eNeuro

Research Article: New Research | *Cognition and Behavior*

Alpha neurofeedback has a positive effect for participants who are unable to sustain their alpha activity

https://doi.org/10.1523/ENEURO.0498-18.2019

Cite as: eNeuro 2019; 10.1523/ENEURO.0498-18.2019

Received: 19 December 2018
Revised: 16 April 2019
Accepted: 24 April 2019

Alpha neurofeedback has a positive effect for participants who are unable to sustain their alpha activity

Abbreviated Title: Sustenance of alpha with neurofeedback

Ankan Biswas[1] and Supratim Ray[1*]

[1]Centre for Neuroscience, Indian Institute of Science, Bangalore, India

AB and SR designed research, analyzed data, wrote the paper. AB performed research.

*Correspondence:

Supratim Ray

sray@iisc.ac.in

Number of figures: 4

Number of tables: 0

Number of Multimedia: 0

Number of words: Abstract: 250, Significance statement: 120 Introduction: 625, Discussion: 2396

Acknowledgements:

We thank Siddhesh Salelkar and Dakshitha Anand for their help in writing the custom Matlab codes required for the experiment. We also thank Vinay Shirhatti, DVPS Murty and Aritra Das for helpful comments and discussions.

Conflict of Interest: The authors declare no competing financial interests.

Funding Sources:

This work was supported by Wellcome Trust/DBT India Alliance (500145/Z/09/Z; Intermediate fellowship to SR), Tata Trusts Grant and DBT-IISc Partnership Programme.

Abstract

Alpha rhythm (8-13 Hz) is linked to relaxed mental state in humans. Earlier reports have shown that individuals can increase their alpha power if provided with a valid feedback, compared to controls who are provided invalid feedback. However, these results remain controversial, partly because controls may be in a different behavioural state, making it difficult to directly compare their alpha power with the valid group. We here address this issue by using an experimental paradigm in which an invalid feedback is given on a fraction of trials, such that both valid and invalid conditions can be obtained from the same participant. Using EEG, we recorded alpha power from the occipital area from 24 humans (9 females) and played a feedback tone which could be valid (tone frequency proportional to alpha power), invalid (tone sequence from a previous valid trial; participants were unaware of this condition), or neutral (constant tone frequency). We found that during eyes closed-state, neurofeedback did not enhance alpha activity beyond pre-trained state within the experimental duration, probably because of saturation of alpha rhythmicity. However, for participants whose alpha power decreased over time within a trial, valid feedback helped them to sustain alpha more than invalid feedback. Further, alpha increase showed a weak negative correlation with their self-reported attentional load but was uncorrelated with relaxation levels. Our results reconcile many conflicting reports in the neurofeedback literature, and show that even under most stringent control, valid neurofeedback can help participants who are otherwise unable to sustain their alpha activity.

Significance Statement

We tested whether providing a real time auditory feedback about the strength of the EEG alpha rhythm helps the participants increase their alpha power. Unlike previous neurofeedback studies that used valid and invalid feedback on different participant groups, we used a design in which valid, invalid and neutral feedback were given to the same participant. We found that for participants whose alpha power reduced over time within a trial, valid feedback helped to sustain the rhythm better than invalid feedback. Further, feedback appeared to be more useful for participants who did not attend the tone. These findings can be used to better screen and design neurofeedback training paradigm, which is now used to treat patients suffering from anxiety and depression.

Introduction

In electroencephalogram (EEG) signals, a brain rhythm in the frequency range between 8-13 Hz, called alpha, is prominently observed in the occipital area of many individuals, especially during an awake and relaxed state with eyes closed (Berger, 1929; Adrian and Matthews, 1934). Although alpha was traditionally believed to be an idling rhythm, recent studies have linked alpha rhythm with high-level cognitive mechanisms such as attention (Kelly et al., 2006a; Klimesch et al., 2007), information retrieval (Klimesch, 2012), and creativity (Fink and Benedek, 2014). Therefore, it has been suggested that learning to control the alpha activity may have a positive effect on the mental state (Escolano et al., 2011; Klimesch, 2012; Nan et al., 2012; Zoefel et al., 2011).

Alpha neurofeedback involves providing individuals a real-time feedback about their alpha power (Kamiya, 2011, 1969), which is typically provided by a tone (Dempster and Vernon, 2009; Kamiya, 1969; Plotkin, 1978; van Boxtel et al., 2012) , or occasionally by a visual signal (Brown, 1970; Dempster and Vernon, 2009; Ros et al., 2013, 2010). Early neurofeedback studies reported that participants could learn to enhance their alpha activity with the aid of neurofeedback training (Kamiya, 1969; Brown, 1970; Nowlis and Kamiya, 1970; Hord and Barber, 1971; Hardt and Kamiya, 1976), which could further have a beneficial effect on their behavioural state, such as reduction in anxiety (Garrett and Silver, 1976; Hardt and Kamiya, 1978) or sleep need (Regestein et al., 1973). However, these findings were subsequently challenged, because the constitutional, physiological and cognitive-attentional state of the participant could vary during training, and that itself could change alpha power (for a review, see Lynch and Paskewitz, 1971; Plotkin and Rice, 1981; Rice and Blanchard, 1982). For example, participants may be anxious/attentive during the beginning because of an unfamiliar setting and may get more relaxed during the training. This alone could increase alpha power over time, irrespective of feedback.

One way to address this concern is to have a "control" group to which invalid or no feedback is provided. Early studies that employed such controls gave conflicting results, with some studies showing an increase in alpha even with no/invalid feedback (Lindholm and Lowry, 1978; Lynch et al., 1974; Strayer et al., 1973), while others showing no increase without valid feedback (Beatty, 1972, 1971). Some studies attributed this discrepancy to methodological differences (Ancoli and Kamiya, 1978; Hardt and Kamiya, 1976; Paskewitz and Orne, 1973; Vernon et al., 2009; Walsh, 1974). Others have suggested that even this design is not sufficient (Biswas and Ray, 2017; Rogala et al., 2016), since the behavioural state of the control and contingent groups may be different. For example, the control group may stop paying attention to the feedback if they realize that it is not helping them. Further, small effects may not be observed due to large inter-participant variability in alpha power across the contingent and control groups (Haegens et al., 2014). To address these concerns, a design is needed in which each participant could potentially be his/her own control (Biswas and Ray, 2017).

To address this, we designed an experiment in which we provided invalid feedback (representing alpha activity from a trial in a previous block) to the participants in 25% of trials, along with valid (50%) and no feedback (25%). The participants were completely unaware about the invalid trials, and therefore the behavioural conditions (for example, amount of attention paid to the feedback tone) were identical to the valid case. We then investigated whether valid feedback had a stronger effect on alpha power than invalid feedback. Further, in our design the participants were free to either use or ignore the feedback, which allowed us to study the correlation between enhancement of alpha power with subjective attention and relaxation levels, which participants provided after the task.

Materials and Methods

Participants

Twenty-four healthy volunteers (mean age: 23.9 years, females: 9) participated in the study. The protocol used for EEG recording was approved by the Institutional Human Ethics Committee of the [Author University]. Prior to conducting the experiment, the participants were briefed about the experimental procedures (see below) and the risks involved, after which written informed consent was obtained. Participants were requested to sit comfortably in front of a computer monitor and to avoid any unnecessary movements during the experiment.

Experimental Paradigm

The experiment was divided into 5 sessions. Each session consisted of a calibration stage (15 seconds), followed by 12 trials of 50 seconds each (Figure 1A). There were three types of trials: valid, invalid, and neutral/constant. During valid trials, the frequency of the feedback tone was directly proportional to the change in alpha power from baseline (computed during the calibration phase). During invalid trials, which were presented from the second session onwards, one of the valid trials from the first session was chosen and the tone sequence for that session was presented. For constant trials, the frequency of the feedback tone was kept constant throughout the trial. The first session (termed "pre-training" phase because the subjects were naïve to the task) consisted of 3 constant and 9 valid trials. From the second session onwards, 3 invalid trials were presented in each session, along with 3 constant and 6 valid trials. The participants were not informed about the invalid trials, so for them, the trial composition was 25% constant and 75% valid for each of the 5 sessions (the actual composition from second session onwards was 50% valid, 25% invalid and 25% constant).

