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Theta EEG neurofeedback benefits early consolidation of motor sequence learning

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Abstract

Procedural learning is subject to consolidation processes believed to depend on the modulation of functional connections involved in representing the acquired skill. While sleep provides the most commonly studied framework for such consolidation processes, posttraining modulation of oscillatory brain activity may also impact on plasticity processes. Under the hypothesis that consolidation of motor learning is associated with theta band activity, we used EEG neurofeedback (NFB) to enable participants to selectively increase either theta or beta power in their EEG spectra following the acquisition phase of motor sequence learning. We tested performance on a motor task before and after training, right after the NFB session to assess immediate NFB effects, 1 day after NFB to assess interaction between NFB effects and overnight sleep-dependent stabilization, and 1 week after the initial session, to assess the effects of NFB on long-term stabilization of motor training. We also explored the extent of the influence of single-electrode NFB on EEG recorded across the scalp. Results revealed a significantly greater improvement in performance immediately after NFB in the theta group than in the beta group. This effect continued for testing up to 1 week following training. Across participants, post-NFB improvement correlated positively with theta/beta ratio change achieved during NFB. Additionally, NFB was found to cause widespread band-power modulation beyond the electrode used for feedback. Thus, upregulating postlearning theta power may yield contributions to the immediate performance and subsequent consolidation of an acquired motor skill.

Descriptors: Procedural, Motor learning, Neurofeedback, EEG, Consolidation

The initial formation of memory traces is followed by time windows during which those traces may be consolidated (Dudai, 2004, 2012; McGaugh, 2000). In procedural learning, consolidation may involve both stabilization, expressed as immunity to retroactive interference, and enhancement, expressed as "offline" improvement in performance without further practice (Robertson, Pascual-Leone, & Miall, 2004). Perhaps the most important process affecting the consolidation of procedural learning is sleep (Albouy, King, Macquet, & Doyon, 2013; Diekelmann & Born, 2010; Inostroza & Born, 2013). A full night's sleep leads to performance improvements without further practice (e.g., Fischer, Nitschke, Melchert, Erdmann, & Born, 2005; Robertson et al., 2004; Walker, Brakefield, Morgan, Hobson, & Stickgold, 2002). Similarly, a 90-min nap shortly after training may also enhance performance (Albouy, Fogel et al., 2013; Backhaus & Junghanns, 2006; Doyon et al., 2009; Korman et al., 2007; Nishida & Walker, 2007).

As consolidation is expressed not only by the preservation of learning in the face of potential interference but also in offline gains in performance, seemingly sleep influences memory not as a state of quiescence, but rather via a range of neuromodulatory and electrophysiological events (Inostroza & Born, 2013; Stickgold, 2013). Spindles occurring during Stage 2 sleep have been especially linked to procedural consolidation (Barakat et al., 2011, 2013; Morin et al., 2008). Such sleep spindles have been reported to entrain neurons throughout neocortex during "up" states of slow wave sleep (Buzsáki, 2005; Steriade, 2003) and are temporally coupled to hippocampal sharp wave–ripple complexes (Siapas & Wilson, 1998; Sirota, Csicsvari, Buhl, & Buzsáki, 2003). This coupling is thought to provide a mechanism for the information transfer between hippocampus and neocortex underlying consolidation (Axmacher, Mormann, Fernandez, Elger, & Fell, 2006). Synchronization of neural activity may enable the replay during sleep of firing patterns that characterized encoding events (Diekelmann & Born, 2010), which may reinforce synaptic plasticity initiated during encoding. Importantly, consolidative replay might occur not only during sleep, but in waking as well (Tambini, Ketz, & Davachi, 2011).

Cortico-hippocampal synchronization and replay are relevant to procedural consolidation, as much evidence has accumulated for a hippocampal role in such learning (Schendan, Searl, Melrose, & Stern, 2003; for review, Albouy, King et al., 2013). This may be because procedural learning requires acquisition not only of

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egocentric motor sequences but of allocentric spatial representations, and of a temporal structure combining series of movements into a coherent unit (Albouy, King et al., 2013), which may also be hippocampus-dependent, especially in early stages of learning.

Posttraining replay leading to consolidation, during waking as well as during sleep, may be amplified by increasing functional connectivity between the substrates of learning. Effective functional connectivity involves increased synchrony of neural firing, which is expressed through greater EEG band power in frequencies characteristic of the relevant cell assemblies (Fries, 2005; Klimesch, 1996). The functional connectivity that best engenders consolidation during waking might be characterized by theta oscillations. A number of studies of declarative memory have noted that increased theta power in the scalp EEG is associated with better memory performance during both encoding and retrieval (e.g., Burke et al., 2013, 2014; Klimesch, Doppelmayr, Schimke, & Ripper, 1997; Klimesch et al., 2001; for reviews, Baastiansen & Hagoort, 2003; Nyhus & Curran, 2010). Widespread cortical and cortico-hippocampal theta phase synchronization found to characterize effective encoding have been proposed to facilitate simultaneous activation of neural assemblies (Fell & Axmacher, 2011). In animal studies, EEG theta rhythm has been reported to index prefrontal tagging of memories for subsequent consolidation during sleep (Benchenane et al., 2010). Accordingly, posttraining theta rhythm modulation might be a method of promoting procedural consolidation.

