the data for the baseline resting-state (RS 1; blue), the NF training session (NF session; orange), and the resting-state period following training (RS 2; green). Increased local and global alpha amplitude following training (RS 2), compared to the baseline (RS 1), was found to be significant (depicted by the continuous black line with the asterisk ($p < 0.05$).

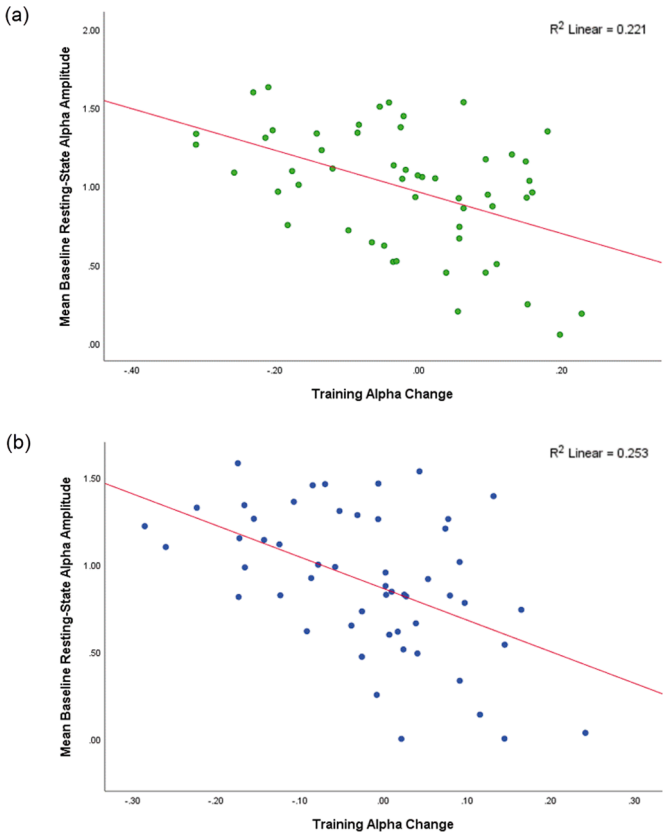

Fig. 6. Representation of the relationship between the mean normalised alpha amplitudes as computed **(a)** from the local Pz electrode channel data and **(b)** from the global all channels data, and the training alpha change. Values < 0 on the x-axis imply greater training alpha change. Thus, higher absolute alpha amplitude at baseline (y-axis) resulted in greater training alpha change.

severity scores, post-intervention.

Post-intervention group comparison: Analysis of the post-intervention clinical interview data found a significant difference between the NF and MI groups on both the PCL-5 ($U = 8$, $p = 0.001$, $d = 2.22$) and HTQ ($U = 7.5$, $p = 0.001$, $d = 2.19$) measures, due to a greater reduction in scores for the NF group. The difference between the NF group and the control group was significant for scores on the PC-PTSD ($U = 18.5$, $p = 0.016$, $d = 1.43$) – also due to a greater reduction in scores for the NF group.

3.2. Subjective mood and stress levels

The brief pre- and post- training (self-report) questionnaires were analysed to assess whether NF and/or MI training improved participants perceived mood and/or level of stress. Overall, evidence of an increase in perceived mood and a decrease in perceived stress was not observed for either group conclusively. Support for improvement in perceived mood was observed for the NF group ($X^2(6) = 12.66$, $p = 0.049$), however, this was not significant when controlling for multiple comparisons ($p > 0.008$).

3.3. Neurofeedback EEG spectral analysis

Wilcoxon signed-rank tests to evaluate changes in alpha amplitude during and following neurofeedback training, compared to baseline, demonstrated both a local (Pz) and a global (all channels) increase in resting-state absolute alpha amplitude following training compared to the baseline resting-state absolute alpha amplitude (local: $Z = -2.235$, $p = 0.025$, $r = -0.31$, and global: $Z = -2.253$, $p = 0.024$, $r = -0.31$), as illustrated in Fig. 5. While a slight decrease in alpha amplitude during feedback sessions, suggestive of successful alpha suppression, was observed – the decrease was not found to be significant either locally or globally ($p > .05$).

However, a Pearson product moment analysis found a negative correlation between baseline resting-state absolute alpha amplitude and training alpha change, both for local and global analyses (local; $R^2 = 0.221$, $r = -.47$, $p < 0.001$, and global; $R^2 = 0.253$, $r = -.503$, $p < 0.001$ – see Fig. 6). The suggestion is that higher amplitude alpha during baseline resting-state was associated with better alpha suppression during the feedback session (see Fig. 6).

Regression analyses to examine the influence of training alpha change on resting alpha change when controlling for baseline resting-state alpha amplitude, as recorded from the Pz sensor (local alpha measurements), found a significant partial correlation, suggesting less alpha suppression (during the NF training) predicted greater alpha increase following training ('rebound') (local; $R^2 = 0.088$, $r_{partial} = 0.315$, $p = 0.023$, and global; $R^2 = 0.056$, $r_{partial} = 0.179$, $p = 0.204$). Previously, this relationship has been found to be negative, i.e., greater training alpha change predicted greater resting alpha change (Kluetsch et al., 2014; Nicholson et al., 2016).

3.4. Motor-imagery BCI EEG spectral analysis

In forty-one runs (out of ninety, performed over multiple sessions), the participants achieved an accuracy rate that was significantly higher during the task period compared to the peak DA obtained for the reference baseline period ($p < 0.05$). DA values obtained from task (Fig. 8 (a)) versus reference baseline periods (Fig. 8 (b)) for these forty-one runs, are illustrated in Fig. 8 below.

The outcome of the Friedman test to determine whether MI training resulted in a reduction of participants parietal theta to parietal alpha ratio index, during the task period (using data for both classes), was not

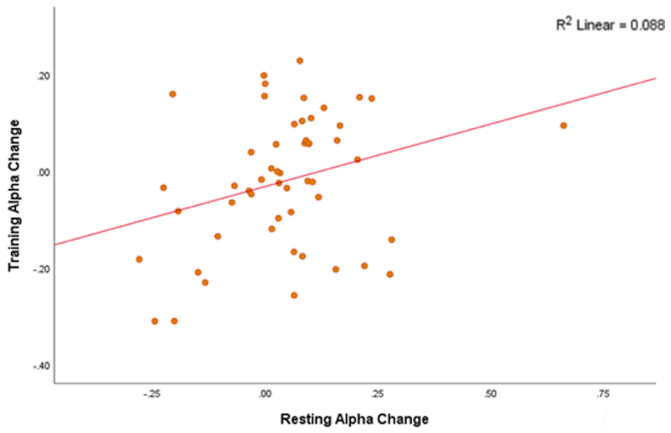

Fig. 7. Illustration of the relationship between training alpha change (<0 reflects greater alpha suppression during NF training) and resting alpha change (>0 implies greater alpha increase in resting period following training). Thus, for these data, less alpha suppression during the NF training period predicted greater increase in resting alpha following training.