The entire trial sequence was generated pseudo-randomly for each participant at the beginning of the experiment. Please note that the first session was not used for analysis because it had no invalid trials and the participants were getting accustomed to the task during this session. However, including the first session data for the analysis yielded very similar results (not shown).

Each session started with a calibration process, in which participants were asked to keep their eyes open without blinking. The calibration process yielded a "baseline" value of the alpha power (average alpha power between 6-15 seconds), which was used for calibrating the pitch of the feedback tone for that session. The calibration process was occasionally repeated if the participants blinked or there was any movement artefact (assessed by manual inspection of the time-frequency spectrum of the EEG signal that showed a broadband response due to such artefacts), although this happened rarely. We did not implement any online artefact rejection. During the neurofeedback training, participants had their eyes closed, so no significant artefacts were observed related to eye movement/blink.

During each trial, for the first 15 seconds, participants were asked to keep their eyes open. From 6^{th} second onwards, a tone was played whose frequency was modulated in three different ways depending on the trial type, as described above. Fifteen seconds after the trial onset, a message was displayed on the monitor screen instructing participants to close their eyes and relax as much as possible. The participants were instructed to try to maximize a "performance score", which reflected the average change in alpha power from the baseline power (measured during calibration time) in the interval between 21 and 50 seconds after trial onset and was displayed at the end of the trial on the monitor screen. This score reflected the true change in power, irrespective of the trial type. Once the trial ended, the tone stopped, and the experimenter asked the participant to open his/her eyes and view their performance score. There was no fixed inter-trial interval; the participants simply indicated by a hand gesture to the experimenter whenever they wanted to start the next trial. The total duration of the experiment was about 1.5 hours.

Importantly, participants were told that the pitch of the feedback tone in non-constant trials was proportional to the relaxation score, but they were not instructed to explicitly pay attention to the feedback tone. Specifically, they were told that they had the liberty to use the feedback tone to improve performance but could also ignore the feedback tone if they felt it was distracting and was not aiding them in increasing the performance score. Indeed, different participants used different strategies, as revealed by their responses to a questionnaire presented at the completion of all the sessions.

Questionnaire

After the experiment, all the participants were required to fill up a questionnaire consisting of the following four questions. A) Was the task relaxing? (Relaxation score: 1 - not at all relaxing, 10 - very relaxing). B) Was the tone acting as a source of disturbance? (Distraction score: 1 -not disturbing, 10 - very disturbing). C) Were you using the feedback provided by the tone? (Attention score: 1 - ignored the tone completely, 10 - paid attention to the tone as much as possible). D) Which method or technique were you using to relax?

Because we asked the participants to fill out the questionnaire only at the end of the experiment, this single evaluation might have been biased by the most recent and vivid experience of the last session only. This issue could have been partially addressed if we had asked them to provide a response at the end of each session (or even perhaps each trial). However, answering questions after each session could have disrupted the continuity of the training/learning and would have increased the duration of the study. Also, we were more interested in the overall effect of neurofeedback that was experienced for the entire duration of the study.

EEG Setup and Data Acquisition

EEG signals were recorded from all the participants using Brain Amp DC EEG acquisition system (Brain Amp DC, Brain Products GmbH). Five electrodes were placed on the occipital region (PO3, O1, O3, O2, PO4) following international 10-20 standard reference scheme. FCz was used as a reference electrode. Impedance value was kept less than 10 k ohms for all the electrodes. Raw EEG signal was sampled at 500 Hz, filtered between 0.016 Hz (first-order filter) and 250 Hz (fifth-order Butterworth filter) and was digitalized at 16-bit resolution (0.1 µV/bit).

Real-time Neurofeedback System Design

The feedback system was developed using custom written codes in Matlab (MathWorks Inc., RRID: SCR_001622) and standard socket programming. TCP/UDP/IP Matlab toolbox (Version: 2.0.6, GNU General Public License) function *pnet* was used to create a TCP/IP connection between the machine hosting Matlab and the RDA server of Brain Vision Recorder, which is the proprietary software provided by Brain Products GmbH. Raw data was acquired from the RDA server via TCP/IP protocol into the system port where Matlab was running. Once the number of data points in the port matched the sampling frequency at which EEG data was acquired by the Brain Vision Recorder (one second of data), it was further processed in Matlab for power estimation.

Power of this one second long signal was estimated using multi taper method using a single taper, implemented in the Chronux package (Bokil et al., 2010), yielding a frequency resolution of 1 Hz. Power was first averaged across electrodes, and then averaged over the alpha range (8-13 Hz) to get alpha power. Because the alpha power varied considerably over time, we took the average power over previous five seconds for generating the feedback tone (see the dotted line in Figure 1C). Consequently, the feedback tone could be provided only from 6th second onwards. We calculated the change in alpha power as follows:

$$\Delta P_{\alpha}(t) = 10 \times \log_{10} \frac{P_e(t)}{P_c} \qquad \text{(Eqn:1)}$$

where $\mathbf{\Delta}P_{\alpha}$ denotes the change in alpha power in decibel (dB) calculated at time t; P_e is the mean alpha power over a 5 second interval preceding t, and P_c is the mean alpha power during the calibration period (taken only once per session). The frequency of the feedback tone (Fs, in Hz), played to the participants using a speaker located in front of them, was calculated according to the following equation:

$$F_s(t) = 1000 + \Delta P_{\alpha}(t) \times 500 \qquad \text{(Eqn:2)}$$

Please note that for estimating alpha power, we did not bandpass filter the EEG data, but instead used multi-taper method and averaged the power in the alpha band instead. Further, this analysis was performed separately at each second of data, and hence there was no overlap in the analysis windows (although we averaged power estimates over the previous five seconds for generating the feedback tone). Once the tone frequency was estimated (equation 2), the tone was generated for one second. The delay between subsequent feedback tone signals was limited to the computational time to perform these analyses once data was collected for that second. Behaviorally, successive feedback tones appeared almost instantaneously with no gap, suggesting that the computation time was negligible.

Statistical Analysis:

All statistical analyses were performed in Matlab (MathWorks Inc.). One-sample two-tailed t-test was used at significance level $\alpha = 0.05$ to check whether the slopes of the regression lines were significantly different from zero. To check whether mean alpha power duirng valid trials was significnaly different compared to invalid trials, two-sample one-tailed t-test was performed at the significance level $\alpha = 0.05$ assuming unequal variances. Bonferroni correction was done to adjust the significance level to $\alpha = 0.0021$ (0.05/24) whenever multiple comparisons across 24 participants were required.

Results

We recorded EEG (Brain Amp DC, Brain Products GmbH) from 24 healthy young adults using 5 active electrodes covering the occipital area. Figure 1A shows the experimental paradigm, which consisted of 60 trials of 50 seconds each, divided into 5 sessions. An auditory feedback was provided in each trial, which could be valid (red), invalid (green; given only from second session onwards), or a constant tone (blue).

Figure 1B shows the change in time-frequency power (in dB) in one valid trial (Trial 16), from a "baseline" power computed in a calibration stage just before the start of the session (in this case, before Trial 13). Alpha power was enhanced by more than 5 dB as soon as this participant closed eyes (16th second onwards) and remained high until the end of the trial (50th second). Figure 1C shows the change in alpha power over time, calculated by averaging the power in the alpha band (between the dotted black lines shown in Figure 1B), which showed a transient peak at the 16th second just when the eyes were closed, and remained high thereafter. This change in alpha power was averaged over a 5-second window (dotted line) and used to set the frequency of the feedback tone (green trace).

