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NEUROFEEDBACK PERFORMANCE UNDER CHALLENGING CONDITIONS: THE THETA-AGENCY INTERPLAY

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ABSTRACT
Neurofeedback (NF) consists in training the self-regulation of some target neural activity. Yet, the neural underpinnings of NF performance remains largely unknown. Here, we investigated Motor Imagery (MI) based NF with EEG, training subjects to regulate motor-related activity in the large β (8-30 Hz) band. We examined the electrophysiological correlates of NF performance across the whole scalp and the frequency spectrum. In addition to the rewarded β activity, fronto-central θ activity predicted NF performance. The association was modulated by the participants' sense of agency over the feedback with stronger effects in participants with lower agency. Fostering agency in NF protocols may reduce cognitive effort and reliance on additional rythms beyond β. Considering these effects could be important for optimizing NF performance.

INTRODUCTION
Neurofeedback (NF) is a cognitive training procedure aiming to train subjects to modulate a specific neural activity, by providing them real-time feedback (FB) on this activity. The premise is that there is a causal link between neural activity and mental (sensory, cognitive, or motor) functions. Mastering control over a targeted activity may improve or restore the corresponding cognitive or sensorimotor ability. However, NF raises several scientific and technical challenges. One of them is the high percentage of non-responders and the variability of NF performance. This raises the question of the neural mechanisms of NF learning and the neural processes associated with NF performance.
Among the possible processes involved, placebo effects [1,2], non-specific training effects [3], and indirect causality effects are debated [4].
In this study, we focused on motor imagery (MI) NF paradigms using electroencephalography (EEG), to train participants to reduce the motor-related β band activity (here considered between 8 and 30 Hz) by imagining right hand movements.
NF learning has been proposed to rely on reinforcement learning, yet this remains untested [5,6]. Psychological factors such as technology acceptance, attention and spatial abilities are known to influence performance [7]. Besides psychological traits, the dynamic cognitive processes contributing to NF success were seldom investigated. These may entail cognitive control, attentional processes, and reward processing among others. These processes are underpinned by rhythms different from the rewarded β activity, hindering the specificity of the training and complicating the interpretation of behavioral or clinical effects [4]. In this line, recent studies have demonstrated functional connectivity outside of the expected motor networks in MI-based NF protocols [8]. Moreover, some NF studies targetting α, β or γ band activities have reported modulations of electrophysiological rhythms beyond the rewarded frequency band [9,10], while others provided evidence for specificity of NF training [11,12].
In this study, we aimed to move past identifying rhythms whose modulation temporally coincided with NF training. We investigated the neural activities associated to successful NF performance beyond the targeted β activity.
Exploratory studies have shown that psychological predictors of NF performance differ between θ and β NF paradigms varies [13]. Additionally, experimental factors such as visual or tactile feedback modality modulate differential rythms [14]. Thus, psychological and experimental factors may modulate the association between non-specific activities and NF performance.
We used an MI-based NF task rewarding the downregulation of activity on central, motor regions in the 8-30 Hz band. Participants were trained with three different FB conditions and we measured their sense of agency i.e. sense of control over the FB. An initial analysis focused on the relationship between agency and NF performance and showed that the subjective sense of agency over FB predicted NF performance [15]. Here, we focused on the electrophysiological correlates of NF performance beyond the rewarded activity and explored activities in the θ (3-7Hz), α (8-12 Hz) and β (13-30Hz) bands across the whole scalp. We also examined whether FB conditions and/or sense of agency interacted with these electrophysiological correlates.

MATERIALS AND METHODS
We used Dussard et al.’s dataset [15]. Full materials and Methods details are provided in [15].

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Participants
Twenty-three healthy right-handed participants (mean age 28 ± 7 years, 11 women) were included in this study approved by the CPP IdF VI ethics committee. Participants gave written informed consent and received financial compensation after participation.