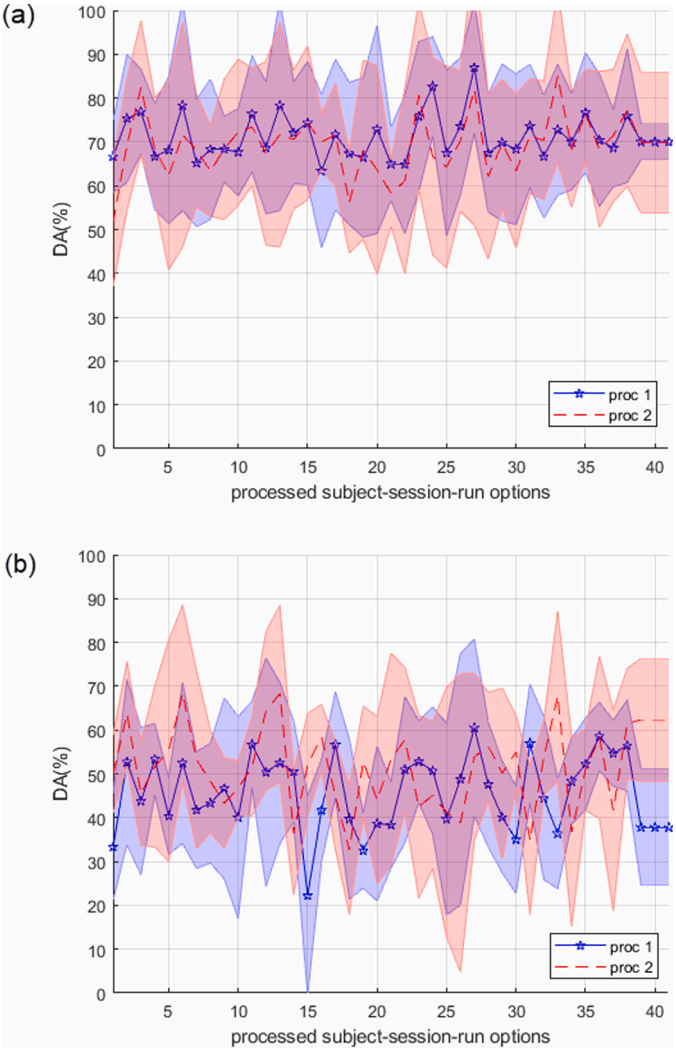

Fig. 8. Presentation of the Decoding Accuracy (DA) rates from runs where peak DA during the task periods **(a)** was significantly higher (one-tailed Wilcoxon signed-rank test, $p < 0.05$) compared to peak DA obtained in the corresponding reference baseline periods **(b)**. Colour code indicates results calculated using a 1s (blue legend; proc 1) width and 2s width (red legend; proc 2) classification window. Thick solid lines and the shaded areas indicate the mean values and standard deviation of peak DA values obtained in six-fold CV, respectively.

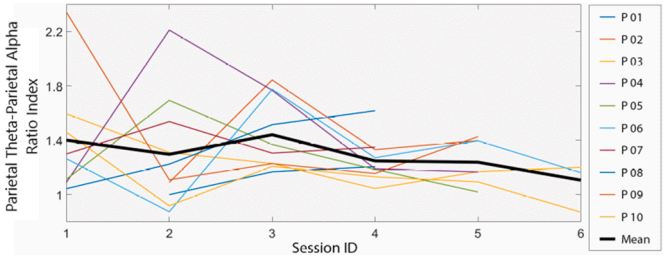

Fig. 9. Illustration of changes in the parietal theta per parietal alpha ratio index, calculated for both classes during the task period, for analysed participants (coloured lines) across all six sessions (x-axis). The trend is represented by the black line. For sessions where there is no value, either the participant was unable to attend, or there was an issue with the dataset (e.g., not enough trials for analysis).

found to be significant (X^2 (5) = 6.619, p =0.251).

Nevertheless, a reduction in the ratio index was observed across sessions (see Fig. 9). A post-hoc analysis using Wilcoxon signed-rank tests found that differences between session 3 – 4 (Z = -1.988, p =0.047) and session 3 – 6 (Z = -2.2, p =0.028) were significant at an alpha level of 0.05. Whilst these differences were determined to be non-significant after the application of a Bonferroni correction (adjusted alpha = 0.008) for multiple comparisons, the results are indicative of a tendency towards a positive effect resulting from the BCI training.

4. Discussion

The current study has examined the effectiveness of NF training using low-cost wearable EEG-based neurotechnology, as a potential treatment for PTSD patients in Rwanda. To evaluate the success of neurofeedback training in the amelioration of PTSD symptoms, pre- and post- clinical interviews assessed participants psychological assessment scores on validated PTSD questionnaire-based measures and also their scores on measures of well-being, resilience and self-efficacy – to provide a thorough assessment of general mental health. EEG spectral analyses of the data from training sessions for both the NF and the MI group were performed to determine whether training resulted in improvements on indices related to alpha power, and to test the efficacy of both types of feedback.

Importantly, the results from the psychological assessment data obtained pre- and post- training, for the complete cohort (N = 29), infer NF training resulted in significant effects which are considered clinically relevant, given 90% of the participants in this group demonstrated a reduction in post-intervention PCL-5 scores of more than 10-points, and 70% who registered above the 3-point threshold on the PC-PTSD pre-intervention measure fell below this threshold post-intervention. Response to treatment is generally evaluated based on the patient's measure of symptom severity on the PCL-5 falling below the cut-off score and furthermore, decreasing greater than 10 points compared to pre-treatment (Hinton et al., 2020; Varker et al., 2020). However, cut-off scores are known to vary as a function of the base-rate prevalence within a given population as well as due to characteristics of the target population (Blevins et al., 2015). Furthermore, research suggests that sub-Saharan populations with PTSD related disability often remain below the threshold on DSM-IV and DSM-V measures, possibly due to an increased propensity to express suffering in terms of somatic symptoms (Hiar et al., 2016; Sacchetti et al., 2020). Therefore, among the Rwandan population, a reduction in symptom severity scores exceeding 10 points, has been posited as a more reliable indicator. Similarly when administering the PC-PTSD, while a score $\geq$ 3 has been established as an optimally sensitive threshold for a diagnosis of PTSD, it has also been noted that population characteristics vary and should be considered when interpreting scores (Prins et al., 2016; Prins and Ouimette, 2004). Moreover, the clinical importance of the improvement in PTSD symptoms was substantiated by large effect sizes for the post-training results on the PTSD measures. The effectiveness of the NF training as a treatment for PTSD symptoms was further supported by the EEG spectral analyses, which found a significant increase in resting-state absolute alpha amplitude after training, compared to the baseline period – a finding that is consistent with previous research, and has been termed the 'alpha rebound effect' (Kluetsch et al., 2014; Nicholson et al., 2018). Although the sample size for the current study is small, the effect size for the increase in resting-state alpha amplitude, as measured both globally and locally, is bordering on medium.