Figure 1D shows the alpha power for all trials for this participant, during eye closed (21-50 seconds after stimulus onset; filled triangles) and eye open (6-15 seconds, open circles) states. The baseline power used for setting the feedback tone frequency (same value for each trial within a session) is shown by a black line, which was comparable to the alpha power during the eyes open state. To test whether feedback training enhanced alpha power over time, we performed linear regression analysis between alpha power and trial number (starting from session 2). For this subject, the slopes were not significant for either eye open or eye closed conditions (Eyes open: Slope = 0.002±0.001, t (47) =1.903, p=0.063; Eyes closed:

Slope = 0.002±0.002, t (47) =0.655, p=0.516). Results were similar when the analysis was restricted to trials of the same type (data not shown).

Across the population of 24 participants, the mean slopes of alpha power versus trial number were 0.002±0.0005 and 0.001±0.0006 for eyes open and eyes closed states, respectively. For eyes open condition, the mean slope was significantly different from zero (N=24, t (23) = 2.936, p=0.007). However, the behaviour of the participants was not well controlled during this condition; it is possible that they made different strategies during this phase early during the experimental session, which could have lowered their alpha power. Importantly, the slopes were not significantly different from zero (N=24, t (23) = 1.594, p=0.125) during the eyes closed condition, during which their behaviour was more controlled, and their alpha power was much higher than the eyes open condition. Therefore, during the eyes closed period, neurofeedback training did not significantly enhance alpha power over the entire course of the experiment.

To test whether the type of feedback had any effect on alpha power within a trial, we plotted the change in alpha power from baseline averaged over the three trial types (Figure 1E). For all trial types, a peak was observed as soon as this participant closed the eyes (16^{th} second), which may be the "alpha squeak" effect upon eye closure (van Leeuwen et al., 1960). During the later period (after ~25 seconds), however, alpha power decreased for the invalid and constant trials, but remained relatively more elevated for valid trials. To quantify this, we again performed linear regression analysis between change in alpha power and time between 21-50 seconds. For this subject, slopes were significantly negative for invalid and constant trials, but not for valid trials. Consequently, the average change in alpha power was about ~1 dB larger for valid as compared to invalid trials (7.43 versus ~6.47 dB). Note that although the invalid condition had the same stimulus statistics and presumably the same behavioural state as the valid one, the alpha power for invalid condition was actually more similar to the constant condition for which the tone was constant and un-informative.

Figure 2 shows the same analysis as shown in Figure 1E for all 24 participants, sorted in decreasing order of significance of the difference in mean alpha power (averaged between 21-50 seconds) between valid and invalid conditions. The alpha power between valid and invalid conditions was significantly different for 11 (6 after Bonferroni correction for the number of participants) out of 24 participants, suggesting that the effect of neurofeedback was subtle and not applicable to all participants. Interestingly, like Figure 1E, alpha power in the invalid condition was similar to the constant condition for several subjects who showed a positive effect of neurofeedback, even though the stimulus and behavioural aspects for invalid condition were matched to the valid condition. This suggests that the evolution of alpha power over time may actually depend on the 'usefulness' or 'information' provided by the feedback, since both invalid and constant trials were, on average, equally un-informative.

A closer look at Figure 2 revealed an interesting trend for the participants who showed a significant effect: for most of these participants, alpha power appeared to decrease over time, suggesting that these participants could not sustain their alpha rhythm. To quantify this effect, for each participant, we plotted the slope of alpha power versus time for the constant trials (blue line in Figure 1E) versus the overall change in alpha power between the valid and invalid conditions (Figure 3). Indeed, the participants who showed a significant increase in alpha power also tended to have negative slopes, and there was a strong negative correlation between the two variables (Slope = -7.668 ± 1.591, t (23) = -4.817, $p = 8.22\times10^{-5}$). This suggests that neurofeedback mainly helped participants increase their alpha power who could not otherwise maintain their alpha activity.

Finally, we tested whether the change in alpha power was correlated with subjective experience (Figure 4). Interestingly, we found a negative trend between change in power and how much participants paid attention to the feedback tone (Figure 4A; Slope = -0.130 ± 0.076, t (23) = -1.703, p = 0.103); the results failed to reach significance only because of one outlier participant who completely ignored the tone; removing this participant from analysis yielded a slope of -0.261 ± 0.086, t (22) = -3.036, p = 0.006) suggesting that participants who were actively attending to the feedback tone did not benefit from neurofeedback. Indeed, the participants who had the strongest effect of neurofeedback (Participants 1-6, filled black triangles) were the ones who were neither fully attending nor fully ignoring the tone. There was, however, no such trend between alpha power and the participant's self-reported level of relaxation (Figure 4B; Slope = -0.127 ± 0.189, t (23) = -0.670, p = 0.510) or whether they were disturbed by the tone (Figure 4C, Slope = 0.077 ± 0.080, t (23) = 0.964, p = 0.346). However, all the participants reported relaxation score of 5 and above (mean score 7.958 ± 0.213), indicating that they felt relaxed after the neurofeedback task (Figure 4B).

Discussion

Using a novel design in which each participant was his/her own control, we tested whether participants were able to enhance their alpha power with valid neurofeedback more than false or no feedback. We found no enhancement of alpha power (during eyes closed state) over trials, although valid neurofeedback was provided during the major part of the experiment (33 out of the 60 trials; 50 seconds each). However, we found that in participants who could not sustain their alpha power, providing valid neurofeedback helped in sustaining alpha power within a trial more than when false or no feedback was provided. Surprisingly, participants who showed enhancement in alpha power with valid neurofeedback were the ones who did not pay too much attention to the neurofeedback tone. Overall, our results suggest that alpha neurofeedback, even when compared against a very stringent control condition, can help in the maintenance of the alpha power in some participants, and further recommend "passive attention" to the neurofeedback for best results.

Comparison with previous studies

Our results are consistent with earlier studies where alpha enhancement beyond pre-training levels was not observed (Cho et al., 2008a; Lynch and Paskewitz, 1971; Lynch et al., 1974; Paskewitz and Orne, 1973; Plotkin, 1978, 1979; van Boxtel et al., 2012; Walsh, 1974), and in contrast to studies which reported alpha enhancement (Brown, 1970; Hart, 1968; Kamiya, 1969). The temporal profile of alpha power, which tended to decrease with time, as well as the effect of neurofeedback, which helped to better maintain the power at elevated levels, are also in line with a previous study (Cho et al., 2008).

As discussed earlier, in our experimental design, the duration of feedback was short (50 seconds per trial), and valid feedback was inter-mixed with neutral and false feedback, in order to minimize the difference between valid and invalid conditions. We were especially concerned that prolonged invalid feedback might evoke a "surprise effect" because the feedback may be very different from what the participant may be feeling, or the participant may start ignoring the feedback if they realized that it was not valid or useful. Although such effects cannot be completely ruled out even in our design (in fact, in any neurofeedback design), having short duration of invalid feedback trials and inter-mixing these with a higher proportion of valid/neutral trials is likely to reduce these effects. Also, previous studies have typically used taped feedback from a different, control group of participants (Fath et al., 1976; Hammond, 2005; Nan et al., 2012; Watson and Herder, 1980; Zoefel et al., 2011) or feedback based on a different frequency band (Egner et al., 2002; van Boxtel et al., 2012). The rate at which power varies in another individual or in a different frequency band is likely to be different, such that the statistics of the feedback signal (for example, how fast it varies with time) itself may be different across valid and invalid conditions, leading to a larger "surprise effect". Further, it is possible that alpha power may depend on how the feedback tone varies over time (irrespective of the trial type), which may be different for valid versus invalid conditions in previous studies. In our study, these confounds are largely ruled out because the invalid feedback tone was based on the subjects' own alpha power during a previous, valid trial. Therefore, the statistics of the tone signal was identical for valid versus invalid conditions. Indeed, when we asked the participants (after the completion of recording from all the participants) about the existence of the third (invalid) type of trials, all the participants who were reachable and remembered the experimental details (18 out of 24) were ignorant about the invalid trials (we did not ask the participants about the existence of the invalid trials immediately after their own recording because of the possibility of the inter-participant discussion about the experimental details). Further, keeping a short trial duration ensured that participants did not get drowsy or tired during the trial, which may also influence alpha power.