In an earlier study, we demonstrated that motor sequence learning (MSL) after neurofeedback (NFB), in which theta power was augmented for 45 min, led to subsequent benefits in explicit MSL, relative to conditions during which beta power was augmented, or during which participants passively viewed movies (Reiner, Rozengurt, & Barnea, 2014). Importantly, as in sleep consolidations studies, theta NFB led not only to preservation of learning, but to offline improvement relative to best prior performance.

In the current study, we attempted to confirm and expand upon that initial finding in several ways. First, we strove to constructively replicate the previous findings using a slightly different MSL task (employing key presses instead of finger tapping), to explore the task specificity of the effect, as well as to prevent technical confounds of repetitive touches and finger swiping. Second, we reduced the duration of the posttraining NFB session from 45 to 30 min, to explore the minimum conditions for effect emergence. Third, we examined whether providing theta-augmenting NFB using Pz versus Fz electrodes would affect the memory benefit. Fourth, as opposed to our earlier study in which we employed a single electrode, in the current study we used a montage of 19 electrodes, in order to examine the effects of Fz NFB on the theta and beta power recorded at other scalp locations. As in our prior study, the parameter used to provide positive feedback was theta/beta ratio. This has been reported to better characterize cognitive traits of attention-deficit hyperactivity disorder (ADHD) than absolute theta power (Snyder & Hall, 2006), seemingly by more effectively differentiating the cognitive processes underlying each frequency band (which yet remain to be definitively identified; Loo & Makeig, 2012). As this parameter was found in several studies to be effective not only in diagnosis but in NFB treatment of ADHD (Arns, Conners, & Kraemer, 2013), we chose to use it in our intervention as well, with the aim of providing the optimal differential modulation of theta (target) and beta (control) band activity.

We expected increases in the performance measure of the number of accurate sequences executed per time-limited trial, for both groups, due to the effect of training during the test, and in the post-24-h test, to the effects of sleep. Crucially, we predicted that there would be greater improvement in performance following NFB in the theta group than in the beta group (which served as a control group to rule out nonband-power-specific effects). In addition, we expected that this advantage in performance improvement would remain stable for some time after the NFB session, due to the stability of consolidated MSL.

Method

Participants

Participants were 60 volunteers (35 females; mean age = 27.7, *SD* = 8.9 years), who participated in the study in return for payment and/or academic requirement credit. Participants were right-handed (all scored positively on the Edinburgh Handedness Inventory; Oldfield, 1971), and were in self-reported good health, with no history of psychiatric or neurological disorders nor chronic use of medication. In accordance with instructions that they received before beginning participation, and in response to direct querying by the experimenter, all participants reported more than 6 h of nocturnal sleep per night before and during the week of the experiment, and had no sleep disruptions. Musicians and expert typists were excluded from participation. Participants were unaware of the goals of the experiments. Informed consent was obtained from all participants for a protocol approved by the Institutional Review Board of the Interdisciplinary Center Herzliya.

The initial 50 participants in the study were randomly assigned to theta or beta intervention groups by alternating serial order. In order to balance the two groups for baseline band power values, the final 10 participants were assigned to their intervention conditions following recording of their baseline EEG but before and without reference to their performance in the NFB or MSL stages of the experiment.

Protocols

Motor sequence learning (MSL). The key aim of the present study was to execute a constructive replication of our previous demonstration of the beneficial effects of theta NFB on MSL. In the previous study, we employed the finger-opposition version of the finger-tapping task, in which digits 1–4 (1 is the index finger and 4 is the little finger) tap the thumb in a set sequence (Karni, Tanne, Rubenstein, Askenasy, & Sagi, 1994; Korman, Raz, Flash, & Karni, 2003). In the current study, we employed a keyboard version of the task (Nishida & Walker, 2007; Walker, Stickgold, Alsop, Gaab, & Schlaug, 2005), in which digits 1–4 of the nondominant left hand press ergonomically spaced and clearly marked keys on a standard computer keyboard. Participants were instructed to continuously press the numbered keys in the sequence: 4-1-3-2-4, as rapidly and accurately as possible, until given a stop signal. They performed the instructed presses while sitting comfortably, without visual feedback (i.e., they were instructed to look away from the keyboard throughout the task). Key presses were recorded in a data file for later analysis of errors and number of correct sequences produced during each task epoch.