Alpha oscillations (8 – 12 Hz) are the dominant EEG brain rhythm associated with relaxed wakefulness (Jann et al., 2009; Laufs et al., 2003; Nunez et al., 2001). Alpha and slow beta are the only cortical frequencies to display event-related synchronisation (ERS) and event-related desynchronisation (ERD) in response to sensory stimuli and/or cognitive demands. Under certain conditions requiring the controlled execution of a response, the former (i.e., ERS) reflects inhibition/constraint of the response and the latter (i.e., ERD) a release from that inhibition/constraint (Klimesch, 2012). Thus, the usual assumption that the magnitude of an oscillation is proportional to its functional impact, does not hold for these brain rhythms – however, it is this characteristic of alpha and beta that allows for the cognitive flexibility necessary for tasks such as attention switching and motor planning/execution (Klimesch, 2012; Neuper et al., 2006; Ros et al., 2014). PTSD, when it develops, results from the impact of a trauma on the CEN, DMN, and SN, and these three intrinsic neural networks are subsequently involved in the maintenance of the disorder (Bell et al., 2019; Lanius et al., 2015; Nicholson et al., 2018). Moreover, each network has been demonstrated to be associated with specific PTSD symptom clusters – CEN with cognitive impairments, DMN with an altered sense of self, and SN with hypervigilance and interoception (Lanius et al., 2015). The evidence from recent research suggests that NF training induces plastic changes in the functioning of the CEN, DMN, and SN and the associated network hubs through the restoration of a homeostatic alpha power range that is necessary to ensure the optimum balance between inherent flexibility and stability within these networks and brain regions (Bell, 2018; Bell et al., 2019; Kluetsch et al., 2014; Lanius et al., 2015;

Ros et al., 2014, 2013). Alpha hypoactivity resulting in reduced functional inhibition has been associated with PTSD (Huang et al., 2014), while down regulation of alpha amplitude during NF training has been associated with a subsequent increase 'rebound' in resting-state alpha power following training (Kluetsch et al., 2014; Nicholson et al., 2016). The significance of this return to homeostasis of alpha power, in the healing of the PTSD brain, is supported by the reported reduction in symptom severity, and improvements in functional connectivity within the CEN, DMN, and SN (Bell, 2018; Bell et al., 2019; Gapen et al., 2016; Kluetsch et al., 2014; Lanius et al., 2015; Nicholson et al., 2018).

The findings presented here suggest that NF training significantly reduced PTSD symptoms. Moreover, a significant post-training reduction in PTSD symptom severity was not found for the MI group – thus raising the question, whether MI can provide a practical method of treatment for PTSD symptoms? There are a couple of considerations to be addressed when making this appraisal. Importantly, when users of a BCI fail to become proficient, as determined by the level of accuracy they achieve within a standard training period, this is termed "BCI illiteracy" (Ahn and Jun, 2015). However, it has been argued that this concept presumes, incorrectly, that performance norms are static across BCI systems and users (Thompson, 2019). With this in mind, consideration should be given to the fact that the cohort for this study were not only BCI novices, furthermore, they had very limited experience with technology – for many a feature mobile phone (as opposed to a smart phone) was the most advanced technology they had engaged with, prior to undergoing feedback training. While time was spent on describing the process and allowing for practice on the first occasion, six sessions was very restrictive given the level of engagement the participants had with technology to that point. Nevertheless, of note also is the finding that people who have difficulty reaching expected performance levels demonstrate higher amplitude theta and low amplitude alpha brain rhythms compared to those who do not have difficulty. Furthermore, these differences in amplitude persist during differing mental states, i.e., during motor-imagery, prior to the beginning of the task – and during resting-state (Ahn et al., 2013). Therefore, it is likely that hypoactive alpha associated with PTSD will add to the challenge of successfully operating a BCI using motor-imagery.

Overall, the findings of this project suggest NF training provides an effective, clinically relevant, treatment for the amelioration of the symptoms of PTSD within a Rwandan population. Neurotechnology represents a rapidly growing area of research, contributing to medical applications from prevention to neural rehabilitation. One of the major challenges for neurotechnological solutions in developing countries lies in establishing the usability of these hi-teach applications to address health problems in countries with a struggling economy, given the high cost associated with the technology (Valdes-Sosa, 2012), and the unfamiliarity that exists within the general populations of these countries in relation to computer technologies. The findings presented here lift the lid on erroneous presuppositions that EEG and BCI based treatments will not be accepted in Rwanda, and by inference, other developing countries in Africa. Moreover, the current research has demonstrated the efficacy of the FlexEEG 8-channel wearable EEG, which is a low-cost, unobtrusive, and an ergonomic EEG headset, in the application of NF training within a developing country – and the effectiveness of NF training using this headset in the reduction of PTSD symptom severity. Health service access in Rwanda depends on the subdivision of income/capacity categories. The first two categories get support from the government in most of their health and regular expenses and include members of the population who struggle to put food on the table (~ 16% of the population), up to people who have part time small jobs and either own cheap houses or are able to pay rent (~ 29.8% of the population). Nevertheless, despite important efforts from the Rwandan government, including decentralised mental health care availability at district hospital level, the treatment gap for mental health is still large. According to a recent report (2019), an estimated 599 trained clinical psychologists were in practice in Rwanda (Kalisa et al., 2019). However, given PTSD was found to occur in 27% of genocide survivors, and 3.6% of the general population of Rwanda in 2019 (Never again Rwanda 2019) , the ratio of clinical psychologists to PTSD patients alone during 2019 was approximately 1:721. Prevalence rates have been re-examined more recently which estimate a 37% prevalence of PTSD among genocide survivors and 15% among the general population (Musanabaganwa et al., 2020). Thus, the scale of the problem is vast. Furthermore, the logistics involved in extending services to people in remote regions pose yet another challenge due to a lack of infrastructure. Moreover, a large portion of the population of Rwanda cannot afford to lose a day's wages. The OECD has raised concerns regarding the economic, social and welfare costs imposed on developing countries due to untreated mental health conditions and have thus prioritised treatment strategies at the highest national and international policy levels (OECD, 2019). Novel neurotechnology, that is low-cost, has the potential to disrupt current treatment practices, overcoming the inherent limitations by offering an effective treatment solution that can be delivered where it is needed, at scale, and by trained health workers rather than clinical psychologists. Given effective NF treatment can be provided by a single EEG channel, Pz, as demonstrated here, there is the potential to simplify and minimise the costs of the neurotechnology for treatment delivery at scale.