Although our design minimized the differences between valid and invalid conditions, the absolute effect of neurofeedback may be much smaller than previous studies For example, Ancoli and Kamiya (Ancoli and Kamiya, 1978) suggested three critical factors to see positive effects of alpha feedback training, namely (a) training for at least four sessions (2 hours), (b) using continuous tone for feedback along with periodic scores of progress, and (c) using training trials with duration of at least 10 minutes. Thus, it is possible that more training sessions either on the same day or on different days could have led to long term alpha enhancement, as observed in previous studies (Dekker et al., 2014; van Boxtel et al., 2012). Also, since we had a rather low ratio of valid to invalid trials (2:1), learning during training through operant conditioning may have been inefficient. In our design, the ratio was kept at 2:1 to have enough trials in each type (valid, invalid and constant) to compare the effect of the neurofeedback training across type types. A lower proportion of invalid trials would have increased the duration of each experiment, which could have other disadvantages such as changes in the state of the subject due to drowsiness and fatigue, or changes in the impedance of the EEG electrodes. Further, as trials of different types were presented randomly, there might be a "carryover" effect of the training from one trial to the next. To reduce this effect, we provided sufficiently long inter-trial interval; participants were instructed to indicate when they wanted to start the next trial, such that a typical inter-trial interval was about 10 seconds or more. Even within each trial, participants were asked to keep their eyes open for the first 15 seconds, and the main effect of feedback was studied only after that. However, any "carry-over" training effect that is longer than the inter-trial duration may have influenced the power in the next trial, mixing the effects of valid and invalid feedback.

However, while these factors explain why the effect of neurofeedback was smaller than many previous studies, they cannot explain our main result, which is a significant difference in alpha power between valid and invalid conditions in almost half of the participants (25% after Bonferroni correction). Indeed, the main point here is not that the effect of neurofeedback was weak, but that there was a significant effect of neurofeedback *in spite of* several design limitations that were incorporated to keep the valid and invalid conditions as similar as possible.

One way to overcome the distortion in the learning dynamics because of invalid trials could be to use an alternate strategy in which subjects are asked to up-regulate or down-regulate their alpha power in different blocks of trials, while providing valid feedback in both conditions. To our knowledge, such a design has not been used yet, although both up- and down-regulation have been studied in different experiments (for example, van Boxtel et al., 2012 and Ros et al., 2013). However, such a design need not necessarily provide the same type of control as the invalid trials in our design. For example, participants may use different strategies to control the alpha-power in the up versus down regulation conditions, which might again affect the learning dynamics for either type of task. In case there is a difference in alpha power in up- and down-regulation conditions, it could be due to a subjects' ability to suppress alpha in down-regulation condition instead of enhancement in the up-regulation condition. So, if we are specifically interested in whether alpha can be voluntarily enhanced by valid feedback, an invalid feedback (unknown to the subject) may provide a more direct control. Further, this invalid feedback condition has been used in many earlier studies (albeit always on a different "control" group of participants), so our design follows a popular, well studied paradigm. This alternate strategy of interleaved blocks of up and down-regulation, nonetheless, can be used in future studies to provide a different type of control that can complement the control used in this study.

eNeuro Accepted Manuscript

Neurofeedback and attention

Unlike previous studies where participants were asked to focus on the tone to control their alpha activity (Kamiya, 1969; Nowlis and Kamiya, 1970; Plotkin, 1978), in our study the participants were completely free to ignore the tone if the tone was distracting or did not aid in improving their performance score. We found that participants who used the feedback tone for getting information about their alpha power without focussing too much to it were the ones who could successfully maintain their alpha level. This is consistent with previous reports that have shown that attending to a stimulus leads to reduction in alpha power (Händel et al., 2011; Kelly et al., 2006b; Klimesch et al., 2007; Sadaghiani et al., 2010). Similarly, it is likely that attending to the neurofeedback tone may have reduced alpha power.

In our study, the main analysis was performed when the subjects had their eyes closed. This also may have contributed to the small effect of neurofeedback, since alpha power is much stronger when eyes are closed and may have reached some sort of 'saturation level'. Indeed, some previous studies have shown larger alpha enhancement when eyes were kept open (Brown, 1970; van Boxtel et al., 2012; Zoefel et al., 2011), even with no or invalid feedback (Enriquez-Geppert et al., 2014; Jurewicz et al., 2018; Ros et al., 2013). Even in our results, a weak but significant long-term enhancement in alpha power was indeed observed during the eye open condition. We preferred the eye closed state because this condition has fewer confounding variables, such as saccadic eye movements, which are known to modulate the power and phase in many frequency bands, including alpha (Bartlett et al., 2011; Staudigl et al., 2017). As before, while the eyes closed state may have resulted in a smaller overall effect of neurofeedback, this cannot explain the difference in alpha power between the valid and invalid conditions that we observed.

As opposed to the testing (neurofeedback) period, the baseline power used for calibration was recorded when the eyes were open (during the calibration period). This was done because we were particularly interested in quantifying the effect of neurofeedback in enhancing alpha activity from a baseline level where least amount of alpha activity was present. Furthermore, taking baseline measurement during eyes open state allowed the participants to feel a "definitive signal" when they closed their eyes since the tone frequency increased instantaneously. Comparison of alpha in eye open versus eye closed conditions is complicated, since different subjects might have different levels of alpha synchronisation upon eyes closure which may not be directly related to the eyes open state. In our case, this issue is of less relevance because our main comparison (between the valid and invalid conditions) is always during eye closed state only. Note that taking baseline measurement with eyes closed condition only changes Pc in eqn 1, which only shifts the operating frequency of the feedback tone away from 1000 Hz (refer to the equation 1 and 2) without changing any other dynamics.

Another potential confound could be related to the use of FCz as a reference electrode, since this electrode is near the C3 and C4 electrode positions where mu-rhythms (which approximately have the same frequency range as alpha) might be predominant (Gastaut et al., 1954). However, mu-rhythms are typically associated with planning of motor movements (Pfurtscheller and Neuper, 1997), but our participants were not engaged in any type of motor activity. Thus, it is unlikely that the choice of the reference electrode affected our results.

Mechanisms of Alpha Neurofeedback

Our results show a short-term benefit of valid neurofeedback in alpha power maintenance that does not translate to any long-term benefits. Neural mechanisms behind such short-term effects are unclear. Recent EEG-fMRI studies have demonstrated that neurofeedback can lead to a plastic increase in the connectivity within the salience network, which was detectable several minutes after the termination of training (Ros et al., 2013). Further, the increase in salience (default-mode) network connectivity was negatively (positively) correlated with changes in 'on task' mind-wandering as well as resting state alpha rhythm (Ros et al., 2013). Default mode network, which primarily consists of the ventral medial prefrontal cortex (vmPFC) and posterior cingulate cortex (PCC), shows significant activity while individuals are not engaged in the external environment and are at a resting-state condition (Buckner et al., 2008; Uddin et al., 2009). On the other hand, salience network of the brain is active during the performance of sensory attention task (Sadaghiani et al., 2010). Neurofeedback can also change dynamic resonant loops in the cortical and thalamocortical circuit (Lubar, 1997), potentially by changing their excitability (Ros et al., 2010). Unfortunately, because we only recorded from occipital electrodes, we cannot study the interaction between visual and default mode or salience networks or measure changes in the excitability of different brain structures. Even if we had coverage of the entire brain, significant volume conduction and poor source localization with EEG (Nunez et al., 1997; Nunez and Srinivasan, 2006) would likely have made analysis and interpretation of data difficult. Simultaneous fMRI-EEG recording while providing neurofeedback, similar to the study by Ros and colleagues (2013), may be needed to better understand the effect of neurofeedback at short time scales.