Baseline performance assessment and posttraining tests. These tests (administered immediately after training, after NFB, after 24 h, and after 1 week) consisted of four trials of 30 s each, with a 50-s rest period between the trials. Each trial epoch throughout the experiment was cued to start with the third of three short auditory tones, and cued to stop by a single tone. Participants were

instructed that occasional errors should not be corrected, and to continue without disruption. For the behavioral results reported below (Figure 2 and 3 and related text), we selected the trial with best performance of the four test trials comprising each test session, in order to capture the peak skill capacity afforded by the training, since after sequence errors participants sometimes temporarily ceased execution altogether. We also analyzed mean performance over all four trials, as reported below.

Motor-sequence training. Motor-sequence training consisted of 160 repetitions of the assigned sequence (4-1-3-2-4), divided into 10 training blocks. Each training sequence was paced, being cued by an auditory signal at a rate of 0.4 Hz, so that the subject had 2.5 s per sequence for execution after the cue. We chose a paced-training approach in order to lead participants to be more focused on accuracy in early stages of acquisition, with speeding of subsequent performance more likely to be achieved with less of a speed-accuracy tradeoff. Training blocks were separated by 30-s rest breaks to reduce muscular fatigue.

Neurofeedback (NFB). NFB was performed using EEG recorded with the Mitsar-202 EEG system (Mitsar, St. Petersburg, Russia). Nineteen silver-chloride electrodes were placed on the scalp using an elastic cap, according the standard 10-20 system, at the following sites: Fp1, Fp2, F7, F3, Fz, F4, F8, T3, C3, Cz, C4, T4, T5, P3, Pz, P4, T6, O1, and O2. The input signals were recorded in a monopolar montage, with linked earlobe reference electrodes. The ground electrode was placed on the forehead. Impedance was kept below 5 kΩ. EEG was amplified, band-pass filtered at 0.5–30 Hz, and sampled at the rate of 250 Hz. During online NFB, a 100 μV artifact-rejection threshold was used to interrupt NFB during eye and body movements that produced gross EEG fluctuations.

During NFB, the spectral distribution of the ongoing oscillatory brain activity was derived from EEG in real-time, using WINEEG software (Mitsar), and stored for further offline analysis. This program, running on a portable computer, received digitized EEG data from all channels. Mean absolute spectral power and relative spectral power of the EEG for each bandwidth was calculated for each subject and each particular condition using fast Fourier analysis, with the following parameters: epoch duration of 4,096 ms, epoch overlapping of 50%, time smoothing with the Hann window. The spectral characteristics were computed for frequencies ranging from 1–22 Hz, and analyzed for frequency bands of interest: theta (4–8 Hz), low beta (15–18 Hz), and high beta (18–22 Hz). The intensity of the high beta band increases during motion (Gasser, Schuller, & Gasser, 2005). Therefore, positive NFB was only provided in both experimental groups as described below if the participants also suppressed high beta (> 18 Hz) along with increasing power in their target power band, in order to avoid positive feedback due to motion and to reduce motion artifacts. The values of each of the EEG power spectra were normalized for each participant and for each electrode, relative to overall raw EEG power.

For the recording of resting stage baseline, all participants sat quietly with their eyes open for 3 min. EEG data were recorded and saved for offline analysis. For the beta group, the Fz electrode was employed to provide real-time NFB, as in our previous study (Reiner et al., 2014) and in accordance with the studies of Egner and Gruzelier (2003, 2004). Regarding theta band NFB, reports of the connection of midline frontal theta to memory processes (Mitchell, McNaughton, Flanagan, & Kirk, 2008) led us to attempt to determine whether Fz might be a better electrode to use for learning improvement via NFB than the Pz electrode employed for theta in our prior study (Reiner et al., 2014). Therefore, in the theta group, we provided 21 of the participants with NFB using the Fz electrode, and nine participants with feedback using the Pz electrode. As we report below, there were no differences between these two electrodes in the success of NFB theta upregulation and improvement in performance.

The NFB program was set to provide real-time positive feedback using a visual signal displayed on the computer screen. This took the form of a bar display, in which the height of a vertical green bar was determined by EEG target band power (i.e., theta or beta). A horizontal criterion line was presented overlying the bar, representing the goal band power level. Participants were instructed to keep the bar above the criterion line as much as possible. It was explained to them that bar position is determined by the character of their EEG, and that they must learn to control it by mental effort alone. Theta group participants were told that relaxation and calming would optimize performance, while the beta group was told that concentration would do so. Initially, the WINEEG software automatically adjusted the threshold to be 90% of the participant's mean target band power during the first 2 min of the NFB session. The NFB operator (RR) then manually adjusted the threshold value by visual inspection of the bar and threshold markers, so that the participants were successful in exceeding it 60–80% of the time. Participants generally improve in their ability to increase target band power, so this adjustment continued dynamically until the end of the NFB session (as is common practice in NFB, e.g., Ros et al., 2013).