Experimental protocol
The experiment consisted in one NF session. Participants performed the MI-NF task with three different FB conditions (Figure 1A).
The FB conditions were either visual, with 1) a pendulum (PENDUL) oscillating to the right, 2) a clenching virtual hand (HAND) or multimodal, with 3) a clenching virtual hand combined with motor illusion vibrations (HAND+VIB).
For each FB condition, participants performed 2 runs of 5 trials (Figure 1B). We presented the FB in separate blocks to avoid the potential cognitive cost of trial-by-trial FB switching. The order of the FB conditions was counterbalanced across participants.
Each NF trial lasted 24s and featured 16 FB movements lasting 1.5s (Figure 1C). Participants were trained and instructed to perform MI at the pace of the rhythmic visual FB movements.
The sense of agency was measured after each run of 5 trials with a 11-point Likert scale in response to the question: “Did you feel like you were controlling the movements of the pendulum/hand?”.

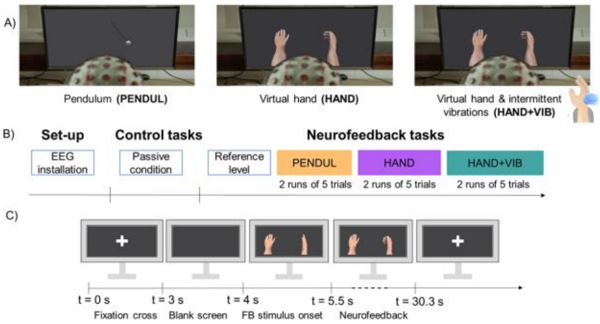

Figure 1. Illustration of the experimental protocol. A. Representation of the different FB conditions, i.e., PENDUL, HAND and HAND+VIB. B. Time course of the experiment. C. Time course of an example trial in the HAND condition

To control for the effect of FB stimulus on EEG activity, participants also underwent control tasks consisting in passive trials where they observed random movements of the pendulum or the virtual hand and eventually received additional vibrations (Figure 1B).

A 2x30s resting state recording with eyes open on a fixation cross established NF reference threshold, based on median 8-30Hz activity on C3 electrode (computed as the Laplacian between C3 and FC1, FC5, CP1, CP5) (Figure 1B). Then, during the NF trials, a 10% reduction of this activity induced positive FB in the form of movement on screen and over 55% reduction triggered maximal amplitude of FB movement (either swing for the pendulum or clenching for the virtual hand). Activity reduction between these upper and lower limits triggered a linearly proportional movement amplitude. Twenty-one out of 23 participants obtained positive visual FB.
For HAND+VIB FB, vibrations were delivered by a vibrator attached on the right-hand extensor tendons. They were triggered every 6s if the participant maintained an average of 30% reduction in the previous 6s. Tactile FB was intermittent to avoid habituation-related opposite direction movement illusions [16].

EEG Data acquisition
EEG signal was recorded with an actiCHamp Plus system (Brain Products GmbH) using a 32-active electrode cap (ActiCAP snap, Brain Products GmbH). The signal was referenced to Fz electrode. The ground electrode was Fpz. The data were recorded at 1 kHz with a band-pass filter of DC-280Hz. Data were transmitted to OpenViBE 2.2.0.

Online EEG signal processing
A laplacian filter was computed over the C3 electrode by subtracting the signals from CP5, FC5, CP1 and FC1 electrodes. The signal was epoched into 1s time windows with 0.75s overlap then filtered in the 8-30 Hz band. The signal values were squared and averaged over time in each epoch. These epoch values were streamed to a Unity application using Lab Streaming Layer (LSL) communication protocol. Each FB movement was determined by the mean of four consecutive epochs. This mean was compared to the pre-determined reference threshold. The amount of reduction in β power was conveyed by the amplitude of FB movements.

Offline EEG signal processing
We performed offline analyses of the event-related desynchronisation/synchronisation (ERD/ERS) during trials with MNE Python. The continuous raw data were filtered with 0.1 Hz high-pass, 90 Hz low-pass, and two zero-phase notch filters (50 and 100 Hz cut-off). The signal was epoched into NF and control trials. We excluded the trials with muscular artifacts. We rejected electrodes around the maxillary regions from analysis due to frequent muscular artifacts. We removed ocular artifacts with independent component analysis. The data were average-referenced and downsampled to 250 Hz. We computed EEG power between 3 and 30 Hz with a Morlet wavelet transform with 1 Hz frequency bins. We averaged the resulting time-frequency data across trials, for each run of each FB condition, in each participant. We normalised power values relative to a 2s fixation cross baseline before the trial onset using a log-ratio. Finally, we averaged the obtained ERD/ERS data across time in each condition.