Behaviourally, neurofeedback training was perceived relaxing by almost all the participants, with an average subjective relaxation score of 7.96 ± 0.21 out of 10, consistent with previous studies (Brown, 1970; Kamiya, 1969; Nowlis and Kamiya, 1970), even though there was no increase in alpha power over trials and the change in alpha power between valid and invalid trials was uncorrelated with the relaxation score (Figure 4B). Instead, this relaxation may be attributed to various factors described by Plotkin, which include sensory deprivation, sustained alertness, concentration/meditation, introspective sensitization, expectation, perceived success at the feedback task due to the isolated setting during the neurofeedback training (Plotkin, 1979, 1978). Thus, while we show that neurofeedback indeed leads to an increase in alpha power even under the most stringent control conditions and show that this works best for subjects who otherwise cannot sustain their alpha power and when they attend to the feedback "passively" (that is, have intermediate attention scores), we do not comment on its potential beneficial physiological effects. Since such different types of feedback are inter-mixed in our design, such questions are beyond the scope of our study.

References

Adrian ED, Matthews BHC (1934) The Berger Rhythm: Potential changes from the occipital lobes in Man. Brain 57:355–385.

Ancoli S, Kamiya J (1978) Methodological issues in alpha biofeedback training. Biofeedback and Self-Regulation 3:159–183.

Bartlett AM, Ovaysikia S, Logothetis NK, Hoffman KL (2011) Saccades during Object Viewing Modulate Oscillatory Phase in the Superior Temporal Sulcus. J Neurosci 31:18423–18432.

Beatty J (1972) Similar effects of feedback signals and instructional information on EEG activity. Physiol Behav 9:151–154.

Beatty J (1971) Effects of initial alpha wave abundance and operant training procedures on occipital alpha and beta wave activity. Psychon Sci 23:197–199.

Berger H (1929) Über das Elektrenkephalogramm des Menschen. Archiv f Psychiatrie 87:527–570.

Biswas A, Ray S (2017) Control of alpha rhythm (8–13 Hz) using neurofeedback. Journal of the Indian Institute of Science 97:527–531.

Bokil H, Andrews P, Kulkarni JE, Mehta S, Mitra PP (2010) Chronux: a platform for analyzing neural signals. J Neurosci Methods 192:146–151.

Brown BB (1970) Recognition of aspects of consciousness through association with EEG alpha activity represented by a light signal. Psychophysiology 6:442–452.

Buckner RL, Andrews-Hanna JR, Schacter DL (2008) The brain's default network. Annals of the New York Academy of Sciences 1124:1–38.

Cho MK, Jang HS, Jeong S-H, Jang I-S, Choi B-J, Lee M-GT (2008a) Alpha neurofeedback improves the maintaining ability of alpha activity. Neuroreport 19:315–317.

Cho MK, Jang HS, Jeong S-H, Jang I-S, Choi B-J, Lee M-GT (2008b) Alpha neurofeedback improves the maintaining ability of alpha activity. Neuroreport 19:315–317.

Dekker MKJ, Sitskoorn MM, Denissen AJM, van Boxtel GJM (2014) The time-course of alpha neurofeedback training effects in healthy participants. Biological Psychology, SAN (Society of Applied Neuroscience) Special issue on Neurofeedback 95:70–73.

Dempster T, Vernon D (2009) Identifying Indices of Learning for Alpha Neurofeedback Training. Appl Psychophysiol Biofeedback 34:309.

Egner T, Strawson E, Gruzelier JH (2002) EEG signature and phenomenology of alpha/theta neurofeedback training versus mock feedback. Appl Psychophysiol Biofeedback 27:261–270.

Enriquez-Geppert S, Huster RJ, Scharfenort R, Mokom ZN, Zimmermann J, Herrmann CS (2014) Modulation of frontal-midline theta by neurofeedback. Biological Psychology, SAN (Society of Applied Neuroscience) Special issue on Neurofeedback 95:59–69.

Escolano C, Aguilar M, Minguez J (2011) EEG-based upper alpha neurofeedback training improves working memory performance. Conf Proc IEEE Eng Med Biol Soc 2011:2327–2330.

Fath SJ, Wallace LA, Worsham RW (1976) The effect of intermittent auditory stimulation on the occipital alpha rhythm. Physiological Psychology 4:185–188.

Fink A, Benedek M (2014) EEG alpha power and creative ideation. Neurosci Biobehav Rev 44:111–123.

Garrett BL, Silver MP (1976) The use of EMG and alpha biofeedback to relieve test anxiety in college students. Biofeedback, behavior therapy, and hypnosis Chicago7 Nelson-Hall.

Gastaut H, Dongier M, Courtois G (1954) On the significance of "wicket rhythms" ("rhythmes en arceau") in psychosomatic medicine. Electroenceph Clin Neurophysiol 6:687–688.

Haegens S, Cousijn H, Wallis G, Harrison PJ, Nobre AC (2014) Inter- and intra-individual variability in alpha peak frequency. Neuroimage 92:46–55.

Hammond D (2005) Neurofeedback with anxiety and affective disorders. Child and Adolescent Psychiatric Clinics of North America 14:105–123.

Händel BF, Haarmeier T, Jensen O (2011) Alpha Oscillations Correlate with the Successful Inhibition of Unattended Stimuli. Journal of Cognitive Neuroscience 23:2494–2502.

Hardt JV, Kamiya J (1978) Anxiety change through electroencephalographic alpha feedback seen only in high anxiety subjects. Science 201:79–81.

Hardt JV, Kamiya J (1976) Conflicting results in EEG alpha feedback studies. Biofeedback and Self-Regulation 1:63–75.

Hart JT (1968) Autocontrol of EEG alpha. Psychophysiology 4:506–506.

Hord D, Barber J (1971) Alpha control: Effectiveness of two kinds of feedback. Psychon Sci 25:151–154.

Jurewicz K, Paluch K, Kublik E, Rogala J, Mikicin M, Wróbel A (2018) EEG-neurofeedback training of beta band (12–22Hz) affects alpha and beta frequencies – A controlled study of a healthy population. Neuropsychologia 108:13–24.

Kamiya J (2011) The first communications about operant conditioning of the EEG. Journal of Neurotherapy 15:65–73.

Kamiya J (1969) Operant control of the EEG alpha rhythm and some of its reported effects on consciousness. Alerted states of consciousness 489.

Kelly SP, Lalor EC, Reilly RB, Foxe JJ (2006a) Increases in alpha oscillatory power reflect an cctive retinotopic mechanism for distracter duppression during sustained visuospatial attention. Journal of Neurophysiology 95:3844–3851.

Kelly SP, Lalor EC, Reilly RB, Foxe JJ (2006b) Increases in Alpha Oscillatory Power Reflect an Active Retinotopic Mechanism for Distracter Suppression During Sustained Visuospatial Attention. Journal of Neurophysiology 95:3844–3851.

Klimesch W (2012) Alpha-band oscillations, attention, and controlled access to stored information. Trends in Cognitive Sciences 16:606–617.

Klimesch W, Sauseng P, Hanslmayr S (2007) EEG alpha oscillations: The inhibition–timing hypothesis. Brain Research Reviews 53:63–88.