Target band power for the electrophysiological and psychophysiological analyses reported below (presented in Figure 1 and 4 and related text) was averaged across the entire NFB session lasting 30 min (three 10-min sessions), for the relevant target electrode (i.e., Fz or Pz, as described above). Those comprehensive averages were used to calculate correlations between band power changes in the target electrodes and the other 18 electrodes reported below (Figure 5 and related text). For offline analysis, independent component analysis instantiated in WINEEG software was used for removing blink artifacts. In order to remove other artifacts from the EEG recording, a comparison between the signal parameters and the threshold values was used, based on several criteria: deviation of the potentials from the isoline exceeding 75 μV, deviation of the low frequency (0–1 Hz) signal component exceeding 50 μV, and deviation of the high frequency (20–35 Hz) signal component exceeding 35 μV. Following artifact removal, mean EEG band power for each relevant frequency for each participant was derived from the WINEEG software (using fast Fourier analysis as described above), to be subjected to analyses of variance (ANOVA) to characterize group differences as well as relationships between frequency change and MSL performance.

In our previous study (Reiner et al., 2014), we included a third group of participants, who did not engage in posttraining NFB at all, but rather watched movies for an equal period of time. As we had found no difference between that group and the beta NFB group in any of the performance measures, we did not include a no-NFB condition in the present study.

Procedure

After assignment to one of the two experimental groups, participants were prepared for EEG recording by placement of the electrode cap and application of electrode gel. They then engaged in the initial MSL assessment test as described above, followed by MSL training, and were then administered a posttraining test.

Baseline EEG was recorded, and participants then immediately engaged in NFB for a period of 30 min (three 10-min sessions with short rest breaks), after which they underwent post-NFB MSL testing. Participants were instructed not to practice the MSL and to sleep regularly that night. They returned to the lab 24 h after the initial session for a follow-up MSL test, which took approximately 15 min. That test was intended to determine the interaction of post-training NFB and sleep on consolidation of MSL. Participants returned again 1 week after the initial session for the final MSL test (also approximately 15-min duration), intended to assess the stability of MSL consolidation effects engendered by NFB. One participant did not complete the post-24-h test or the post-1-week test, and three other participants did not complete the post-1-week test.

Analyses

NFB effects on EEG band power modulation were examined with repeated measures ANOVA, with factors of group (theta, beta) and stage (resting baseline, NFB). The dependent variables were mean theta power, mean beta power, and theta/beta ratio during the relevant stages. Follow-up separate repeated measures ANOVA were executed as appropriate. NFB effects on MSL were examined with repeated measures ANOVA with between-subjects factor of group and within-subject factor of stage, for the dependent variable of percent change in number of correct sequences executed per best trial relative to the prior test stage. To examine the effect of band power changes on MSL performance across participants, we conducted a regression analysis in which the dependent variable was percent change in performance after NFB and the predictor was change in theta/beta ratio during NFB. This was followed up by separate regressions calculated for each group.

Results

NFB Modulation of EEG Power

As mentioned above, for 21 members of the theta NFB group, Fz was used as the feedback electrode and Pz for the other nine members of the group (for the beta group, only the Fz electrode was used). Accordingly, the first step in our analysis was to determine whether this manipulation affected modulation of theta band power. One-way ANOVA comparing these subgroups for the dependent measure of band power change during NFB relative to baseline revealed that differences between feedback electrodes were not significant for theta change, $F(1,28) < 1.0$; beta change, $F(1,28) = 2.6$, $p > .1$; or theta/beta ratio change, $F(1,28) = 1.9$, $p > .1$. Furthermore, as we will report below, NFB caused target band changes not only in the feedback electrodes but over most scalp locations. We therefore collapsed across the two theta feedback electrodes for theta group data in all further analyses.

We then proceeded to examine whether NFB achieved its intended effects of differentially increasing target band power relative to resting baseline, in both theta and beta groups. We examined these NFB effects with repeated measures ANOVA, with factors of group (theta, beta) and stage (resting baseline, NFB). The dependent variables were mean theta power, mean beta power, and theta/beta ratio during the relevant stages.

For theta power (Figure 1A), there was a main effect of stage, $F(1,58) = 22.0$, $p < .01$, partial $\eta^2 = .275$, and an interaction of Group × Stage, $F(1,58) = 17.1$, $p < .01$, partial $\eta^2 = .228$, while the main effect of group was not significant, $F(1,58) = 3.0$, $p > .09$. We examined the interaction by conducting ANOVA comparing groups, with percent change in mean theta band power from resting baseline to NFB stage as the dependent variable. This revealed that theta band change in theta group (42.2% increase) was higher than in the beta group (8.4% increase), $F(1,58) = 11.2$, $p < .01$. The change in theta power in the theta group was significant, $F(1,58) = 33.1$, $p < .01$, partial $\eta^2 = .533$, and in the beta group it was not significant, $F(1,29) < 1.0$.