4.1. Limitations

The study findings presented here should be considered hypothesis generating and provide important information for future studies. However, care should be taken with interpretation, mainly due to two key limitations, which were sample size and the sparse coverage of the scalp with the FlexEEG montage. While the latter was necessary to test the efficacy of the FlexEEG, which a is a low-cost wearable headset, the limited surface coverage increases the probability of false negative results as it is difficult to find changes in uncovered regions. Furthermore, the ability to compare results from specific channels or adjust based on global baselines/trends, is restricted due to sparse coverage.

Regarding the sample, in the interests of efficiency, given the logistical challenges of the project, participants were recruited from a cohort of PTSD patients who had previously engaged in a study investigating the transgenerational transmission of PTSD, conducted at the University of Rwanda (UR), as the PTSD patient group (for details see Rudahindwa et al., 2018). For this previous study the experiment group were necessarily all female (they had been pregnant at the time of the genocide). Furthermore, the sample size was small – ideally, to reach 80% power, the sample would require 34 – 40 participants per group. Of further consequence, is that while all participants had a pre-existing diagnosis of PTSD, the diagnosis had been received approximately one-year prior to the onset of this study. Again, given the tight timeline for data-collection, clinical interviews for all three groups, were conducted within four days of the first intervention session, and within four days following the final intervention session. On analysis of the clinical

interview data, it was noted that three control, two MI group, and one NF group participant(s) did not meet the threshold for a diagnosis of PTSD at baseline. However, cultural variability in cut off scores has been documented in the literature (Blevins et al., 2015; Hiar et al., 2016; Prins et al., 2016; Prins and Ouimette, 2004; Sacchetti et al., 2020), and parameters have not yet been established for the Rwandan population.

All data collection for this study took place in public buildings, and it was difficult to eliminate noise from the environment. While the environment was therefore not an optimal experiment setting, in terms of adding ecological validity to the outcome of the process, this limitation can be considered a strength. The principal aim of the research was both, to determine whether the FlexEEG neurotechnology could effectively deliver NF to PTSD patients in Rwanda, and to establish what the impact of NF training provided in this way would have on subjective symptom severity. Therefore, it was necessary to assess the outcome of the training within the context, and under the conditions, that will be prevalent for the future use of the neurotechnology. To establish the efficacy of NF as a treatment for PTSD within African populations, more research is needed that includes a larger sample, of both genders; that looks at different causes of trauma; and studies participants from different cultures/geographical locations.

5. Conclusion

This research has demonstrated a clinically important effect of NF training on symptom severity for PTSD patients within a group of genocide survivors in Rwanda – representing the first evidence of a neurotechnological solution for the treatment of PTSD in Rwanda. Reduced symptom severity in PTSD patients through training self-regulation of alpha power has been shown previously, and is considered to be related to improved functional connectivity of intrinsic neural networks (Kluetsch et al., 2014), which facilitate fundamental processes that are not reliant on external stimulation (Thomann et al., 2017). In line with the findings of Kluetsch et al., 2014, the results presented here infer that the NF participants successfully achieved alpha 'rebound', or an increase in resting-state alpha following each training session, which has been associated with reduced anxiety (Kluetsch et al., 2014). While the findings for the MI group were not found to be significant, there was an observed decrease in the ratio index of parietal theta power to parietal alpha power for participants across BCI sessions, becoming more pronounced across the latter three (of six) sessions. Focus on task irrelevant information results in an increased parietal theta/alpha power ratio, therefore, a decrease across sessions supports improved CEN function and network switching (Emami and Chau, 2020). Importantly, the success of the NF training using the wearable, low-cost electroencephalography, within uncontrolled experimental conditions outside the laboratory, present evidence of a potential treatment for PTSD in Rwanda and other developing countries. Affordability and accessibility rank very high on the list of priorities when considering a treatment in the African context, as the most vulnerable are those who live in remote communities, where there are limited healthcare systems and poor transport infrastructures in place. This initial study will underpin the next stage of the research to conduct a large-scale randomised controlled trial that considers gender, patient groups and countries, with the goal of evidencing the efficacy of NF and/or MI treatment, to be promoted as a public health solution in developing countries – particularly in developing post-conflict countries.

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Declaration of Competing Interest

Prof Damien Coyle is Founder, CEO and shareholder of NeuroCONCISE Ltd, the supplier of the FlexEEG wearable Neurotechnology used in this study. The other authors declare no conflict of interest.

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References

Abdallah, C.G., Averill, C.L., Ramage, A.E., Averill, L.A., Goktas, S., Nemati, S., Krystal, J. H., Roache, J.D., Resick, P.A., Young-McCaughan, S., Peterson, A.L., Fox, P., 2019. Salience Network Disruption in U.S. Army Soldiers With Posttraumatic Stress Disorder. Chronic Stress 3, 247054701985046. https://doi.org/10.1177/2470547019850467.

Ahn, M., Cho, H., Ahn, S., Jun, S.C., 2013. High theta and low alpha powers may be indicative of BCI-illiteracy in motor imagery. PLoS One 8. https://doi.org/10.1371/journal.pone.0080886.

Ahn, M., Jun, S.C., 2015. Performance variation in motor imagery brain-computer interface: A brief review. J. Neurosci. Methods 243, 103–110. https://doi.org/10.1016/j.jneumeth.2015.01.033.

Alderson, T., Bokde, A.L.W., Kelso, J.A.S., Maguire, L., Coyle, D., 2018. Metastable neural dynamics in Alzheimer's disease are disrupted by lesions to the structural