Lindholm E, Lowry S (1978) Alpha production in humans under conditions of false feedback. Bull Psychon Soc 11:106–108.

Lubar JF (1997) Neocortical dynamics: implications for understanding the role of neurofeedback and related techniques for the enhancement of attention. Appl Psychophysiol Biofeedback 22:111–126.

Lynch JJ, Paskewitz DA (1971) On the mechanisms of the feedback control of human brain wave activity. Journal of Nervous and Mental Disease 153:205–217.

Lynch JL, Paskewitz DA, Orne MT (1974) Some factors in the feedback control of human alpha rhythm. Psychosomatic Medicine 36:399–410.

Nan W, Rodrigues JP, Ma J, Qu X, Wan F, Mak P-I, Mak PU, Vai MI, Rosa A (2012) Individual alpha neurofeedback training effect on short term memory. International Journal of Psychophysiology 86:83–87.

Nowlis DP, Kamiya J (1970) The control of electroencephalographic alpha rhythms through auditory feedback and the associated mental activity. Psychophysiology 6:476–484.

Nunez PL, Srinivasan R (2006) Electric fields of the brain. New York: Oxford University Press.

Nunez PL, Srinivasan R, Westdorp AF, Wijesinghe RS, Tucker DM, Silberstein RB, Cadusch PJ (1997) EEG coherency: I: statistics, reference electrode, volume conduction, Laplacians, cortical imaging, and interpretation at multiple scales. Electroencephalography and Clinical Neurophysiology 103:499–515.

Paskewitz DA, Orne MT (1973) Visual Effects on Alpha Feedback Training. Science 181:360–363.

Pfurtscheller G, Neuper C (1997) Motor imagery activates primary sensorimotor area in humans. Neuroscience Letters 239:65–68.

Plotkin WB (1979) The alpha experience revisited: Biofeedback in the transformation of psychological state. Psychological Bulletin 86:1132–1148.

Plotkin WB (1978) Long-term Eyes-closed Alpha-enhancement Training: Effects on Alpha Amplitudes and on Experiential State. Psychophysiology 15:40–52.

Plotkin WP, Rice KM (1981) Biofeedback as a placebo: anxiety reduction facilitated by training in either suppression or enhancement of alpha brainwaves. J Consult Clin Psychol 49:590–596.
Regestein QR, Buckland GH, Pegram GV (1973) Effect of daytime alpha rhythm maintenance on subsequent sleep. Psychosomatic medicine 35:415–418.
Rice KM, Blanchard EB (1982) Biofeedback in the treatment of anxiety disorders. Clinical Psychology Review 2:557–577.
Rogala J, Jurewicz K, Paluch K, Kublik E, Cetnarski R, Wróbel A (2016) The Do's and Don'ts of Neurofeedback Training: A review of the controlled studies using healthy adults. Front Hum Neurosci 301.
Ros T, Munneke MAM, Ruge D, Gruzelier JH, Rothwell JC (2010) Endogenous control of waking brain rhythms induces neuroplasticity in humans. Eur J Neurosci 31:770–778.
Ros T, Théberge J, Frewen PA, Kluetsch R, Densmore M, Calhoun VD, Lanius RA (2013) Mind over chatter: Plastic up-regulation of the fMRI salience network directly after EEG neurofeedback. NeuroImage 65:324–335.
Sadaghiani S, Scheeringa R, Lehongre K, Morillon B, Giraud A-L, Kleinschmidt A (2010) Intrinsic connectivity networks, alpha oscillations, and tonic alertness: a simultaneous electroencephalography/functional magnetic resonance imaging study. Journal of Neuroscience 30:10243–10250.
Staudigl T, Hartl E, Noachtar S, Doeller CF, Jensen O (2017) Saccades are phase-locked to alpha oscillations in the occipital and medial temporal lobe during successful memory encoding. PLOS Biology 15:e2003404.
Strayer F, Scott WB, Baken P (1973) A re-examination of alpha feedback training: operant conditioning or perceptual differentiation? Can J Psychol 27:247–253.
Uddin LQ, Clare Kelly AM, Biswal BB, Castellanos FX, Milham MP (2009) Functional connectivity of default mode network components: correlation, anticorrelation, and causality. Hum Brain Mapp 30.
van Boxtel GJM, Denissen AJM, Jäger M, Vernon D, Dekker MKJ, Mihajlović V, Sitskoorn MM (2012) A novel self-guided approach to alpha activity training. International Journal of Psychophysiology 83:282–294.
van Leeuwen WS, Kemp A, Kniper J (1960) Concerning the Squeak' phenomenon of the alpha rhythm. Electroencephalogr. Clin. Neurophysiol In: ELECTROENCEPHALOGRAPHY AND CLINICAL NEUROPHYSIOLOGY , pp244–244. ELSEVIER SCI IRELAND LTD CUSTOMER RELATIONS MANAGER, BAY 15, SHANNON ….
Vernon D, Dempster T, Bazanova O, Rutterford N, Pasqualini M, Andersen S (2009) Alpha neurofeedback training for performance enhancement: reviewing the methodology. Journal of neurotherapy 13:214–227.
Walsh DH (1974) Interactive Effects of Alpha Feedback and Instructional Set on Subjective State. Psychophysiology 11:428–435.
Watson CG, Herder J (1980) Effectiveness of alpha biofeedback therapy: Negative results. Journal of Clinical Psychology 36:508–513.
Zoefel B, Huster RJ, Herrmann CS (2011) Neurofeedback training of the upper alpha frequency band in EEG improves cognitive performance. NeuroImage 54:1427–1431.

Figure Legends

Figure 1: Effect of neurofeedback training on alpha power in a representative participant.

A) Details of the experimental paradigm. Three types of trials, namely Valid (red), Invalid (green), and Constant (blue) were presented for 5 sessions, each consisting of 12 trials. Each trial was 50 seconds long. Each block started with a calibration stage (not shown). The first session, in which invalid trials were not presented, was not used for analysis.

B) Time-frequency spectogram of a single valid trial showing change in power from baseline (computed during the calibration stage). Broken lines at 8 and 13 Hz indicate the alpha range.

C) Change in instantaneous alpha power for the same trial as in B (brown trace; left y-axis). Dotted orange line depicts alpha power smoothed by averaging across the previous 5 seconds, which was used to set the frequency of the feedback tone (green trace; right y-axis).

D) Raw alpha power versus trial number during calibration (thick black line; same value for each block of 12 trials), eyes open (open circles) and eyes closed state (solid triangles). Regression lines between raw alpha power versus trial number (13-60) are shown for eyes open (grey trace) and eyes closed states (brown trace). Corresponding slopes and p-values are indicated in the panel in respective colours. Error bar indicates SEM.

E) Change in alpha power with respect to time for three types of trials: valid (red), invalid (green), and constant (blue), averaged over trials 13-60 (24 valid, 12 invalid and 12 constant trials). Regression lines plotted between mean change in alpha power and time (21-50 s) are also shown in corresponding colours. Average change in power in decibels (between 21 to 50 second) $\pm$ SEM for the three types trials are indicated at top right corner (in corresponding colours). Slopes of the regression lines along with their p-values are indicated at bottom right corner.

Figure 2: Modulation of alpha power for three types of trials for all participants.

