Selective neuromodulation induced by alpha-based neurofeedback learning: A double-blind randomized study

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Highlights

- Randomized double-blind study of neuromodulation induced by EEG-neurofeedback (NF)
- Sham feedback (FB) was used for the control group
- Targeted alpha activity increased selectively over the 12 NF training sessions
- This neuromodulation was observed only in the real NF training group
- The feeling of control across sessions increased more for real than sham FB group

Abstract

Background:

The neuromodulation induced by neurofeedback training (NFT) remains a matter of debate. Investigating the modulation of brain activity specifically associated with NF requires controlling for multiple factors, such as reward, performance, congruency between task and targeted brain activity. This can be achieved using sham feedback (FB) control condition, equating all aspects of the experiment but the closed loop between brain activity and FB.

Objective:

We aimed at investigating the modulation of individual alpha EEG activity induced by NFT in a double-blind, randomized, sham-controlled study.

Methods:

Forty-eight healthy participants were assigned to either NF (n=25) or control (n=23) group and performed 12 NFT sessions of alpha upregulation with a wearable EEG device. Participants of the NF group received FB based on their individual alpha activity. The control group received the auditory FB of participants of the NF group.

Results:

An increase of alpha activity across training sessions was observed in the NF group only ($p<0.001$). This neuromodulation was selective in that it was not observed for theta (4-8Hz) and low beta (13-18Hz) activities. It was associated with an increased feeling of control ($p<0.001$), more marked for NF than control group. Anxiety level decreased and relaxation feeling increased with training in both groups.

Conclusions:

NFT across multiple sessions can induce specific brain modulation, suggesting a neuroplasticity

selective of the targeted brain activity. Our results pave the way to self-learnt, NF-based neuromodulation with light-weighted, wearable EEG systems for various applications (e.g. epilepsy, sleep, attention).

Keywords

Neurofeedback; controlled sham condition; alpha oscillations; relaxation; neuromodulation; wearable EEG

Introduction

Neurofeedback (NF) is a cognitive training that exploits the causal relationship between brain activity and cognitivo-motor abilities. It consists in providing real-time, closed-loop— auditory, visual, or tactile—feedback of a subject's brain activity to train self-regulation of specific brain patterns related to a targeted ability. For example, some NF protocols target electroencephalographic (EEG) activity in the alpha band (7-13Hz), aiming at its reduction or enhancement, in order to train participants to focus attention sustainably or to relax, respectively [1]–[3]. NF applications have been developed since the 70's in non-clinical [4], [5] and clinical settings, such as epilepsy [6], attention-deficit hyperactivity disorder [7]–[11], depression [9], [10], and anxiety [12], [14]–[16]. However, the understanding of the neurocognitive mechanisms and effects of NF training (NFT) remains elusive; it has become a full swing topic for the scientific and medical community [17].

NF can be considered as a particular case of reinforcement learning, by which the subject is rewarded through the feedback for modulating the targeted brain activity. This modulation is usually learnt through a cognitive strategy enforced by task instruction and related to the cognitivo-motor ability to be improved or restored. The ensuing cognitive or motor improvements are typically used as the primary outcome measures to assess NFT efficiency, in particular in clinical applications [14], [18], [19]. Control conditions are quite variable, not only aiming at the closed loop between brain activity and feedback but also varying the task or the procedure [20]. For example, in clinical NF application studies, where NFT aimed at reducing behavioral symptoms associated with various disorders (anxiety [14]–[16], depression [12], [13], [21], addiction [22]–[25], attention deficit [7]–[11], [26]), NF performance was typically compared with other procedures, such as cognitive therapy, mental exercise, and treatment-as-usual [20]. Thus, the behavioral or clinical benefits of NFT may be related to an ensemble of specific and non-specific mechanisms, including psychosocial

influences [27], cognitive and attentional/motivational factors [28], test-retest improvement, as well as spontaneous clinical improvement or cognitive development [17], contributing to the ongoing debate about NF efficiency [15], [19].

A key question concerns the neuromodulation associated with NFT, that is, induced by the closed loop between the subject's brain activity and feedback. Addressing this question requires a control condition equating every other aspect of the NF protocol—such as instruction, task, reward. In some NF studies, the control condition was based on linking the feedback to another brain activity than the targeted one [20]. This results in an incongruity between the activity that drives the feedback and the task—hence the cognitive efforts—of the subject, with potential impacts not only on performance, but also on reward and motivation. Although this type of control condition may pinpoint the cognitivo-motor changes specifically associated with the targeted brain activity [20], it does not allow to reveal the neuromodulation induced by NFT. A sham feedback (sham-FB) condition, where the feedback in the control group is matched on the feedback in the experimental group, is necessary to allow investigation of the self-learnt neuromodulation specifically associated with NF. To date, few studies have used such feedback, with mixed results. For instance, Witte et al. used EEG-based NFT of sensorimotor rhythm regulation over multiple sessions but did not find evidence for between session neuromodulation [29]. Naas et al. [30] used an NF protocol targeting upper alpha band over four training sessions in four days and did not reveal any significantly different positive improvement of the targeted activity between groups over time. In contrast, Beatty [31] showed an increase of the trained alpha activity in the NF group but not in the sham-FB condition during a unique NF session.