Statistical analyses
ERD/ERS predictors of NF performance
We used a mass univariate approach based on linear mixed-effects regression (LMER) models to explore the relationship between NF performance and ERD/ERS computed between 3 and 30 Hz over the whole scalp. Thus, for each electrode i and each frequency j, we computed a model with NF performance as the outcome

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variable and the ERD/ERS value at the electrode i for the frequency j (ERD_ERSvaluei,j) as fixed effect factor. We included runs as a fixed effect covariate and a random intercept of the NF performance across participants.

The models were written in R 4.0.4 with the lme4 package, as follows: NF_performance ~ $ERD\_ERS_{i,j}$ + run + (1 | participant_id)
Model parameters were estimated using Restricted Maximum Likelihood and p-values were estimated using Type III ANOVA. Parameter estimates of the fixed effect of ERD/ERS were extracted for each electrode and frequency and tested for significance with false discovery rate (FDR) correction for multiple comparisons applied to the p values (n = 756: 28 electrodes x 27 frequencies).
This analysis allowed the identification of a fronto-central θ activity predictive of NF performance. We investigated further this activity in subsequent analyses.

Impact of FB condition on fronto-central θ activity
To control for the potential effect of vibrations in the HAND+VIB condition, we repeated the initial LMER analysis by excluding the vibration periods from the trial data, before averaging the ERD/ERS data across time. For this, we excluded NF performance values of cycles 4, 8, 12 and 16, which could feature vibrations.

Potential modulators of fronto-central-θ predictor
We tested if FB condition and sense of agency modulated the identified fronto-central θ activity. To do so, we averaged the ERD/ERS values that significantly predicted NF performance after FDR-correction on fronto-central electrodes in the θ band. We used LMER analysis to assess the interaction between this averaged fronto-central θ activity and i) agency, ii) FB condition. Thus, the model was the following:
NF_performance ~ ERD/ERS_Theta*Agency + ERD/ERS_Theta*FB + Run + (1 + FB + Agency + ERD/ERS_Theta | participant_id)
We chose this random-effects structure to control for Type I error while allowing model convergence.
We ran the same analysis on the left central β cluster (corresponding to the rewarded activity) as a control.

RESULTS

Electrophysiological correlates of NF performance
First, we examined the ERD/ERS patterns that accounted for NF performance by computing LMER models over the scalp and the frequency spectrum.
Decreased power in the rewarded 8-30Hz band over the left central regions was positively associated with NF performance (Figure 2A). This was expected since our design trained participants to reduce this activity and FB (aka. NF performance) was computed on the basis of 8-30 Hz band activity on C3 through OpenVibe. This effect seemed particularly marked in the 13-30 Hz band and extended bilaterally; it extended on parietal electrodes in the high-β band. Such activity is typical of MI task [17].

Moreover, power in the low θ band (3-4Hz) over fronto-central regions was positively associated with NF performance: increased fronto-central low θ power predicted higher NF performance (Figure 2A and 2B).