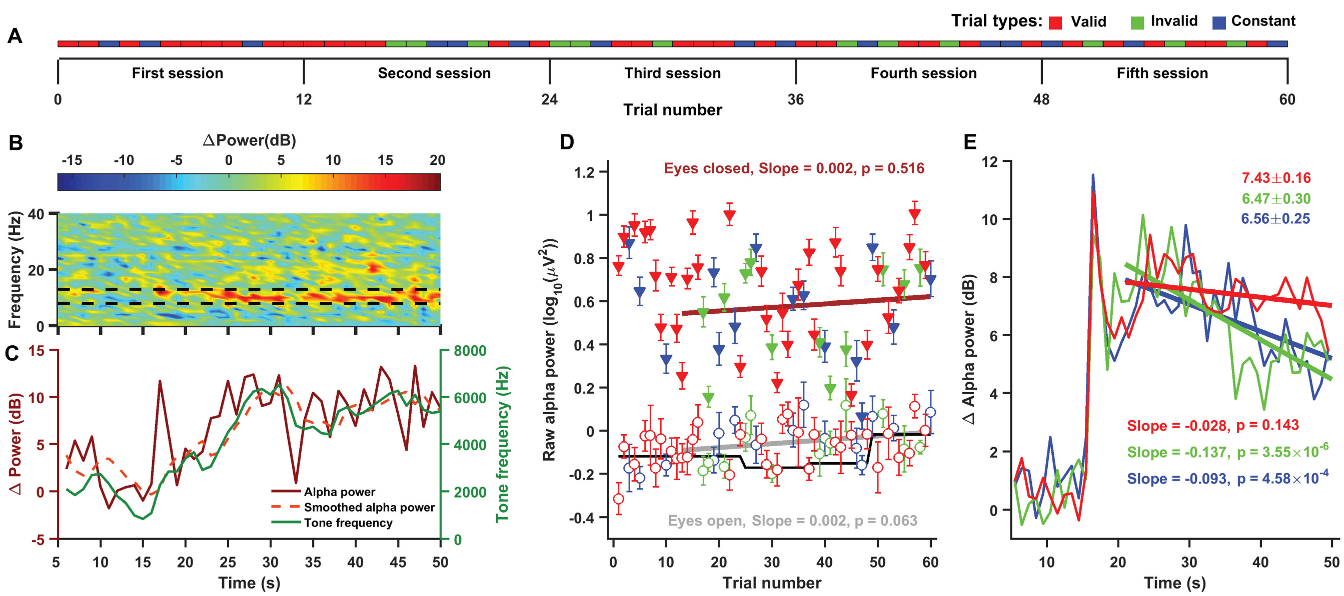
Same as Figure 1E, separately for each of the 24 participants, in descending order of significance of the difference between change in alpha power between valid and invalid trials (estimated using t-test and shown in the plots, along with the mean changes in alpha power for the three trial types).

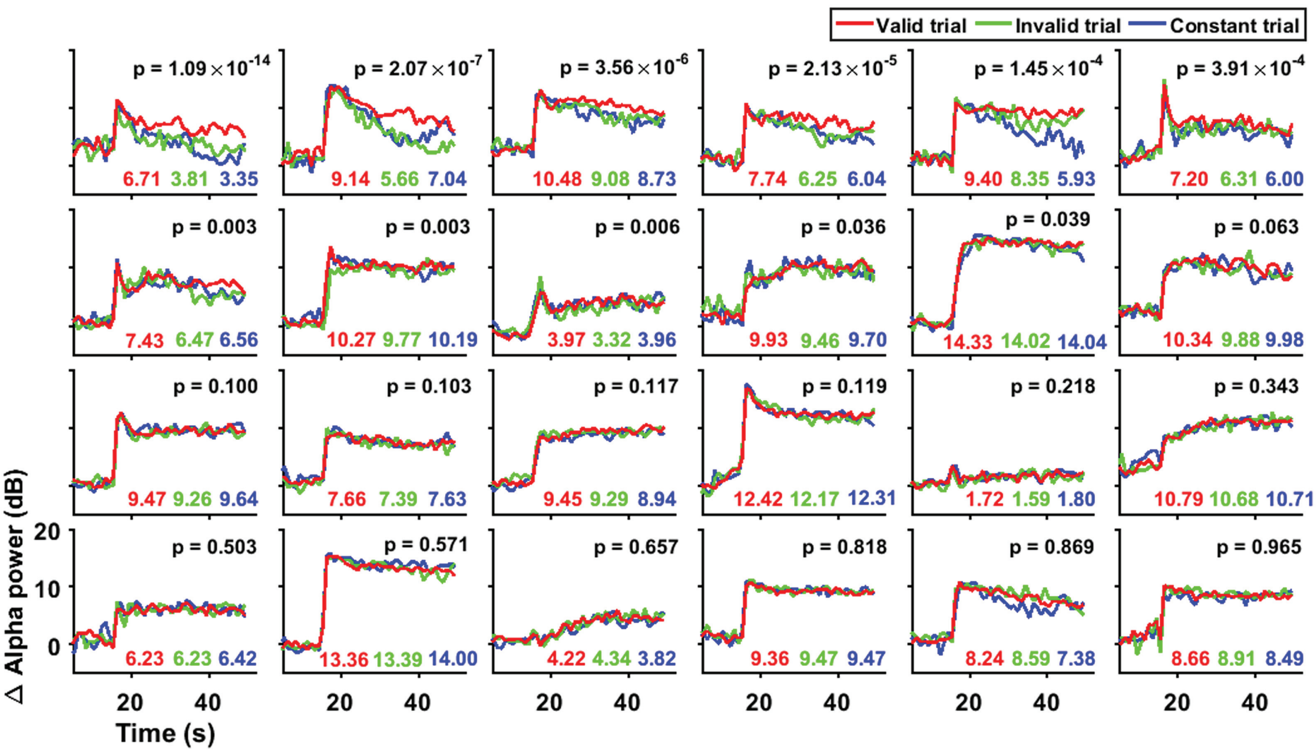
Figure 3: Effect of Neurofeedback depends on sustenance of alpha power.

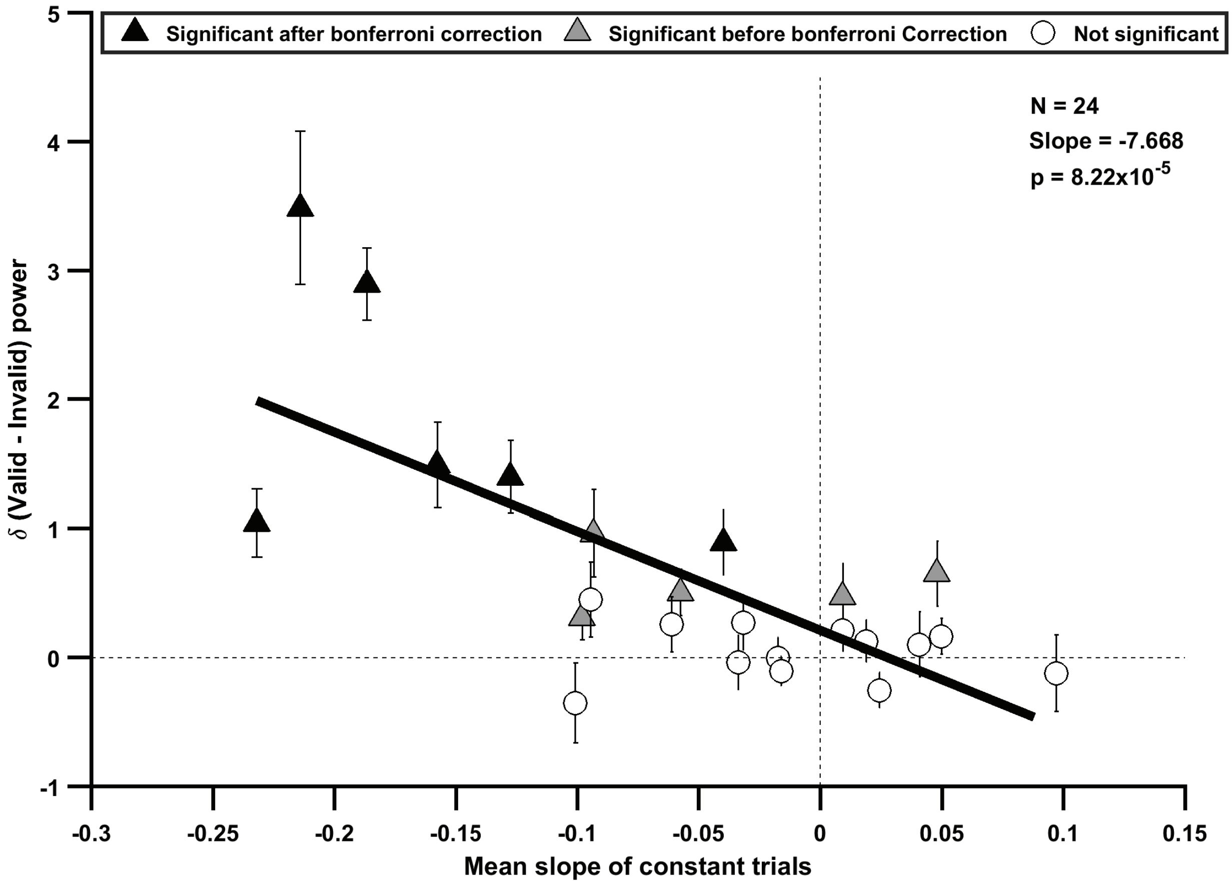
Scatterplot shows difference in power between valid and invalid trials (*Δ* Power) and slope for the constant trials for all the 24 participants. Thick black line shows a regression line; slope and p-values are indicated in the panel. Participants 1-6, for which mean change in alpha power between valid and invalid trials was significant after Bonferroni correction are indicated using filled black triangles. Participants 7-11, for which the difference was significant before Bonferroni correction are indicated using grey triangles. Remaining participants are indicated using open circles. Error bar indicates SEM.