For beta power (Figure 1B), there was a main effect of stage, $F(1,58) = 4.7$, $p < .05$, partial $\eta^2 = .075$, but not of group, $F(1,29) < 1.0$. The interaction of Group × Stage did not reach significance, $F(1,58) = 2.8$, $p = .1$, but to characterize the relative magnitude of the effects, we examined beta change in each group separately. In the beta group, there was a 21.0% increase in beta power, which was significant, $F(1,29) = 4.5$, $p < .05$, partial $\eta^2 = .135$, while in the theta group there was a 7.9% increase, which was not significant, $F(1,29) < 1.0$.

For theta/beta ratio change (Figure 1C), there was a main effect of stage, $F(1,58) = 9.4$, $p < .01$, partial $\eta^2 = .140$, but not of group, $F(1,58) = 3.4$, $p < .07$, and a significant interaction of Group × Stage, $F(1,58) = 25.7$, $p < .01$, partial $\eta^2 = .307$. We examined the interaction by conducting separate repeated measures ANOVA for each group, with theta/beta ratio change as the dependent variable. This revealed that theta/beta ratio increased only in theta group

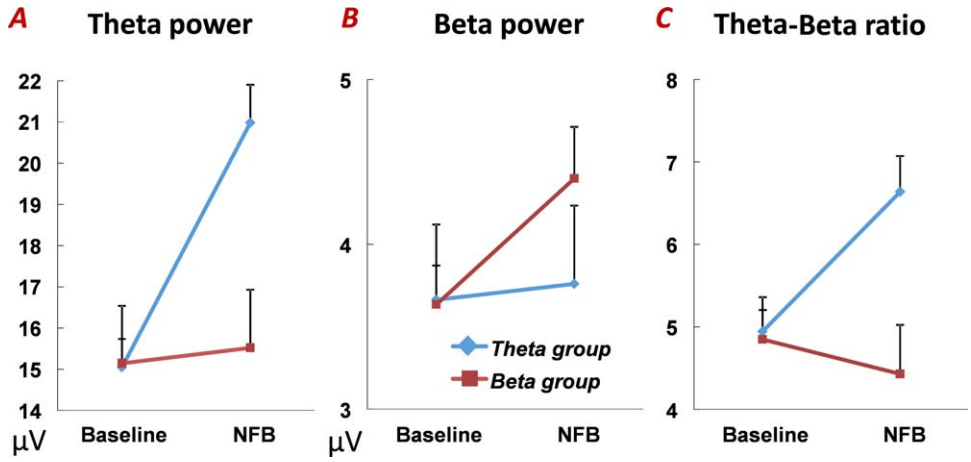

Figure 1. Group differences in changes in mean power between baseline and neurofeedback (NFB), in microvolts (μV), for (A) theta band power, and (B) beta band power. C: Group differences in change in theta/beta ratio. Brackets indicate *SEM*s.

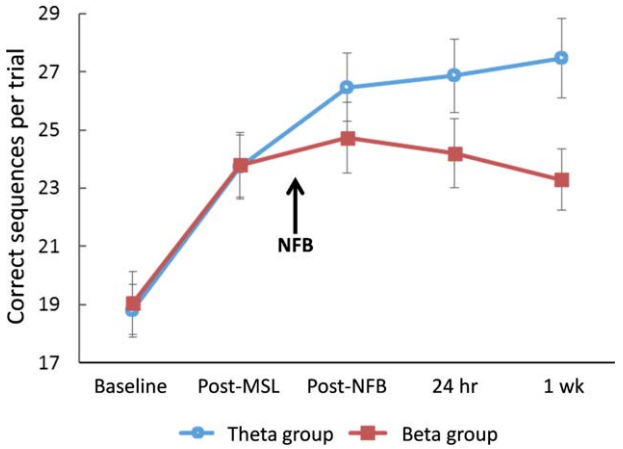

Figure 2. Motor sequence learning mean performance scores during each block of each stage of the experiment, for theta and beta NFB groups. Brackets indicate *SEM*s.

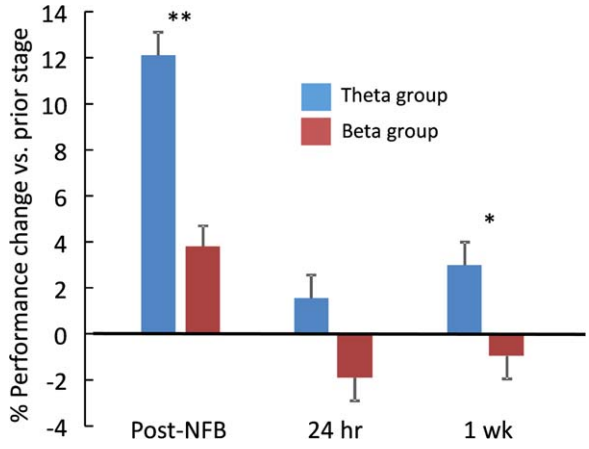

Figure 3. Motor sequence learning percent change scores over the post-NFB stages of the experiment, for theta and beta NFB groups. Asterisks between arrows indicate significant differences between groups in change over stages. $^{**}p < .01$; $^{*}p < .05$.