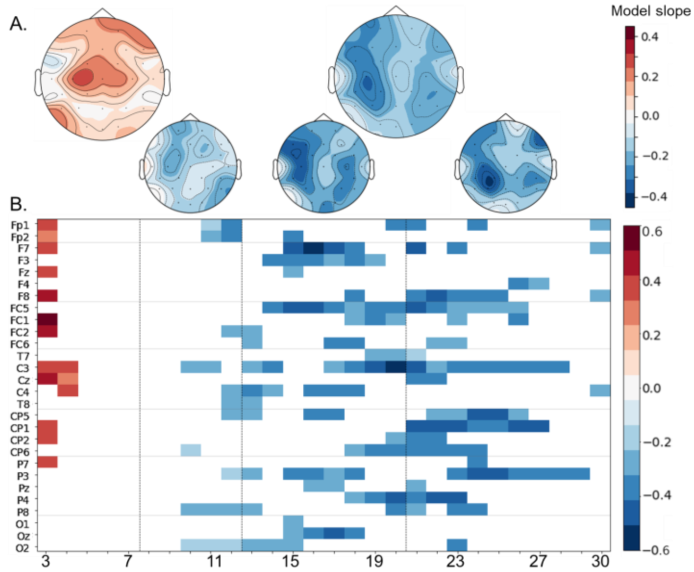

Figure 2. Parameter estimates of the effect of ERD/ERS on NF performance across electrodes and frequencies. Blue indicates negative estimates, that is, decreased power predicts higher NF performance. Red color indicates positive estimates increased power predicts higher NF performance. A. Topographic maps of the parameter estimates averaged in different frequency bands. Topmost maps: left map for 3-7 Hz and right map for 8-30 Hz. Lower maps depict from left to right: 8-12 Hz, 13-20 and 21-30 Hz. B. Electrode-frequency representation of parameter estimates, with electrodes in ordinate (from frontal electrodes on the top to occipital electrodes on the bottom) and frequencies in abscissa. Only statistically significant parameter estimates at p<.05 with FDR correction are displayed.

We then focused on this fronto-central θ pattern, which stood out as it was not rewarded in our NF protocol and is not typically associated with MI.

Impact of FB condition on fronto-central θ activity
First, we investigated if this fronto-central θ activity was influenced by the FB condition. Our previous findings showed vibration-locked patterns of θ synchronisation in the time-frequency representations [16] (see Figure 3A and 3B).
If θ activity was a byproduct of the vibratory FB, this could confound our result since the vibrations were by design associated with successful NF performance.
The effect of the vibratory FB on the θ band was further illustrated by displaying topographical maps of θ activity averaged over the time periods of the vibrations, during the NF trials (Figure 3A top) and the passive, control trials (Figure 3B, top).

The fronto-central pattern θ ERS was concomitant of the vibrations. Yet, it was somewhat more central in the passive condition (Figure 3B, top).
The θ ERS was short-lived, lasting ~0.5s of the 2s vibration duration. Its amplitude decreased from the first to last vibration in the passive condition.

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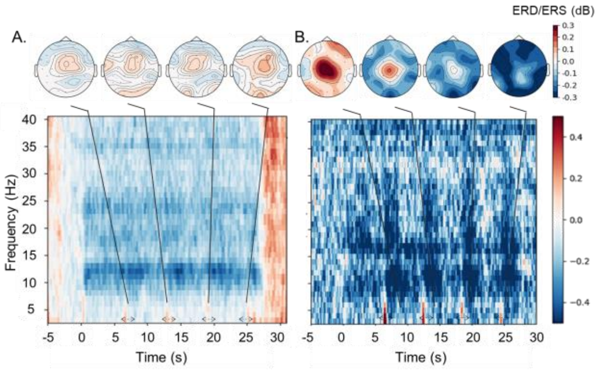

Figure 3. A. Grand average data of the NF HAND+VIB trials. B. Grand average data of the passive condition with virtual hand and vibration stimuli. Top: Topographical maps of the 3-7Hz ERD/ERS during the vibration periods. Bottom: Time-frequency representation of ERD/ERS on C3 electrode.

As an additional control, we re-ran our LMER analysis by excluding the vibration periods in the HAND+VIB trials. The results remained unchanged. This suggests that the fronto-central θ effect on NF performance was not attributable to a confounding effect of the vibratory FB.

Potential modulators of fronto-central θ predictor

We then investigated whether FB conditions and/or sense of agency modulated the association between the fronto-central θ activity and NF performance. Indeed, our original analysis showed that subjective sense of agency over FB was a significant predictor of NF performance [16].

For this analysis, we extracted and averaged the ERD/ERS values on the electrodes and the low θ frequencies (3-4Hz) where a significant effect on NF performance had been found. We then ran an LMER analysis taking into account the effects of FB condition and agency and their potential interaction with the fronto-central θ effect.