connectome. Neuroimage 183, 438–455. https://doi.org/10.1016/J.NEUROIMAGE.2018.08.033.
Alderson, T.H., Bokde, A.L.W., Kelso, J.A.S., Maguire, L., Coyle, D., 2020. Metastable neural dynamics underlies cognitive performance across multiple behavioural paradigms. Hum. Brain Mapp. 1–23. https://doi.org/10.1002/hbm.25009.
Alimardani, M., Nishio, S., Ishiguro, H., 2014. Effect of biased feedback on motor imagery learning in BCI-teleoperation system. Front. Syst. Neurosci. 8, 1–8. https://doi.org/10.3389/fnsys.2014.00052.
Allman, J.M., Watson, K.K., Tetreault, N.A., Hakeem, A.Y., 2005. Intuition and autism: A possible role for Von Economo neurons. Trends Cogn. Sci. 9, 367–373. https://doi.org/10.1016/j.tics.2005.06.008.
Alonso, J., Petukhova, M., Vilagut, G., Chatterji, S., Heeringa, S., Üstün, T.B., Alhamzawi, A.O., Viana, M.C., Angermeyer, M., Bromet, E., Bruffaerts, R., De Girolamo, G., Florescu, S., Gureje, O., Haro, J.M., Hinkov, H., Hu, C.Y., Karam, E.G., Kovess, V., Levinson, D., Medina-Mora, M.E., Nakamura, Y., Ormel, J., Posada-Villa, J., Sagar, R., Scott, K.M., Tsang, A., Williams, D.R., Kessler, R.C., 2011. Days out of role due to common physical and mental conditions: Results from the WHO World Mental Health surveys. Mol. Psychiatry 16, 1234–1246. https://doi.org/10.1038/mp.2010.101.
Ang, K.K., Chin, Z.Y., Wang, C., Guan, C., Zhang, H., 2012. Filter bank common spatial pattern algorithm on BCI competition IV datasets 2a and 2b. Front. Neurosci. 6, 1–9. https://doi.org/10.3389/fnins.2012.00039.
Bell, A.N., 2018. Tuning the traumatized brain: Loreta Z-score neurofeedback and heart rate variability biofeedback for chronic PTSD. NeuroRegulation 5, 152–153. https://doi.org/10.15540/nr.5.4.150.
Bell, A.N., Moss, D., Kallmeyer, R.J., 2019. Healing the neurophysiological roots of trauma: A controlled study examining loreta z-score neurofeedback and HRV biofeedback for chronic PTSD. NeuroRegulation 6, 54–70. https://doi.org/10.15540/nr.6.2.54.
Bigirimana, A.D., Siddique, N., Coyle, D., 2020. Emotion-Inducing Imagery Versus Motor Imagery for a Brain-Computer Interface. IEEE Trans. Neural Syst. Rehabil. Eng. 28, 850–859. https://doi.org/10.1109/TNSRE.2020.2978951.
Blevins, C.A., Weathers, F.W., Davis, M.T., Witte, T.K., Domino, J.L., 2015. The Posttraumatic Stress Disorder Checklist for DSM-5 (PCL-5): Development and Initial Psychometric Evaluation. J. Trauma. Stress 28, 489–498. https://doi.org/10.1002/jts.
Bonnelle, V., Ham, T.E., Leech, R., Kinnunen, K.M., Mehta, M.A., Greenwood, R.J., Sharp, D.J., 2012. Salience network integrity predicts default mode network function after traumatic brain injury. Proc. Natl. Acad. Sci. U. S. A. 109, 4690–4695. https://doi.org/10.1073/pnas.1113455109.
Breslau, N., Kessler, R.C., Chilcoat, H.D., Schultz, L.R., Davis, G.C., Andreski, P., 1998. Trauma and Posttraumatic Stress Disorder in the Community. Arch. Gen. Psychiatry 55, 626–632. https://doi.org/10.4088/jcp.v69n0501.
Connor, K.M., Davidson, J.R.T., 2003. Development of a new Resilience scale: The Connor-Davidson Resilience scale (CD-RISC). Depress. Anxiety 18, 76–82. https://doi.org/10.1002/da.10113.
Coyle, D., Stow, J., McCreadie, K., McElligott, J., Carroll, Á., 2015. Sensorimotor modulation assessment and brain-computer interface training in disorders of consciousness. Arch. Phys. Med. Rehabil. 96, S62–S70. https://doi.org/10.1016/j.apmr.2014.08.024.
Deiber, M.P., Hasler, R., Colin, J., Dayer, A., Aubry, J.M., Baggio, S., Perroud, N., Ros, T., 2020. Linking alpha oscillations, attention and inhibitory control in adult ADHD with EEG neurofeedback. NeuroImage Clin 25, 102145. https://doi.org/10.1016/j.nicl.2019.102145.
Des Forges, A., 1999. Leave None to Tell the Story. Human Rights Watch, New York.
Emami, Z., Chau, T., 2020. The effects of visual distractors on cognitive load in a motor imagery brain-computer interface. Behav. Brain Res. 378, 1–10. https://doi.org/10.1016/j.bbr.2019.112240.
Emami, Z., Chau, T., 2018. Investigating the effects of visual distractors on the performance of a motor imagery brain-computer interface. Clin. Neurophysiol. 129, 1268–1275. https://doi.org/10.1016/j.clinph.2018.03.015.
g.NAUTILUS RESEARCH | Wearable EEG Headset | g.tec medical engineering [WWW Document], 2020. URL https://www.gtec.at/product/gnautilus-research/(accessed 5.24.20).
Gapen, M., van der Kolk, B.A., Hamlin, E., Hirshberg, L., Suvak, M., Spinazzola, J., 2016. A Pilot Study of Neurofeedback for Chronic PTSD. Appl. Psychophysiol. Biofeedback 41, 251–261. https://doi.org/10.1007/s10484-015-9326-5.
Goulden, N., Khusnulina, A., Davis, N.J., Bracewell, R.M., Bokde, A.L., McNulty, J.P., Mullins, P.G., 2014. The salience network is responsible for switching between the default mode network and the central executive network: Replication from DCM. Neuroimage 99, 180–190. https://doi.org/10.1016/j.neuroimage.2014.05.052.
Greicius, M.D., Krasnow, B., Reiss, A.L., Menon, V., 2003. Functional connectivity in the resting brain: A network analysis of the default mode hypothesis. Proc. Natl. Acad. Sci. U. S. A. 100, 253–258. https://doi.org/10.1073/pnas.0135058100.
Hiar, S., Thomas, C.L., Hinton, D.E., Salles, J., Goutaudier, N., Olliac, B., Bui, E., 2016. Somatic symptoms mediate the relationship between trauma during the arab spring and quality of life among tunisians. J. Nerv. Ment. Dis. 204, 153–155. https://doi.org/10.1097/NMD.0000000000000446.