(38.8% increase, $F(1,29) = 32.6$, $p < .01$), partial $\eta^2 = .529$, but decreased in the beta group (−5.3%); this decrease was not significant, $F(1,29) = 2.0$, $p > .16$.

Differences between the groups in EEG band power change may theoretically be a function of initial differences in EEG band power, with lower initial EEG power possibly allowing for greater change, irrespective of the NFB intervention. We therefore examined between-group differences in baseline power (as portrayed in Figure 1). ANOVA confirmed that group differences in baseline theta band power, beta band power, and theta-beta ratio were not significant, all Fs < 1.0.

As mentioned above, NFB was programmed to give positive feedback signaling increase in target band power for both groups only if accompanied by suppression of motion-related high beta (> 18 Hz). The 48 participants for whom we had raw data available for examination (some raw data was lost due to hard disk failure before this analysis could be performed) were successful in reducing the amount of high beta power during NFB (3.8 μV) versus baseline (4.5 μV), paired sample $t(47) = 2.52$, $p < .02$. This was particularly the case in the theta group (NFB: 4.0 μV, baseline 4.8 μV), $t(25) = 2.20$, $p < .05$; the reduction in the beta group (3.7 μV vs. 4.2 μV) was not significant.

NFB Effects on Posttraining MSL Improvement

MSL performance scores for both NFB groups during training and test stages are displayed in Figure 2. As described in the Method section, there were four trials at every test, and the best trial of each test was chosen for comparisons. We first determined by one-way ANOVA that performance (expressed as number of correct sequences executed per best trial) in the initial, pretraining stage did not differ significantly between groups, nor did the performance following initial training, both Fs(1,58) < 1.0. Additionally, there was no difference between groups in the percent change in performance from baseline to posttraining (theta group, 27.2%; beta group, 27.4%), $F(1,58) < 1.0$. These analyses indicate that later effects of NFB cannot be attributed solely to prior group differences in baseline ability or in motor training.

We then examined the impact of NFB on task performance changes, by conducting repeated measures ANOVA with between-subjects factor of group (theta, beta) and within-subject factor of stage (from posttraining to after NFB; from after NFB to next day; from next day to next week; Figure 3), for the dependent variable of percent change in number of correct sequences executed per best trial relative to the prior test stage. This revealed a main effect of group, $F(1,54) = 50.1$, $p < .01$, partial $\eta^2 = .481$, a main effect of stage $F(2,108) = 22.6$, $p < .01$, partial $\eta^2 = .295$, and a marginal interaction of Group × Stage, $F(2,108) = 2.7$, $p = .07$, partial $\eta^2 = .047$. We explored the marginal interaction by conducting separate one-way ANOVA for differences between the groups in performance improvement at each of the stages following NFB. Immediately after NFB, there was a significant improvement of 12.1% in the theta group relative to the pre-NFB test, $F(1,29) = 108.6$, $p < .01$, partial $\eta^2 = .789$. The 3.8% improvement in the beta group relative to the pre-NFB test was also significant, $F(1,29) = 10.9$, $p < .01$, partial $\eta^2 = .272$. Importantly, theta group improvement was significantly greater than that of the beta group, $F(1,58) = 28.2$, $p < .01$. Regarding changes between the after-NFB test to the next day's test, there was a nonsignificant improvement in the theta group of 1.6% and a nonsignificant decrease in the beta group of −1.9%. Testing a week later revealed an additional significant improvement relative to the prior test of 3.0% in the theta group, $F(1,23) = 8.9$, $p < .01$, partial $\eta^2 = .278$, and a nonsignificant −0.5% decrease in the beta group; the group differences were significant, $F(1,54) = 4.8$, $p < .05$. Overall, the change from posttraining pre-NFB baseline to the final test a week later was 17.4% in the theta group and 1.2% in the beta group. The differences between theta and beta groups in performance improvement were also obtained not only for the best trial of each test stage, but also for the average scores across all four trials: For the immediate post-NFB comparison, theta group improvement (12.3%) was greater than beta group improvement (5.0%), $F(1,58) = 25.3$, $p < .01$; for the next day's test, theta group (1.6%) and beta group (−1.8%) differences were marginal, and for the testing a week later, the theta group had a 3.1% improvement while the beta group declined −1.9%, a significant difference, $F(1,54) = 8.7$, $p < .01$. Thus, NFB had a notable impact on MSL performance, both immediately and in follow-up testing.