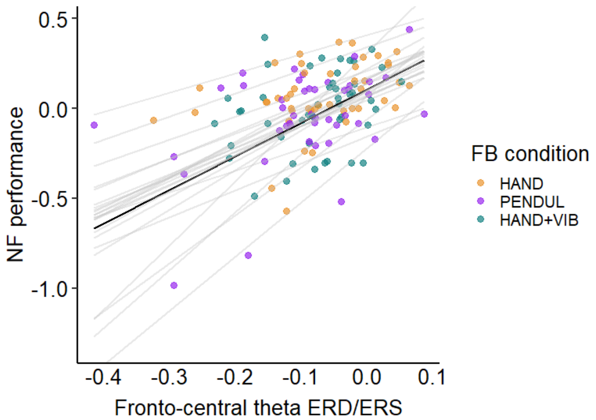

Figure 4. Relation between NF performance and fronto-central θ activity. Individual data for each FB condition (HAND in orange, PENDUL in purple and HAND+VIB in turquoise). Thin gray lines represent the individual random slopes and intercepts of the effect of fronto-central θ on NF performance. The black thick line represents the estimated fixed effect of fronto-central θ on NF performance.

This analysis showed when accounting for the effects of FB condition and agency, the main effect of fronto-central θ on NF performance remained significant (parameter estimate: = 1.87, 95% CI [0.93, 2.81]; $F(1, 71.9) = 18.8$, $p < 0.001$) (Figure 4). Thus, fronto-central θ activity was neither a mere electrophysiological correlate of sense of agency nor of FB condition.
There was no significant interaction between fronto-central θ and FB conditions ($F(2, 81.4) = 0.55$, $p = 0.58$). Therefore, fronto-central θ activity seemed associated with NF performance regardless of FB condition.

In contrast, there was a significant interaction between fronto-central θ and sense of agency (parameter estimate = -0.22, 95% CI [-0.34, -0.10]; $F(1, 93.3) = 12.5$, $p < 0.001$). To illustrate this interaction, we represented NF performance as a function of fronto-central θ values, splitting the data according to different scores of agency (1st tercile [0-3] in red, 2nd tercile [4,7] in brown and 3rd tercile of agency scores [8-10] in green, in Figure 5). We represented the model predictions by plotting the estimated slopes of fronto-central θ effect on NF performance at three fixed agency values (2, 6 and 8) (colored lines in Figure 5).

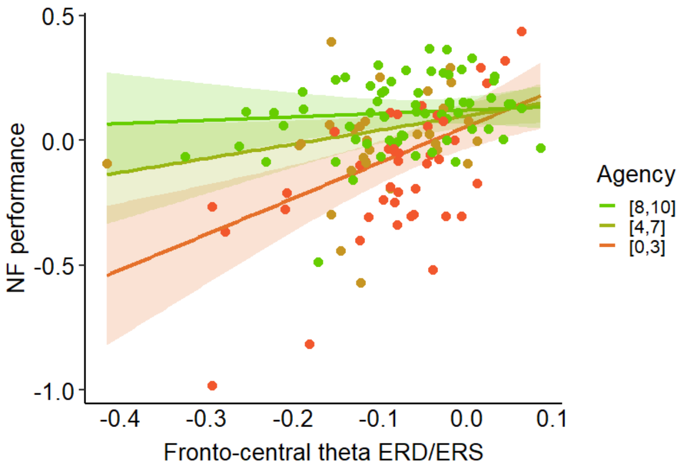

Figure 5. Relation between NF performance and fronto-central θ activity as a function of agency. Dots represent the individual data for each run and each FB condition, colored by agency bin (1st tercile in red-orange, 2nd tercile in light brown, 3rd tercile in green). The colored lines represent the estimated slopes of fronto-central θ effect on NF performance for the median agency values of each tercile (agency values of 2, 6 and 8), with shaded areas indicating 95% confidence intervals around these slopes.