Here, we aimed at studying the neuromodulation specifically induced by alpha-based NFT over multiple sessions in healthy participants, by contrasting it to a carefully controlled sham-FB condition in a randomized double-blind study. We used a new compact and wearable EEG-based NF device designed for relaxation and stress self-management, the Melomind™ device (myBrain Technologies,

Paris, France) [32]. The protocol consisted in a 12-week NF program. Participants, immersed in a relaxing soundscape delivered by headphones, were engaged in learning to decrease the volume of a sound indicator, which was based on the individual alpha-band activity recorded by two parietal dry electrodes. EEG activity in the alpha-band is used in most NF protocols aiming at anxiety reduction, stress-management or well-being [1], [2], [14], [15]. The participants in the sham-FB group received 'yoked' feedback, based on the individual alpha activity of randomly-chosen subjects from the NF group at the same stage of learning. Hence, this feedback was similar in every aspect to the one in the NF group, except that it was not the result of an established closed loop between the subject's alpha-band activity and the auditory stream. In particular, it controlled for reward and performance across both groups [20]. We expected a selective increase of the targeted neural activity across the program only for the participants of the NF group. We also examined behavioral outcomes in terms of anxiety level, relaxation, and feeling of control.

Materials and Methods

Participants

Forty-eight healthy volunteers participated in this study (mean age: 33.3 years; age range: 18-60; see Supplementary Table A.1 for more details). All declared having normal or corrected-to-normal vision, no hearing problem, no history of neurological or psychiatric disorders, no ongoing psychotropic drug treatment. Participants were randomly and blindly assigned either to the *NF group*—who received real NFT—or to the *control group*—who received sham-FB, except for the first few participants who—for the purpose of the sham-FB—were assigned to the *NF group.* The experimenter was also blind to the assignment.

All participants gave written informed consent to participate in the study. All procedures were carried out in accordance with the Declaration of Helsinki. The experimental protocol was identical to the experimental protocol of the clinical study approved by French ethical committee (CPP SUD-OUEST OUTRE-MER I, study nb. 2017-A02786-47), registered on ClinicalTrials.gov (ref. NCT04545359).

EEG recording and preprocessing

Brain activity was recorded by two gold-coated dry electrodes placed on parietal regions (P3 and P4) with the CE marked Melomind™ device (myBrain Technologies, Paris, France; https://www.melomind.com/; Fig. 1). Ground and reference were silver fabric electrodes, placed on the left and right headphones respectively, in mastoid regions. The headset communicated via Bluetooth with a mobile NF application, which processed EEG data every second to give the user auditory feedback about his alpha-band activity (see below).

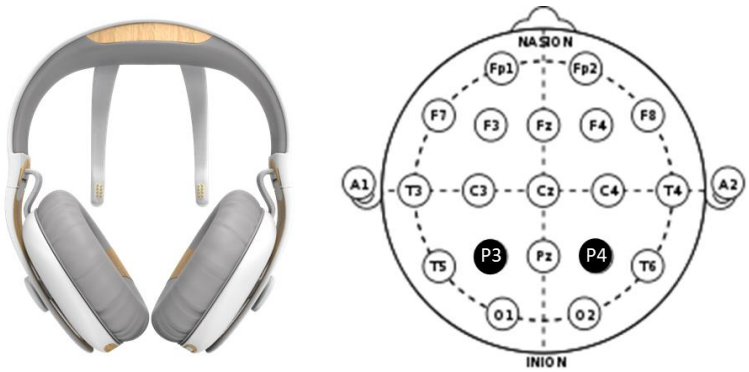

Fig. 1 **Melomind™ device.** Left column: The device comprises an audio headset and two posterior branches at the end of which two gold-coated dry electrodes are inserted. Right column: These electrodes are positioned at P3 and P4 locations (indicated in black) according to the extended 10-20 International System.

EEG signals were amplified and digitized at a sampling rate of 250 Hz, band-pass filtered from 2Hz to 30Hz in real time and sent to the mobile device by embedded electronics in the headset. Then, real-

time estimation of signal quality was performed by a dedicated machine learning algorithm [33] to discard noisy segments before computing the feedback.

Experimental protocol

The protocol consisted of 12 NFT sessions with Melomind™ device, with one session per week (Fig. 2). Each session was composed of 7 exercises of 3 minutes (total: 21 minutes). At the beginning and end of each session, two-minute resting state recording was performed and the participant completed the Spielberger State-Trait Anxiety Inventory (*STAI*, *Y-A* form, in French, [29])—to assess his/her anxiety state level—and a 10-cm visual analog scale indicating his/her subjective relaxation level (r*elax-VAS*). Moreover, at the end of each exercise, the participant indicated his/her subjective level of feedback control on a 10-cm visual analog scale (*control-VAS*). We also collected psychometric trait measures before and after the NF program to assess psychological stress (Perceived Stress Scale - PSS) [35], trait anxiety (*STAI-Y-B*) [29], and affectivity (Positive and Negative Affect Schedule - PANAS). Participants completed the protocol in three different locations: at the Center for NeuroImaging Research (CENIR) of the Paris Brain Institute (ICM, Paris, France) (N=20 participants), at the workplace 14 (N=14), or at home (N=14).