While the analysis reported above demonstrated the effectiveness of NFB in increasing band target power for each respective group, seemingly leading to the group performance differences as demonstrated, we asked whether the degree to which individual participants modulated their relative band power specifically

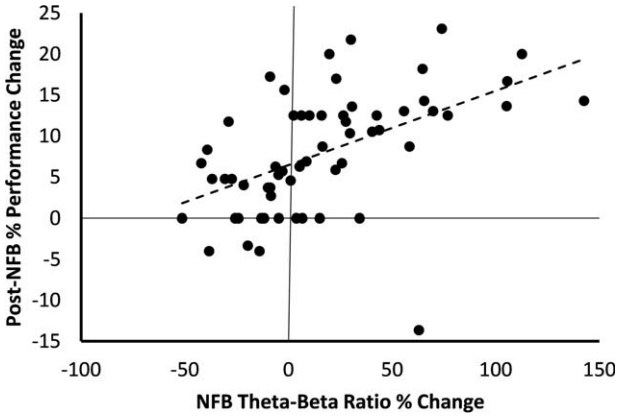

Figure 4. Percent performance improvement following NFB compared to immediate posttraining measures, as a function of the degree of change in theta-beta power ratio during NFB compared to baseline, for $N = 59$ participants.

affected their performance improvements. We therefore conducted regression analysis, initially performed for the whole sample and then for each group separately. The dependent variable was percent change in performance after NFB and the predictor was change in theta/beta ratio during NFB. One participant from the beta group, whose performance after NFB declined more than 2 *SD*s, was removed from this analysis as an outlier. The regression was significant, $F(1,57) = 36.7$, $p < .01$, $R = .63$ (Figure 4); that relationship held for both groups separately, ps $< .02$. The same pattern of effects was obtained when regressing performance change on change in theta alone. The regression for the whole sample was significant, $F(1,57) = 13.8$, $p < .01$, $R = .44$. However, further analysis revealed that regression was marginally significant only in the theta group, $F(1,28) = 3.7$, $p = .07$, $R = .34$, while the regression in beta group was not significant, $F(1,27) = 1.3$, $p = .25$, $R = .21$. Regressing performance change on beta change across both groups yielded a minor positive but nonsignificant relationship, $F(1,57) = 1.9$, $p = .18$, $R = .11$; the correlations were not significant for either group separately, Fs < 1.0. Thus, there appears to be a direct linear relationship between increase in theta power during NFB and the degree of performance enhancement; this effect does not seem to be attributable to reduction in beta power. Finally, post-NFB performance was correlated not only with change in theta/beta ratio, but with absolute theta/beta ratio during NFB, $F(1,57) = 15.9$, $p < .01$, $R = .47$; this relationship held for the theta group separately, $F(1,28) = 4.8$, $p < .05$, $R = .38$, but not for the beta group, $F(1,27) = 1.2$, $p = .29$, $R = .20$.

Distribution of NFB Effects on Target Band Power Across Electrode Locations

Although participants were provided with feedback regarding the change in target band power using a single electrode (Fz for the beta group; Pz or Fz for the theta group, which did not differ in their modulation of theta power, as reported above), in the current study we were able to measure the extent to which that single-channel feedback caused more widespread changes in the other 18 electrodes from which EEG was recorded. This relationship may be examined by many comparisons, but that most relevant to understanding differential NFB effects on performance changes is the correlation in theta/beta ratio change during NFB versus baseline between the electrode used for NFB and all other electrodes.

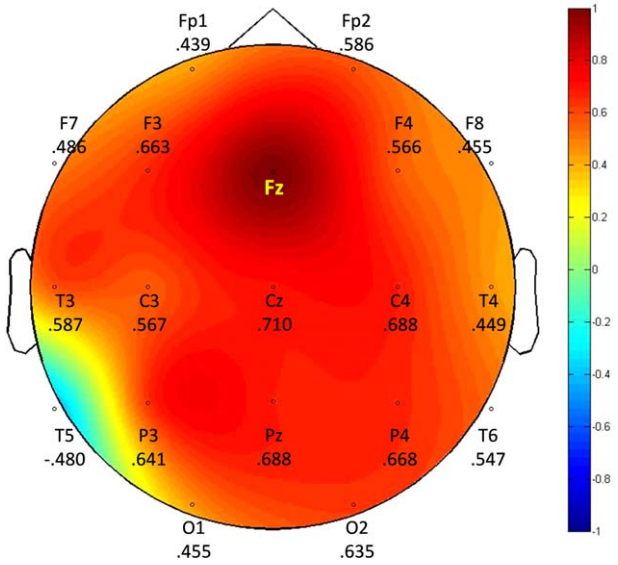

Figure 5. Map of correlations (Pearson's R) between the Fz electrode used for NFB and other scalp electrodes in theta/beta band power ratio change in NFB vs. baseline, for $N = 44$ participants. All correlations except for T5 electrode are significant at $p < .01$.

Since this measure takes into account power changes in both bands, it enables the synoptic examination of all participants regardless of their specific group.