This showed a positive correlation between NF performance and fronto-central θ for low scores of agency. With higher scores of agency, the slope declined gradually, reflecting that NF performance was less associated to fronto-central θ.
The same analysis run on the C3 β cluster showed a significant main effect of β on NF performance ($F(1, 53.9) = 8.03$, $p = 0.006$). In contrast to the fronto-central θ activity, we did not find any interaction between FB and C3 β ($F(2, 57.9) = 1.86$, $p = 0.17$) or between sense of agency and β ($F(1, 79.5) = 1.47$, $p = 0.23$).

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DISCUSSION

This study investigated the electrophysiological correlates of NF performance in an MI-based EEG NF protocol. We found significant associations between NF performance and ERD/ERS patterns in the central motor region in the rewarded β band. Additionally, fronto-central θ activity consistently predicted NF performance. Diving deeper, we identified an interaction between this fronto-central θ activity and sense of agency. NF performance was more strongly associated with fronto-central θ activity in participants with lower agency.

EEG patterns of NF performance

Our results showed that NF performance was associated with power reduction in the rewarded 8-30Hz range in left central regions. Left central μ-β desynchronisation is reliably associated with right-hand MI-BCI performance [18,19]. Our study extends these findings by examining performance correlates across different FB conditions in a within-subject NF design.

In addition to the rewarded left central β activity, fronto-central θ power predicted NF performance. In line with this result, both pre-cue [20,21] and on-task θ power [22] were shown to predict BCI performance.

Frontal θ activity notably emerges in response to perceived conflict [23] such as negative FB in NF. Negative FB processing would enable for adjustement of the NF strategy towards better NF performance. In line with this interpretation, an α NF study reported that θ activity differentiated sham from NF participants. This was seen as a constancy of conflict/error-prediction signals in the sham group, while the NF group reduced conflict by improving NF performance [24].

MI modulates frontal θ activity more than motor execution, highlighting increased mental effort [25]. Specifically, frontal θ shows higher involvment in kinesthetic than visual MI [26]. Mental demand has been correlated to a θ-β combination in a BCI paradigm [27]. Studying within-trial dynamics of θ activity and NF performance may reveal if θ activity arises locally in response to negative FB or if it reflects overall attention and cognitive effort.

Impact of FB condition on fronto-central θ activity

Vibrations in the HAND+VIB condition were associated with fronto-central θ synchronisation in the NF tasks. Midfrontal θ oscillations have been proposed to encode the value of tactile delay [28]. This is especially relevant because the vibrations were delivered following the integration of a 6s time segment i.e: they constituted a delayed, asynchronous FB. In contrast, during the passive task, θ patterns were more central, potentially reflecting sensory processing. Vibrations modulate activity on central θ activity [29].

However, the relationship between NF performance and fronto-central θ activity remained significant after excluding vibration segments from the analysis.

Agency is a modulator of the fronto-central-θ predictor

Both sensorimotor β [30] and fronto-central θ [31, 32] relate to sense of agency. Yet, our analysis showed that both θ and β predictors remained significant after accounting for agency.

Further analysis showed that sense of agency modulated the association between θ and NF performance: a stronger association was observed in participants with low sense of agency. We suggest that participants reporting high sense of agency may have required less mental effort to achieve NF performance. Our findings resonate with recent reinforcement learning research, which reports differences in θ and β in response to positive and negative FB between agent and passive participants [33]. Negative FB elicited more fronto-central θ activity than positive FB. Crucially, the difference between positive and negative FB more pronounced difference in agent participants. This contrasts with our observations that θ dynamics in the NF context were heightened in participants with a low sense of agency. Altogether, these results suggest a potential role for sense of agency in shaping strategies employed during reinforcement learning tasks, including NF.

CONCLUSION

This study shed some light on the neurophysiological correlates of NF performance, highlighting the role of θ activity and its interaction with sense of agency. All in all, sense of agency allows for better performance, associated with a more specific pattern of modulation. It is important to consider that participants can mobilize different processes to manage NF performance. It is key to control for the activities that are modulated with NF training as they may contribute to non-specific effects. Monitoring such activities could be important for some clinical applications of NF where neurophysiological specificity is of crucial importance.

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