Hinton, M., O'Donnell, M., Cowlishaw, S., Kartal, D., Metcalf, O., Varker, T., McFarlane, A.C., Hopwood, M., Bryant, R.A., Forbes, D., Howard, A., Lau, W., Cooper, J., Phelps, A.J., 2020. Defining post-traumatic stress disorder recovery in veterans: Benchmarking symptom change against functioning indicators. Stress Heal. https://doi.org/10.1002/smi.3019.
Huang, M.X., Yurgil, K.A., Robb, A., Angeles, A., Diwakar, M., Risbrough, V.B., Nichols, S.L., McLay, R., Theilmann, R.J., Song, T., Huang, C.W., Lee, R.R., Baker, D. G., 2014. Voxel-wise resting-state MEG source magnitude imaging study reveals neurocircuitry abnormality in active-duty service members and veterans with PTSD. NeuroImage Clin 5, 408–419. https://doi.org/10.1016/j.nicl.2014.08.004.
Jann, K., Dierks, T., Boesch, C., Kottlow, M., Strik, W., Koenig, T., 2009. BOLD correlates of EEG alpha phase-locking and the fMRI default mode network. Neuroimage 45, 903–916. https://doi.org/10.1016/j.neuroimage.2009.01.001.
Jokić-begić, N., Begić, D., 2003. Quantitative electroencephalogram (qEEG) in combat veterans with post-traumatic stress disorder (PTSD). Nord. J. Psychiatry 57, 351–355.
Kalisa, J., Schäfer, I., Püschel, K., Mutesa, L., Sezibera, V., 2019. Fostering the training of professionals to treat trauma and PTSD in Rwanda : a call for structured training curriculum.
Kessler, R.C., Sonnega, A., Bromet, E., Hughes, M., Nelson, C.B., 1995. Posttraumatic Stress Disorder in the. National Comorbidity Survey. Arch. Gen. Psychiatry 52, 1048–1060. https://doi.org/10.1001/archpsyc.1995.03950240066012.
Klimesch, W., 2012. Alpha-band oscillations, attention, and controlled access to stored information. Trends Cogn. Sci. 16, 606–617. https://doi.org/10.1016/j.tics.2012.10.007.
Kluetsch, R.C., Ros, T., Théberge, J., Frewen, P.A., Calhoun, V.D., Schmahl, C., Jetly, R., Lanius, R.A., 2014. Plastic modulation of PTSD resting-state networks and subjective wellbeing by EEG neurofeedback. Acta Psychiatr. Scand. 130, 123–136. https://doi.org/10.1111/acps.12229.
Korik, A., Sosnik, R., Siddique, N., Coyle, D., 2019. Decoding imagined 3D arm movement trajectories from EEG to control two virtual arms-a pilot study. Front. Neurorobot. 13, 1–22. https://doi.org/10.3389/fnbot.2019.00094.
Korik, A., Sosnik, R., Siddique, N., Coyle, D., 2018. Decoding imagined 3D hand movement trajectories from EEG: Evidence to support the use of mu, beta, and low gamma oscillations. Front. Neurosci. 12, 1–16. https://doi.org/10.3389/fnins.2018.00130.
Lambert, J.E., Holzer, J., Hasbun, A., 2014. Association Between Parents' PTSD Severity and Children's Psychological Distress: A Meta-Analysis. J. Trauma. Stress 27, 9–17. https://doi.org/10.1002/jts.21891.
Lanius, R.A., Frewen, P.A., Tursich, M., Jetly, R., McKinnon, M.C., 2015. Restoring large-scale brain networks in ptsd and related disorders: A proposal for neuroscientifically-informed treatment interventions. Eur. J. Psychotraumatol. 6, 1–12. https://doi.org/10.3402/ejpt.v6.27313.
Laufs, H., Holt, J.L., Elfont, R., Krams, M., Paul, J.S., Krakow, K., Kleinschmidt, A., 2006. Where the BOLD signal goes when alpha EEG leaves. Neuroimage 31, 1408–1418. https://doi.org/10.1016/j.neuroimage.2006.02.002.
Laufs, H., Kleinschmidt, A., Beyerle, A., Eger, E., Salek-Haddadi, A., Preibisch, C., Krakow, K., 2003. EEG-correlated fMRI of human alpha activity. Neuroimage 19, 1463–1476. https://doi.org/10.1016/S1053-8119(03)00286-6.
Lewis, S.J., Arseneault, L., Caspi, A., Fisher, H.L., Matthews, T., Moffitt, T.E., Odgers, C. L., Stahl, D., Teng, J.Y., Danese, A., 2019. The epidemiology of trauma and post-traumatic stress disorder in a representative cohort of young people in England and Wales. The Lancet Psychiatry 6, 247–256. https://doi.org/10.1016/S2215-0366(19)30031-8.
Lotte, F., Congedo, M., Lécuyer, A., Lamarche, F., Arnaldi, B., 2007. A review of classification algorithms for EEG-based brain-computer interfaces. J. Neural Eng. 4 https://doi.org/10.1088/1741-2560/4/2/R01.
Lotte, F., Guan, C., 2011. Regularizing common spatial patterns to improve BCI designs: Unified theory and new algorithms. IEEE Trans. Biomed. Eng. 58, 355–362. https://doi.org/10.1109/TBME.2010.2082539.
Lotze, M., Cohen, L.G., 2006. Volition and imagery in neurorehabilitation. Cogn. Behav. Neurol. 19, 135–140. https://doi.org/10.1097/01.wnn.0000209875.56060.06.
Mathworks, 2015. Simulink - Simulation and Model-Based Design - MATLAB & Simulink [WWW Document]. URL https://uk.mathworks.com/products/simulink.html (accessed 5.24.20).
McFarland, D.J., Miner, L.A., Vaughan, T.M., Wolpaw, J.R., 2000. Mu and beta rhythm topographies during motor imagery and actual movements. Brain Topogr 12, 177–186. https://doi.org/10.1023/A:1023437823106.
Menon, V., 2011. Large-scale brain networks and psychopathology: A unifying triple network model. Trends Cogn. Sci. 15, 483–506. https://doi.org/10.1016/j.tics.2011.08.003.
Millán, J.D.R., Rupp, R., Müller-Putz, G.R., Murray-Smith, R., Giugliemma, C., Tangermann, M., Vidaurre, C., Cincotti, F., Kübler, A., Leeb, R., Neuper, C., Müller, K.R., Mattia, D., 2010. Combining brain-computer interfaces and assistive