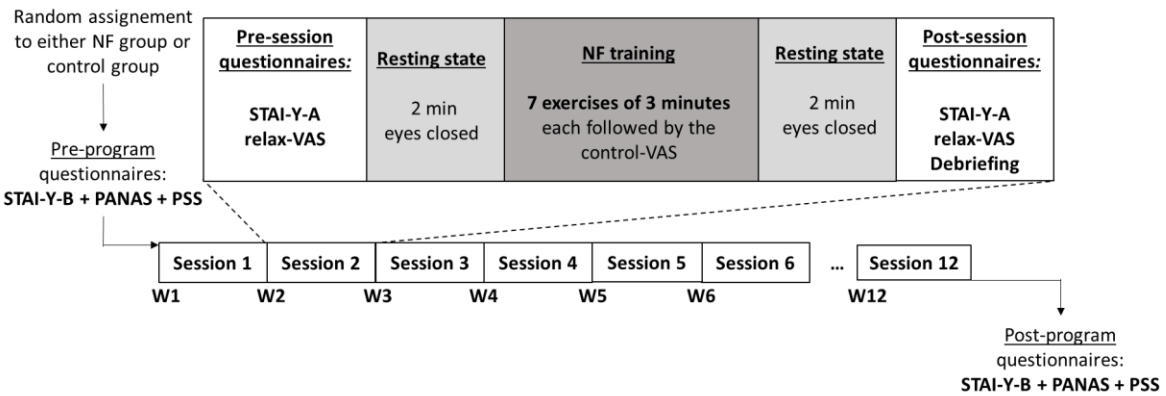

Fig. 2 **Timeline of the experimental protocol.**

Neurofeedback training procedure

The NF paradigm targeted alpha rhythm centered on the individual alpha frequency (IAF). Before each NFT session, a 30-second calibration phase allowed computing IAF using an optimized, robust estimator dedicated to real-time IAF estimation based on spectral correction and prior IAF estimations [36]. During the NF exercises, participants were instructed to close their eyes, be relaxed and try to reduce the auditory feedback volume by their own strategies (not provided or advised by the experimenter; see Supplementary Material for the reported mental strategies). A relaxing landscape background (e.g. forest sounds) was played at a constant, comfortable volume on each exercise. The audio feedback was an electronic chord sound added to this background with a volume intensity derived from EEG signals using a proprietary algorithm. More precisely, the individual alpha amplitude was computed in consecutive 1-second epochs as the root mean square (RMS) of EEG activity filtered in IAF±1Hz band (*NF index*); it was normalized to the calibration baseline activity to obtain a 0-1 scale, which was used to modulate the intensity of the feedback sound during the exercises in the NF group (0: silent feedback; 1: maximal volume). For the participants in the control group, the instruction was identical but they received sham-FB, which was the replayed feedback variations from a randomly chosen subject in the NF group at the same training level (i.e. session) [20].

Data analysis

NF index and learning score

For each participant and each training session, we first computed the average value of the NF index (before normalization) for every exercise. Second, we built an NF learning score ($\Delta D(t)$)—inspired from [37]—from the NF index variations across exercises and sessions: we computed the median value (*med*) of the NF index across the 7 exercises of the first session; then, for each following

session *t*, we computed *D(t)* the number of NF index values above or equal to *med*. This corresponded to a cumulated duration because the NF index value was computed every second. It was divided by the total duration of the training session (21 minutes) in order to express *D(t)* by minute, and transformed into percent change relative to the first session, as follows (Eq. (1)):

$$\Delta D(t) = \left(\frac{D(t)}{D(t=1)} - 1\right) \times 100 \qquad (1)$$

Theta and low beta activities

To study the selectivity of the neuromodulation to the targeted alpha activity, we analyzed the between-sessions evolutions of theta (4-7Hz) and low beta (13-18Hz) activities. For each subject, on each exercise and session, theta activity was computed every second as the RMS of EEG activity filtered between 4 and 7Hz in 4-second sliding windows, on epochs with high or medium quality (see [33] for details about signal quality computation). We then averaged these RMS values for each session. Similar computation was performed for low beta activity, with EEG activity filtered between 13 and 18Hz.

Signal quality

As encouraged in [17], the quality of EEG signals was analyzed to test bad EEG data prevalence between groups and across training sessions. For each participant and session, during each exercise, the quality of each 1-second EEG epoch on each electrode was determined by a classification-based approach according to three labels: HIGHq, MEDq, and LOWq (see [33] for more details). A quality index *Q* was then computed for each electrode, during each exercise, as in Eq. (2):

$$Q = \frac{\#HIGHq + 0.5*\#MEDq}{N + \#LOWq} \qquad (2)$$

with: #HIGHq, #MEDq, #LOWq indicating the number of high, median, low quality epochs and N, the total number of quality labels, across the 21-min training. Finally, the average value of *Q* was computed across both electrodes for each exercise.

Behavioral outcomes

The raw scores of the *STAI-Y-A* (between 20 and 80) and *relax-VAS* (between 0 and 10) were computed pre- and post-session. The subjective level of feedback control was measured within- and between-sessions on the *control-VAS* (between 0 and 10).

Statistical analyses

All statistical analyses were performed using R (v.4.0.2; R Core Team, 2020) and *lme4* package [38]. We used Linear Mixed Models (LMMs) and type III Analyses of Variance (anova) on these models [39], [40], because LMMs allow handling missing data, variability in effect sizes across participants, and unbalanced designs (see [41]). Available data in this study are detailed in Supplementary Table C.1. For the LMM analyses, the NF group at the first session was set as the level of reference in order to specifically estimate the effects of NFT in this group. A random effect structure with random intercept by participant (subject_id) was fit. Parameter estimates (β) for the effects of interest were obtained by fitting the models on the data (see below), using the Restricted Maximum Likelihood (REML) approach. P-values were estimated via t-tests using the Satterthwaite approximation to degrees of freedom with *lmerTest* package [42]. We considered $p<0.05$ as statistically significant.