Figure 4. Subjective experience of the neurofeedback training for all participants.

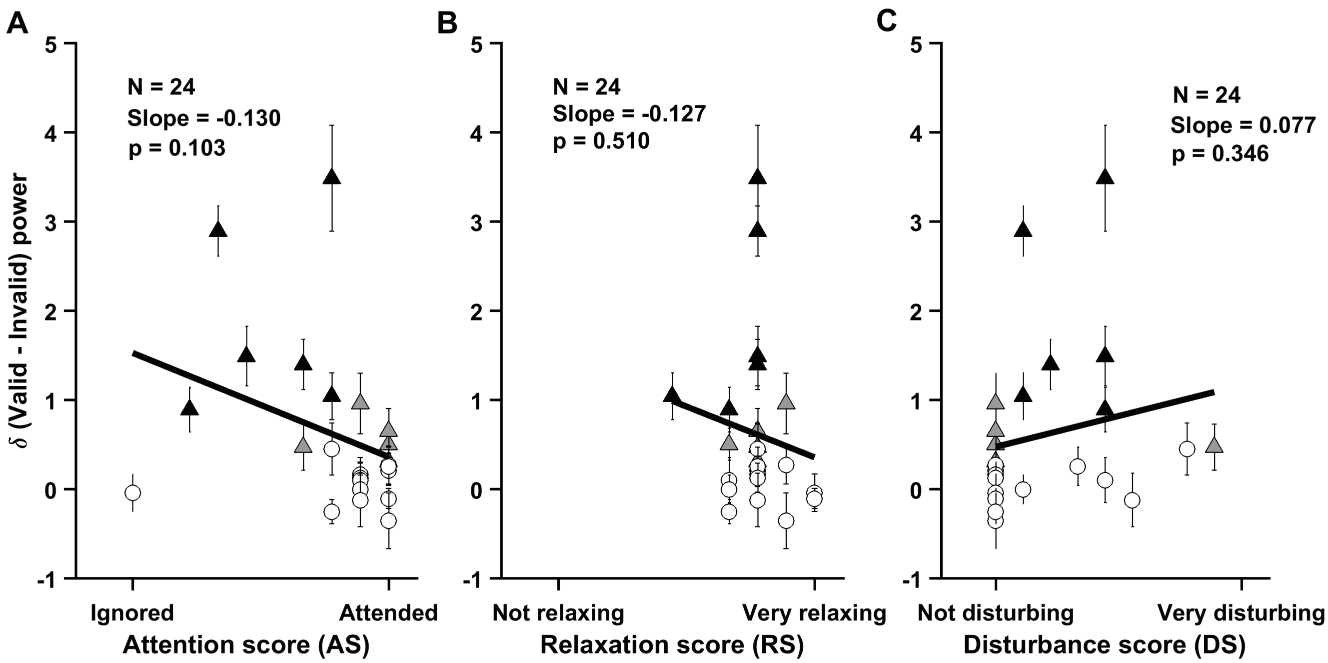
Scatterplot showing difference in alpha power between valid and invalid trials with respect to A) Feedback scores (FS), B) Relaxation Score (RS), and C) Disturbance scores (DS). For each plot, regression line is shown in thick black, and slope and p-values are indicated in the panel. Same markers as in Figure 3. Error bar indicates SEM.


A
Trial types: Valid Invalid Constant
First session
Second session
Third session
Fourth session
Fifth session
0
12
24
36
48
60
Trial number
B
ΔPower(dB)
-15 -10 -5 0 5 10 15 20
Frequency (Hz)
C
Δ Power (dB)
Tone frequency (Hz)
Alpha power
Smoothed alpha power
Tone frequency
Time (s)
D
Raw alpha power ($log_{10}(\mu V^2)$)
Eyes closed, Slope = 0.002, p = 0.516
Eyes open, Slope = 0.002, p = 0.063
Trial number
E
Δ Alpha power (dB)
7.43±0.16
6.47±0.30
6.56±0.25
Slope = -0.028, p = 0.143
Slope = -0.137, p = 3.55×10^{-6}
Slope = -0.093, p = 4.58×10^{-4}
Time (s)


Valid trial
Invalid trial
Constant trial
p = 1.09×10^-14
6.71 3.81 3.35
p = 2.07×10^-7
9.14 5.66 7.04
p = 3.56×10^-6
10.48 9.08 8.73
p = 2.13×10^-5
7.74 6.25 6.04
p = 1.45×10^-4
9.40 8.35 5.93
p = 3.91×10^-4
7.20 6.31 6.00
p = 0.003
7.43 6.47 6.56
p = 0.003
10.27 9.77 10.19
p = 0.006
3.97 3.32 3.96
p = 0.036
9.93 9.46 9.70
p = 0.039
14.33 14.02 14.04
p = 0.063
10.34 9.88 9.98
p = 0.100
9.47 9.26 9.64
p = 0.103
7.66 7.39 7.63
p = 0.117
9.45 9.29 8.94
p = 0.119
12.42 12.17 12.31
p = 0.218
1.72 1.59 1.80
p = 0.343
10.79 10.68 10.71
p = 0.503
6.23 6.23 6.42
p = 0.571
13.36 13.39 14.00
p = 0.657
4.22 4.34 3.82
p = 0.818
9.36 9.47 9.47
p = 0.869
8.24 8.59 7.38
p = 0.965
8.66 8.91 8.49
Δ Alpha power (dB)
20
10
0
20
40
Time (s)



Significant after bonferroni correction
Significant before bonferroni Correction
Not significant
N = 24
Slope = -7.668
p = 8.22x10^-5
δ (Valid - Invalid) power
Mean slope of constant trials
5
4
3
2
1
0
-1
-0.3
-0.25
-0.2
-0.15
-0.1
-0.05
0
0.05
0.1
0.15


A
B
C
δ (Valid - Invalid) power
N = 24
Slope = -0.130
p = 0.103
N = 24
Slope = -0.127
p = 0.510
N = 24
Slope = 0.077
p = 0.346
5
4
3
2
1
0
-1
Ignored
Attended
Attention score (AS)
Not relaxing
Very relaxing
Relaxation score (RS)
Not disturbing
Very disturbing
Disturbance score (DS)