technologies: State-of-the-art and challenges. Front. Neurosci. 4, 1–15. https://doi.org/10.3389/fnins.2010.00161.
Mulder, T., 2007. Motor imagery and action observation: Cognitive tools for rehabilitation. J. Neural Transm. 114, 1265–1278. https://doi.org/10.1007/s00702-007-0763-z.
Munyandamutsa, N., Nkubamugisha, P.M., Gex-Fabry, M., Eytan, A., 2012. Mental and physical health in Rwanda 14 years after the genocide. Soc. Psychiatry Psychiatr. Epidemiol. 47, 1753–1761. https://doi.org/10.1007/s00127-012-0494-9.
Musanabaganwa, C., Jansen, S., Fatumo, S., Rutembesa, E., Mutabaruka, J., Gishoma, D., Uwineza, A., Kayiteshonga, Y., Alachkar, A., Wildman, D., Uddin, M., Mutesa, L., 2020. Burden of post-traumatic stress disorder in postgenocide Rwandan population following exposure to 1994 genocide against the Tutsi : A meta- analysis. J. Affect. Disord. 275, 7–13. https://doi.org/10.1016/j.jad.2020.06.017.
Neuper, C., Wörtz, M., Pfurtscheller, G., 2006. Chapter 14 ERD/ERS patterns reflecting sensorimotor activation and deactivation. Prog. Brain Res 159, 211–222. https://doi.org/10.1016/S0079-6123(06)59014-4.
Bazivamo, C., 2004. Dénombrement des victimes du génocide, Rapport Final, Version révisée.
Never again Rwanda [WWW Document], 2019. URL http://neveragainrwanda.org/reports/.
Nicholson, A.A., Rabellino, D., Densmore, M., Frewen, P.A., Paret, C., Kluetsch, R., Schmahl, C., Théberge, J., Ros, T., Neufeld, R.W.J., McKinnon, M.C., Reiss, J.P., Jetly, R., Lanius, R.A., 2018. Intrinsic connectivity network dynamics in PTSD during amygdala downregulation using real-time fMRI neurofeedback: A preliminary analysis. Hum. Brain Mapp. 39, 4258–4275. https://doi.org/10.1002/hbm.24244.
Nicholson, A.A., Ros, T., Frewen, P.A., Densmore, M., Théberge, J., Kluetsch, R.C., Jetly, R., Lanius, R.A., 2016. Alpha oscillation neurofeedback modulates amygdala complex connectivity and arousal in posttraumatic stress disorder. NeuroImage Clin 12, 506–516. https://doi.org/10.1016/j.nicl.2016.07.006.
Nunez, P.L., Wingeier, B.M., Silberstein, R.B., 2001. Spatial-temporal structures of human alpha rhythms: Theory, microcurrent sources, multiscale measurements, and global binding of local networks. Hum. Brain Mapp. 13, 125–164. https://doi.org/10.1002/hbm.1030.
OECD, 2019. Recommendation of the Council on Responsible Innovation in Neurotechnology [WWW Document]. Oecd/Legal/0457. URL. https://legalinstruments.oecd.org/en/instruments/OECD-LEGAL-0434.
Olff, M., Langeland, W., Gersons, B.P.R., 2005. The psychobiology of PTSD: Coping with trauma. Psychoneuroendocrinology 30, 974–982. https://doi.org/10.1016/j.psyneuen.2005.04.009.
Othmer, S., Othmer, S.F., 2009. Post Traumatic Stress Disorder—The Neurofeedback Remedy. Biofeedback 37, 24–31. https://doi.org/10.5298/1081-5937-37.1.24.
Pfurtscheller, G., Allison, B.Z., Brunner, C., Bauernfeind, G., Solis-Escalante, T., Scherer, R., Zander, T.O., Mueller-Putz, G., Neuper, C., Birbaumer, N., 2010. The hybrid BCI. Front. Neurosci. 4, 1–11. https://doi.org/10.3389/fnpro.2010.00003.
Pfurtscheller, G., Brunner, C., Schlögl, a, Lopes da Silva, F.H., 2006. Mu rhythm (de) synchronization and EEG single-trial classification of different motor imagery tasks. Neuroimage 31, 153–159. https://doi.org/10.1016/j.neuroimage.2005.12.003.
Pfurtscheller, G., Neuper, C., Flotzinger, D., Pregenzer, M., 1997. EEG-based discrimination between imagination of right and left hand movement. Electroencephalogr. Clin. Neurophysiol. 103, 642–651. https://doi.org/10.1016/S0013-4694(97)00080-1.
Pfurtscheller, G., Neuper, C., Guger, C., Harkam, W., Ramoser, H., Schlögl, A., Obermaier, B., Pregenzer, M., 2000. Current trends in Graz Brain-Computer Interface (BCI) research. IEEE Trans. Rehabil. Eng. 8, 216–219. https://doi.org/10.1109/86.847821.
Pohjalainen, J., Räsänen, O., Kadioglu, S., 2015. Feature selection methods and their combinations in high-dimensional classification of speaker likability, intelligibility and personality traits. Comput. Speech Lang. 29, 145–171. https://doi.org/10.1016/j.csl.2013.11.004.
Prasad, G., Herman, P., Coyle, D., McDonough, S., Crosbie, J., 2010. Applying a brain-computer interface to support motor imagery practice in people with stroke for upper limb recovery: a feasibility study. J. Neuroeng. Rehabil. 7, 60. https://doi.org/10.1186/1743-0003-7-60.
Prins, A., Bovin, M.J., Smolenski, D.J., Marx, B.P., Kimerling, R., Jenkins-Guarnieri, M. A., Kaloupek, D.G., Schnurr, P.P., Kaiser, A.P., Leyva, Y.E., Tiet, Q.Q., 2016. The Primary Care PTSD Screen for DSM-5 (PC-PTSD-5): Development and Evaluation Within a Veteran Primary Care Sample. J. Gen. Intern. Med. 31, 1206–1211. https://doi.org/10.1007/s11606-016-3703-5.
Prins, A., Ouimette, P., 2004. Erratum: The Primary Care PTSD screen (PC-PTSD): Development and Operating Characteristics (Primary Care Psychiatry)). Prim. Care Psychiatry 9, 151.
Reiter, K., Andersen, S.B., Carlsson, J., 2016. Neurofeedback treatment and posttraumatic stress disorder:Effectiveness of neurofeedback on posttraumatic stress disorder and the optimal choice of protocol. J. Nerv. Ment. Dis. 204, 69–77. https://doi.org/10.1097/NMD.0000000000000418.
Resnick, H.S., Kilpatrick, D.G., Dansky, B.S., Saunders, B.E., Best, C.L., 1993. Prevalence of Civilian Trauma and Posttraumatic Stress Disorder in a Representative National Sample of Women. J. Consult. Clin. Psychol. 61, 984–991.
Ros, T., Baars, B.J., Lanius, R.A., Vuilleumier, P., 2014. Tuning pathological brain oscillations with neurofeedback: A systems neuroscience framework. Front. Hum. Neurosci. 8, 1–22. https://doi.org/10.3389/fnhum.2014.01008.