Similarly to [43], we analyzed the within- and between-sessions NFT effects on the NF index using an LMM with the session, the training exercise, the group, and the 2-way interactions between session and group and between exercise and group as fixed effects (Eq. (3) as coded in R):

Y ~ 1 + session + exercise + group + session:group + exercises:group + 1|subject_id (3)

Preliminary analyses indicated that the effect of exercises followed a U curve. Therefore, the exercises were coded as a quadratic term, that is, exercises 1 to 7 were coded as 9, 4, 1, 0, 1, 4, and 9. The sessions were coded as a numeric variable between 0 and 11. Eq. (3) was also used for the analysis of the *control-VAS* scores.

For the analysis of NF learning score, theta activity, low beta activity, and the signal quality index, we used the following LMM equation (Eq.(4)):

$$Y \sim 1 + session + group + session{:}group + 1|subject_id \quad (4)$$

For the behavioral outcomes (*relax-VAS* and *STAI-Y-A*), we used an LMM with session, phase (pre- or post-session), group, and the 2-way interactions between session and group and between phase and group as fixed effects (Eq. (5)):

$$Y \sim 1 + session + phase + group + session{:}group + phase{:}group + 1|subject_id \quad (5)$$

Results

Neuromodulation induced by NF

The analysis of the NF index showed a statistically significant effect of session. This reflected a significant linear increase of the NF index across sessions in the NF group (slope estimate (β) = 0.04, 95% Confidence Interval (CI) [0.03, 0.06], $p < .001$). We found a significant interaction between group and session (β = -0.08, CI [-0.10, -0.06], $p < .001$), which revealed that the increase of the NF index across sessions was specific to the NF group (Fig. 3a) (see Supplementary Table D.1 for details of the parameter estimates for each factor).

The analysis of the NF learning score confirmed this specific NF-based neuromodulation. It showed a significant effect of session (β = 1.08, CI [0.17, 2.00], $p < .05$) and a significant interaction between session and group (β = -1.40, CI [-2.72, -0.09], $p < .05$) (see Supplementary Table D.2), reflecting that that the NF learning score increased across sessions in the NF group only (Fig. 3b). Additional individual linear regressions of the NF learning score (see Supplementary Fig. D.3 and D.4) showed that 76% (19/25) of the participants from the NF group had a positive regression slope across the 12 sessions, while the slope was positive for 43.5% (10/23) of the participants from the control group.

In addition, there was a significant effect of exercise on the NF index, reflecting the quadratic pattern of the NF index across exercises for the NF group (β = 0.03, CI [0.02, 0.05], $p < .001$). The non-significant interaction between exercise and group indicated that this effect did not differ between both groups (β = 1.64e-03, CI [-0.02, 0.02], p = 0.88) (Fig. 4).

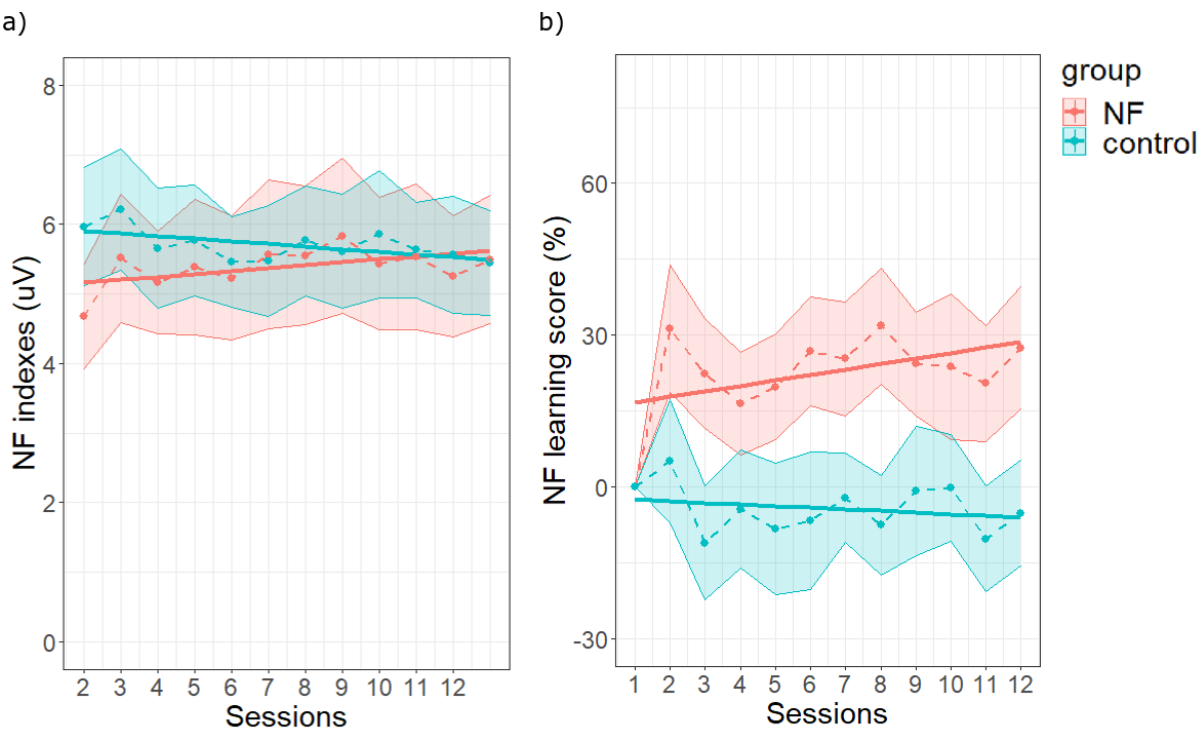

Fig. 3 **Neuromodulation induced by NFT. a) Evolution of the NF index across sessions, for the NF (in red) and the control (in blue) groups.** Dotted lines and points represent the values of the NF index along the 12 sessions, averaged across participants for each group; the shaded areas represent the

standard errors of the means. The solid lines represent the session effect estimated for each group from the LMM. **b) Evolution of the NF learning score across sessions.** Same legend as in a).

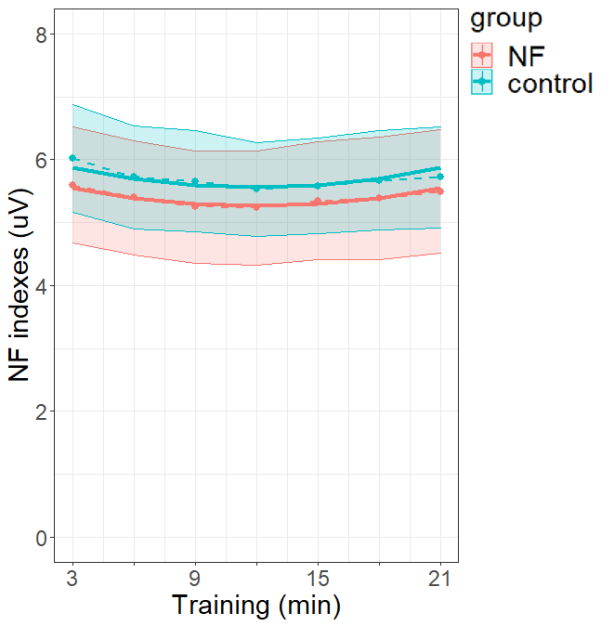

Fig. 4 **Within-sessions modulation of NF index for the NF (in red) and the control (in blue) groups.** The dotted lines and points represent the values of the NF index along the training exercises, averaged across sessions and participants for each group. Training exercises are expressed in minutes (each exercise lasted 3 minutes, with 7 exercises—21 minutes training—in each session). Shaded areas represent the standard errors of the means. The solid lines represent the exercise effect estimated for each group from the LMM.

Selectivity of the neuromodulation on alpha activity

To investigate the selectivity of the neuromodulation relative to the targeted alpha activity, we analyzed EEG activity in two adjacent bands (theta and low beta). For theta activity, there was a significant effect of session (β = 0.06, CI [0.02, 0.10], $p < .01$), without any interaction between group and session (β = -0.04, CI [-0.10, 0.01], p = 0.15). This reflected an increase of theta activity, which

was not specific to the NF group. For low beta activity, no significant effect was observed (see Supplementary Tables D.3, D.4 and Supplementary Fig. D.5 for details).

Signal quality

The estimate of the slope of the quality index evolution across sessions was significantly negative (β = -2.04e-03, CI [-3.52e-03, -5.55e-04], $p < .01$), without any interaction between group and session (β = -1.01e-03, CI [-3.14e-03, 1.12e-03], $p = 0.35$) (see Supplementary Table E.1). Thus, there was a slight decrease of signal quality across sessions and it did not differ between both groups. See Supplementary Fig. E.1.

Behavioral outcomes

Relaxation and anxiety levels

STAI-Y-A – The state anxiety level decreased significantly from pre- to post-session for the NF group (parameter estimate for phase: β = -2.46, CI [-3.45, -1.46], $p < .001$). This decrease was significantly greater for the control than the NF group as indicated by the interaction between phase and group (β = -2.13, CI [-3.55, -0.71], $p < .01$) (Fig. 5a). Moreover, there was a significant linear decrease of *STAI-Y-A* scores across sessions (β = -0.20, CI [-0.34, -0.06], $p < .01$). This decrease in anxiety level was not different between groups (β for the interaction between session and group = 9.73e-03, CI [-0.20, 0.22], $p = 0.93$) (Fig. 5b). See Supplementary Table F.1 for more details.