Ros, T., Théberge, J., Frewen, P.A., Kluetsch, R., Densmore, M., Calhoun, V.D., Lanius, R. A., 2013. Mind over chatter: Plastic up-regulation of the fMRI salience network directly after EEG neurofeedback. Neuroimage 65, 324–335. https://doi.org/10.1016/j.neuroimage.2012.09.046.
Rudahindwa, S., Mutesa, L., Rutembesa, E., Mutabaruka, J., Qu, A., Wildman, D.E., Jansen, S., Uddin, M., 2018. Transgenerational effects of the genocide against the Tutsi in Rwanda: A post-traumatic stress disorder symptom domain analysis. AAS Open Res 1, 10. https://doi.org/10.12688/aasopenres.12848.1.
Rusiniak, M., Wróbel, A., Cieśla, K., Pluta, A., Lewandowska, M., Wójcik, J., Skarżyński, P.H., Wolak, T., 2014. The relationship between alpha burst activity and the default mode network. Acta Neurobiol Exp 78, 92–106. https://doi.org/10.21307/ane.
Sacchetti, E., Garozzo, A., Mussoni, C., Liotta, D., Novelli, G., Tamussi, E., Deste, G., Vita, A., 2020. Post-traumatic stress disorder and subthreshold post-traumatic stress disorder in recent male asylum seekers: An expected but overlooked "European" epidemic. Stress Heal 36, 37–50. https://doi.org/10.1002/smi.2910.
Sannelli, C., Vidaurre, C., Müller, K.R., Blankertz, B., 2019. A large scale screening study with a SMR-based BCI: Categorization of BCI users and differences in their SMR activity. PLoS ONE. https://doi.org/10.1371/journal.pone.0207351.
Sareen, J., 2014. Posttraumatic stress disorder in adults: Impact, comorbidity, risk factors, and treatment. Can. J. Psychiatry 59, 460–467. https://doi.org/10.1177/070674371405900902.
Schaal, S., Elbert, T., 2006. Ten Years After the Genocide: Trauma Confrontation and Posttraumatic Stress in Rwandan Adolescents. J. Trauma. Stress 19, 95–105.
Schlögl, A., Neuper, C., Pfurtscheller, G., 2002. Estimating the Mutual Information of an EEG-based Brain-Computer Interface. Biomed. Tech. Eng. 47, 3–8. https://doi.org/10.1515/bmte.2002.47.1-2.3.
Schwarzer, R., Jerusalem, M., 1995. Generalized Self-Efficacy scale, in: Measures in Health Psychology: A User's Portfolio. Causal and Control Beliefs 35–37.
Seeley, W.W., Menon, V., Schatzberg, A.F., Keller, J., Glover, G.H., Kenna, H., Reiss, A.L., Greicius, M.D., 2007. Dissociable intrinsic connectivity networks for salience processing and executive control. J. Neurosci. 27, 2349–2356. https://doi.org/10.1523/JNEUROSCI.5587-06.2007.
Sherman, M.D., Gress Smith, J.L., Straits-Troster, K., Larsen, J.L., Gewirtz, A., 2016. Veterans' perceptions of the impact of PTSD on their parenting and children. Psychol. Serv. 13, 401–410. https://doi.org/10.1037/ser0000101.
Smigelsky, M.A., Aten, J.D., Gerberich, S., Sanders, M., Post, R., Hook, K., Ku, A., Boan, D.M., Monroe, P., 2014. Trauma in sub-Saharan Africa: review of cost, estimation methods, and interventions. Int. J. Emerg. Ment. Health 16, 354–365. https://doi.org/10.4172/1522-4821.1000129.
Smith, B.W., Dalen, J., Wiggins, K., Tooley, E., Christopher, P., Bernard, J., 2008. The brief resilience scale: Assessing the ability to bounce back. Int. J. Behav. Med. 15, 194–200. https://doi.org/10.1080/10705500802222972.
Sridharan, D., Levitin, D.J., Menon, V., 2008. A critical role for the right fronto- insular cortex in switching between central-executive and default-mode networks. PNAS 105, 12569–12574. https://doi.org/10.1016/S0076-695X(08)60303-8.
Stewart-Brown, S., Janmohamed, K., 2008. Warwick-Edinburgh Mental Well-being Scale (WEMWBS), User Guide. Version, 1.
Tay, A.K., Mohsin, M., Rees, S., Steel, Z., Tam, N., Soares, Z., Baker, J., Silove, D., 2017. The factor structures and correlates of PTSD in post-conflict Timor-Leste: An analysis of the Harvard Trauma Questionnaire. BMC Psychiatry 17, 1–11. https://doi.org/10.1186/s12888-017-1340-0.
Tennant, R., Hiller, L., Fishwick, R., Platt, S., Joseph, S., Weich, S., Parkinson, J., Secker, J., Stewart-Brown, S., 2007. The Warwick-Dinburgh mental well-being scale (WEMWBS): Development and UK validation. Health Qual. Life Outcomes 5, 1–13. https://doi.org/10.1186/1477-7525-5-63.
Thomann, A.K., Griebe, M., Thomann, P.A., Hirjak, D., Ebert, M.P., Szabo, K., Reindl, W., Wolf, R.C., 2017. Intrinsic neural network dysfunction in quiescent Crohn's. Disease. Sci. Rep. 7, 1–10. https://doi.org/10.1038/s41598-017-11792-y.
Thompson, M.C., 2019. Critiquing the Concept of BCI Illiteracy. Sci. Eng. Ethics 25, 1217–1233. https://doi.org/10.1007/s11948-018-0061-1.
Unity Technologies, 2020. Unity Real-Time Development Platform | 3D, 2D VR & AR Visualizations [WWW Document]. Unity Technol. URL https://unity.com/ (accessed 5.24.20).
Valdes-Sosa, P.A., 2012. Coping with brain disorders using neurotechnology. Malaysian J. Med. Sci. 19, 1–3.
Van Der Kolk, B.A., Hodgdon, H., Gapen, M., Musicaro, R., Suvak, M.K., Hamlin, E., Spinazzola, J., 2016. A randomized controlled study of neurofeedback for chronic PTSD. PLoS One 11. https://doi.org/10.1371/journal.pone.0166752.

Varker, T., Kartal, D., Watson, L., Freijah, I., O'Donnell, M., Forbes, D., Phelps, A., Hopwood, M., McFarlane, A., Cooper, J., Wade, D., Bryant, R., Hinton, M., 2020. Defining response and nonresponse to posttraumatic stress disorder treatments: A systematic review. Clin. Psychol. Sci. Pract. 27, 1–36. https://doi.org/10.1111/cpsp.12355.

Wahbeh, H., Oken, B.S., 2013. Peak high-frequency HRV and peak alpha frequency higher in PTSD. Appl. Psychophysiol. Biofeedback 38, 57–69. https://doi.org/10.1007/s10484-012-9208-z.

Yuan, H., He, B., 2014. Brain-computer interfaces using sensorimotor rhythms: Current state and future perspectives. IEEE Trans. Biomed. Eng. 61, 1425–1435. https://doi.org/10.1109/TBME.2014.2312397.

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