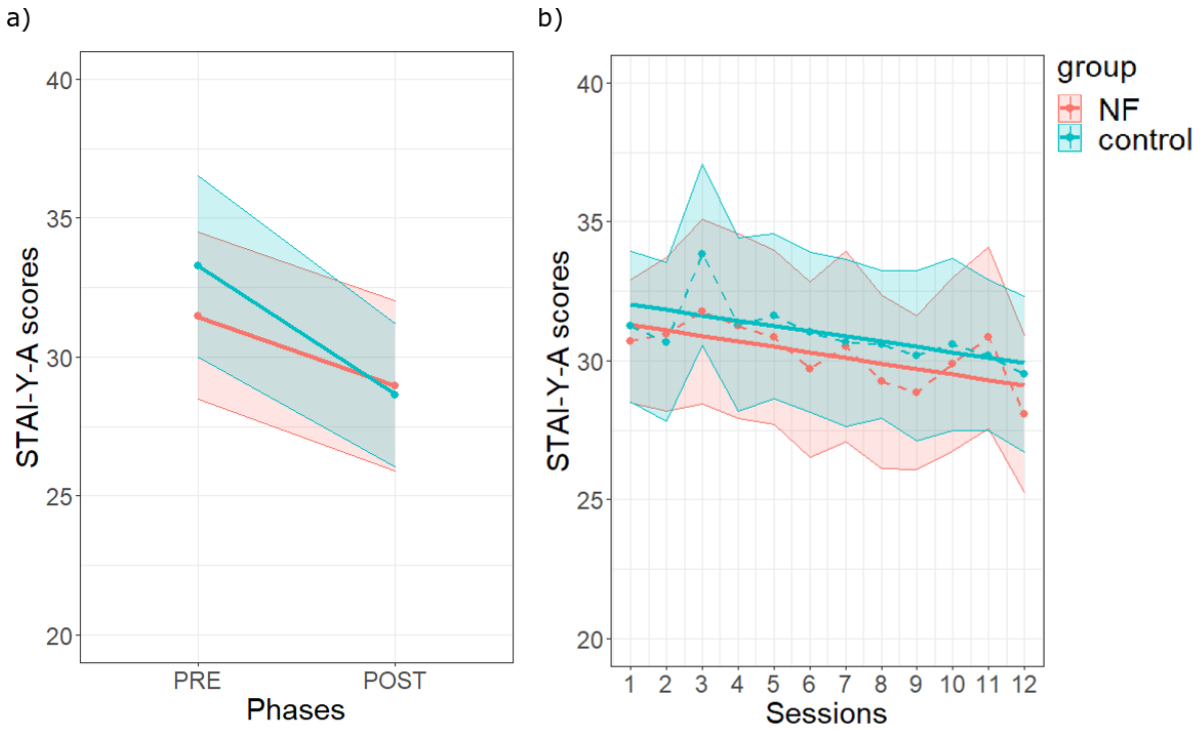

Fig. 5 **Effects of NFT on anxiety level. a) Pre-post (phase) mean effects.** Evolution of the *STAI-Y-A* scores from pre- to post-NF training sessions, averaged across participants and sessions, for the NF (in red) and control (in blue) groups. Shaded areas represent standard errors of the means. **b) Between-sessions effect on *STAI-Y-A* scores in each group.** For each session, the pre- and post-session anxiety levels were averaged. Same legend as in Fig. 3a.

relax-VAS – Relaxation, as measured by the *relax-VAS* scores, increased from pre- to post-session for the NF group (β = 0.85,CI [0.60, 1.09], p < .001) and this effect was not significantly different between groups (β = 0.33, CI [-0.03, 0.68], p = 0.07) (Fig. 6a). Moreover, *relax-VAS* scores showed a significant linear increase across the sessions (β = 0.06, CI [0.03, 0.10], p < .001) and this effect did not differ significantly between groups (β = -0.02, CI [-0.07, 0.03], p = 0.45) (Fig. 6b). See Supplementary Table F.2 for more details.

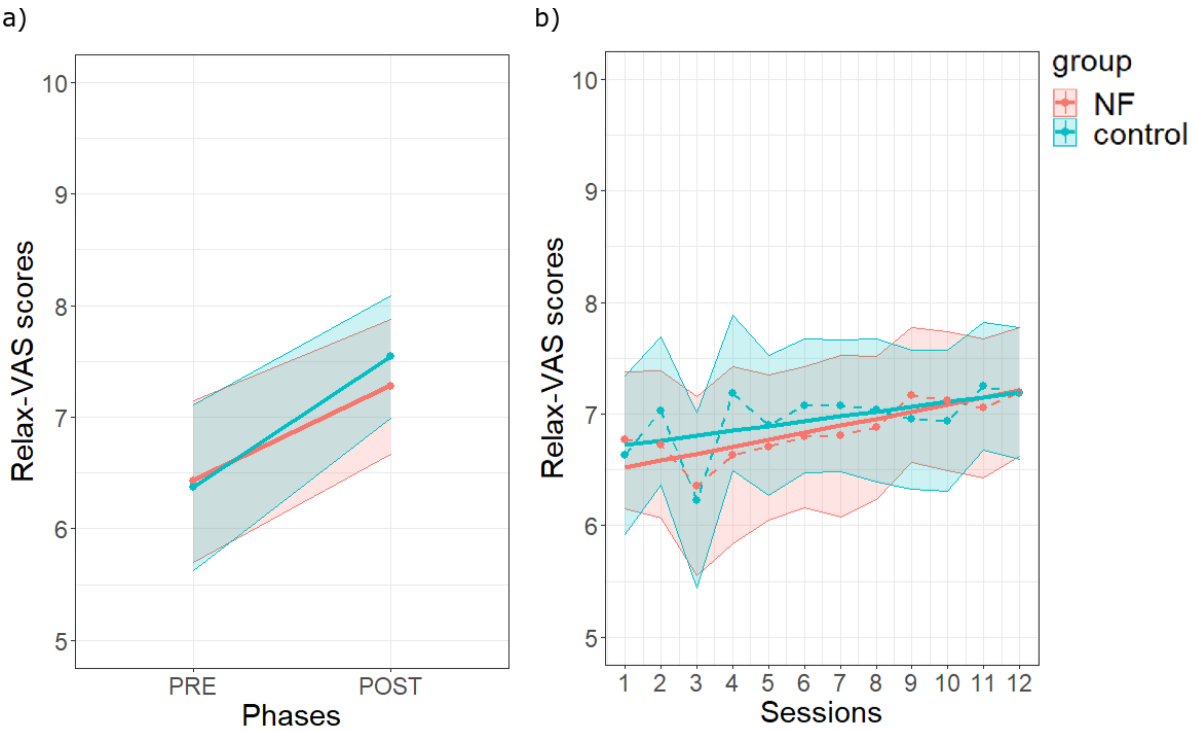

Fig. 6 **Effects of NFT on *relax-VAS* scores. a) Pre-post (phase) mean effects. b) Between-sessions effect on *relax-VAS* scores in each group.** Same legend as in Fig. 5.

Subjective feeling of control

A significant increase of the feeling of control was observed across sessions for the NF group (β = 0.12, CI [0.10, 0.15], $p < .001$). This increase was more marked in the NF group as revealed by the significant interaction between session and group (β = -0.06, CI [-0.10, -0.02], $p < .01$) (Fig. 7). In addition, similarly to the within-session effects of the NF indexes, there was a quadratic fit of control feeling over exercises for the NF group (β = 0.05, CI [0.02, 0.07], $p < .001$) which is not significantly different between groups (β = -0.01, CI [-0.05, 0.02], p = 0.47). See Supplementary Table G.1 and Fig. G.1 for more details.

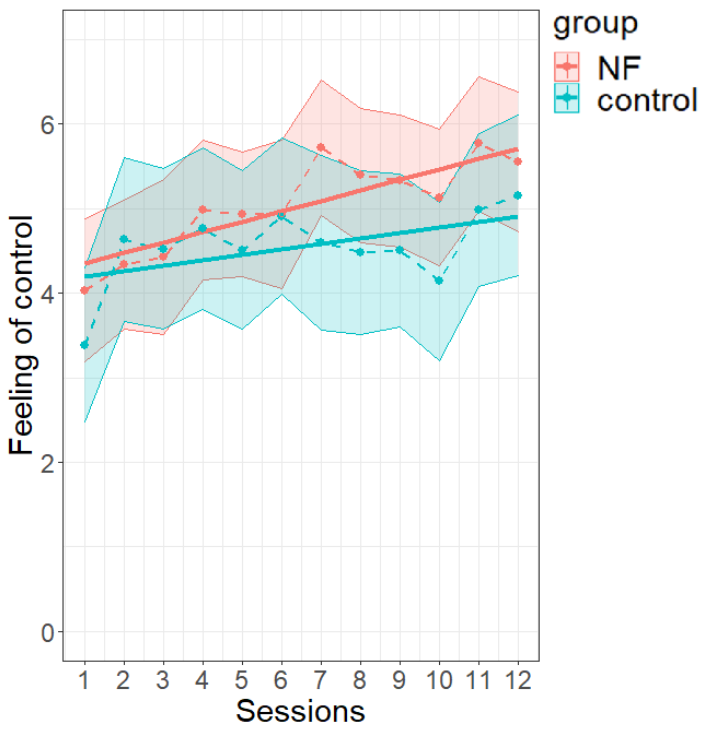

Fig. 7 **Evolution of the between-session effect of feeling of control with NF learning.** See Fig. 3 for a detailed description of the figure.

Discussion

We proposed a double-blind randomized study of the neuromodulation induced by alpha-based NFT over 12 weekly sessions using a strictly controlled sham-FB control condition. We used ecological conditions of NFT based on a wearable, dry sensor headset, which delivers intensity-modulated auditory feedback based on EEG signal amplitude in individual alpha frequency band. To avoid non-contingency between produced efforts and the resulting feedback evolution for the control group [20], the control condition consisted in delivering sham-FB—a feedback signal replayed from a randomly chosen user of the NF group at the same training stage. Hence, all participants benefited from the proposed NFT experience, but only those of the NF group experienced a closed loop between the feedback and their own alpha activity.

NF learning refers to the capacity to self-regulate a targeted activity in the desired direction across training sessions [19]. Here, the NF group was expected to increase individual alpha activity across the training sessions, reflecting lasting effects [44]. This was confirmed by the analysis of the NF index and of the NF learning score, which both demonstrated a specific effect of training sessions in the NF relative to the control group. This finding demonstrates a specific neuromodulation induced by the closed loop between the individual alpha activity and the FB, which could suggest an Hebbian neuroplasticity associated with NFT [19]. The use of a randomized double-blind protocol together with the very strict sham-FB control condition allowed us to control for the many potential confounding factors which may contribute to NFT effects. In particular, it allowed us to control for context, task, reward, and performance, avoiding potential motivational biases between the NF and control conditions [20]. Moreover, we examined the selectivity of the neuromodulation to the targeted activity, which is rarely studied [45], [46]. As proposed in [37], we analyzed two adjacent frequency bands (theta and low beta). We found an overall increase across sessions for the theta band, not specific to the NF group, and no significant change for the low beta band. This provides evidence for the selectivity of the neuromodulation associated with NFT. To the best of our knowledge, this is the first evidence of selective longitudinal alpha-band neuromodulation (over 12 weeks) in a double-blind randomized study implying healthy participants trained with a wearable dry sensors NF device.

Additionally, this study uncovered some interesting aspect of the dynamics of alpha band activity during NF learning, with a U-shape pattern of alpha activity across the exercises. Alpha activity is a spontaneous but complex rhythm associated with an ensemble of cognitive states and processes. Modulation of alpha activity has been predominantly related to vigilance, attention [47], awake but relaxed state with eyes closed [48], [49]. In this study, the NFT procedure was designed to train participants to increase alpha activity with the ultimate aim to improve their relaxation state. Yet, the U-shape of alpha activity change across the training exercises seemed to reflect the different cognitive processes involved by the task: continuous monitoring of the feedback may have required

more focused attention, error detection, and working memory processes, at the start of the training session, that is, during the first exercises, in order for the subjects to be able to progressively adapt their cognitive strategy and mental state to the task. This may have resulted in the initial decrease of the alpha activity over the training exercises [50]–[52]. Then, the subjects managed to adjust their cognitive strategy and mental state to upregulate their alpha activity. The cognitive strategies used mainly included attentional focus on landscape sounds and attention defocusing, which is consistent with the alpha increase after a few exercises. It is important to note that the within-session U-shape pattern of alpha activity was observed in both the NF and control groups. This supports the idea that the sham-FB control condition allowed us to rigorously control for the task performed by the subjects. Altogether, the quadratic fit of alpha activity revealed by the within-session analysis of the NF index values seemed to reflect the combination of multiple cognitive processes in relation with NF learning, while the specific neuromodulation of alpha activity induced by NFT was revealed in the longitudinal effect across the twelve sessions.

We also examined EEG data quality, because it can have a confounding effect on NF learning [17]. We observed a slight decrease of EEG data quality across sessions but this did not differ between both groups of participants. Thus, EEG data quality did not seem to contribute to the specific neuromodulation of alpha activity observed in the NF relative to the control group.

We investigated the behavioral changes in the form of relaxation and anxiety levels pre- and post-session and across the training program. There was a reduction of anxiety level and an increase of relaxation across the training sessions, without any group difference in these effects. This is likely explained by our study protocol. Thanks to the design of the sham-FB condition, participants in the control group experienced the same immersive, relaxing experience as the NF group, without being aware of the yoked feedback. Thus, the behavioral results obtained may be explained by non-specific mechanisms of the NFT, such as the relaxing training context, placebo effect, and repetition-related effect [17]. It may be noted that anxiety decreased more from pre- to post-session in the

control than the NF group. This may be related to the fact that the sham-FB condition allowed the subjects from the control group to be rewarded with somewhat less cognitive effort, which may have reduced their state anxiety level, for example related to their performance during the session [54]. Furthermore, the implication of healthy subjects with low to moderate anxiety levels in this study may have contributed to the lack of difference between groups. Indeed, Hardt and Kamiya [53], in their alpha-upregulation NFT study, observed positive benefits in terms of anxiety level for high but not low anxious subjects. Further investigations should involve a clinical set-up with high anxious participants to study if a specific behavioral effect of NF may be highlighted. Overall, our findings showed that NFT induced positive behavioral benefits for all participants but the part due to neuromodulation remained unclear. Indeed, the links between behavioral outcomes and neurophysiology are complex and include several factors [17], such as cognition, attention, motivation [28], training frequency [55], but also the choice of the neuromarker itself [19]. Further investigations should focus on the research of specific biomarkers related to psychophysiological factors. Moreover, directly relating NF-based neuromodulation and cognitive state dynamics is arduous because of the temporal difference between the electrophysiological and behavioral measures. To investigate this properly, real-time subjective measures would need to be reported by the participant during the NF exercises, but this would impact the performances and the focus on the task. The neurophenomenology approach could be interesting to study the influence of neural activity modulation on the participant's inner experience [56].

Finally, departing from other studies using sham-FB control groups [20], we asked participants to assess their feeling of control during the training [57]. We found an increase of the feeling of control across sessions in both groups, which suggests that participants of the control group were not aware of the non-contingency between their efforts and the feedback signal and had a qualitatively similar experience as those of the NF group in terms of NF performance. This is important to avoid confounding effects of motivation or frustration [20]. That said, the increase in the feeling of control across sessions was more marked in the NF group. This suggests that the more active nature of FB

modulation achieved in the NF group relative to the control group may have resulted in a greater feeling of control, eventually associated with a sense of agency in task performance. Importantly, this result supports the view that the neuromodulation observed in the NF group was due to the subject's gaining control over his/her brain signal, rather than motivational effects [20].

To conclude, our study demonstrates a selective and specific neuromodulation associated with NFT of alpha-band activity with a wearable dry-sensor EEG device. Even if the relationship between the targeted EEG modulation and behavioral outcomes is complex and remains to be fully elucidated, the recent development of such wearable EEG systems is promising to easily perform NF protocols to induce neuromodulation in various applications like Parkinson's disease, epilepsy, sleep, attention or anxiety disorders and better understand underlying mechanisms.

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CRediT authorship contribution statement

Fanny Grosselin: Conceptualization, Data curation, Formal analysis, Investigation, Writing - Original Draft, Writing - Review & Editing, Visualization, Project administration. **Audrey Breton:** Conceptualization, Methodology, Formal analysis, Investigation, Writing - Original Draft, Writing - Review & Editing. **Lydia Yahia-Cherif:** Formal analysis, Writing - Review & Editing. **Xi Wang:** Data curation, Formal analysis, Investigation, Writing - Review & Editing. **Giuseppe Spinelli:** Investigation,

Writing - Review & Editing. **Laurent Hugueville:** Investigation, Resources, Writing - Review & Editing. **Philippe Fossati:** Conceptualization, Methodology, Writing - Review & Editing. **Yohan Attal:** Conceptualization, Methodology, Writing - Review & Editing, Supervision. **Xavier Navarro-Sune:** Conceptualization, Investigation, Writing - Original Draft, Writing - Review & Editing, Project administration. **Mario Chavez:** Methodology, Investigation, Writing - Review & Editing. **Nathalie George:** Conceptualization, Methodology, Writing - Original Draft, Writing - Review & Editing, Supervision, Project administration.

Declaration of competing interest

myBrain Technologies provided the mobile EEG device used in the present study (Melomind™). F.G, A.B., X.W., G.S., Y.A. and X.N.-S. are or were full-time employees of myBrain Technologies and had a role in the study conceptualization, methodology, formal analysis, investigation, supervision, visualization or writing the manuscript. N.G. and L.H have a collaboration agreement with myBrain Technologies for the development of the mobile EEG system constitutive of Melomind™ device. The authors L.Y.-C. and M.C. declare that they have no competing financial interests.

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