Figure 5 is a scalp map portraying the strength of the correlations in percent theta/beta ratio change during NFB versus baseline, between the Fz electrode used to provide NFB and each other non-feedback electrode, for 43 of the participants (seven others were in the theta Pz NFB group, and the raw EEG data of several other participants were lost due to hard disk failure before this analysis could be performed). As is apparent from the figure, there are striking correlations over most of the scalp, with almost all electrodes displaying significant positive correlations at $p < .01$. The only exception was electrode T5, which had a significant negative correlation with the Fz feedback electrode; the reason for this discrepancy appears to be the default setting of the neurofeedback program to use linked earlobes as a reference, so that the correlations of T5 and T6 (adjacent to the ears) with any other electrodes will necessarily have an inverse relationship. This strong overall pattern of correlations indicated that NFB led to the widespread modulation of relative EEG band power, not just in the immediate vicinity of the feedback electrode.

Discussion

Examining the effects of neurofeedback (NFB) on motor sequence learning (MSL), we found that encouraging participants to upregulate the theta power of their EEG following training on the keyboard version of the finger-tapping task led to significantly greater offline performance gains than those exhibited by a control group, who received NFB to increase beta power. Furthermore, 24 h and 7 days following training, the theta NFB group continued to improve in performance, while beta group performance declined. We also found a significant correlation between the degree of theta upregulation and the size of posttraining performance gains. These findings represent a constructive replication of our initial finding of NFB effects on MSL (Reiner et al., 2014), and indicate that 30 min of NFB is sufficient to impact on subsequent MSL performance.

We further determined that NFB focused on both theta and beta EEG bands affected target power not only in the electrodes used for feedback, but also across most of the scalp electrodes.

How might NFB promote consolidation of MSL? In our prior report (Reiner et al., 2014), we suggested that the salutary effects of theta NFB on performance reflect systems consolidation processes, that is, the transfer of the locus of motor representations guiding behavior from the hippocampus to the prefrontal cortex (Dudai, 2004). However, given the immediacy of NFB effects on MSL, it seems more reasonable to attribute them to synaptic consolidation processes, which have been shown to play a major role in the time window immediately following the creation of new memories (Dudai, 2004).

There are several routes by which posttraining theta upregulation might benefit synaptic consolidation. The first candidate process is the replay of firing patterns by neuronal ensembles active during training. This replay is considered to be an important basis of sleep-based consolidation, and has been reported to occur during waking as well (Carr, Jadhav, & Frank, 2011). Interestingly, cortico-hippocampal theta coherence has been related to replay strength and subsequent consolidation (Benchenane et al., 2010). It is possible that increasing theta power by NFB benefits replay, and thereby augments synaptic consolidation through the repeated firing of the neural ensembles that were active during training, yielding Hebbian plasticity.

A second candidate process is the sharpening of memory traces by resetting nontrace neurons that have not crossed a threshold for Hebbian plasticity back to baseline activity levels, thus increasing the representational signal-to-noise ratio. As noted by Hsieh and Ranganath (2014), Norman and colleagues have offered a learning algorithm involving biased competition between representations in a network, in which theta oscillations lead to systemic inhibition. Cycling between high and low inhibition states associated with different theta phases leads to the strengthening of targeted memories by long-term potentiation and weakening of the competitors by long-term depression (Norman, Newman, & Detre, 2007; Norman, Newman, Detre, & Polyn, 2006). This biased competition filtering is asserted to be responsible for sleep consolidation (Albouy, Fogel et al., 2013; Tononi & Cirelli, 2014), and active upregulation of waking theta through NFB could also have such consolidative effects.

A third possibility is that the mental strategies employed to upregulate theta power are more conducive than those yielding greater beta power to the prevention of posttraining interference to MSL. A negative relationship has been reported between theta/beta ratio and trait attentional control (Loo & Makeig, 2012), and increased alertness, manifested by faster responses to target visual stimuli, is accompanied by higher EEG activation in the beta band (Kamiński, Brzezicka, Gola, & Wróbel, 2012). In contrast, theta activity has been associated with meditative states and drowsiness (Cahn & Polich, 2006). Accordingly, the advantage of the theta condition might simply lie in its passively enabling neural plasticity processes to achieve completion by preventing retroactive interference and minimizing competition for brain resources.

Relatedly, it must be acknowledged that, although differences in posttraining performance improvement are correlated with EEG band-power changes, in the protocol employed it was suggested to the two NFB groups to use different mental state strategies to increase their band power targets (relaxation for theta vs. concentration for beta). Although we also encouraged each participant to use whatever idiosyncratic method gave them the best NFB, it is possible that the MSL differences can be attributed to other cognitive or affective factors differentiating the groups rather than to the NFB differences. While the strong correlation across participants between theta upregulation and MSL modulation seems to argue against discounting the contribution of the electrophysiological differences, it cannot be ruled out that they covaried with the degree to which participants maintained relaxation versus concentration states. It should be noted, though, that since NFB by definition requires participant-initiated mental processes in order to be effective, even if no suggestions had been given for strategies to achieve target band power modulation, participants would still have differed in their cognitive or affective approaches to achieving their targets. While it is difficult to separate the contribution of mental states and the EEG differences to MSL performance, it might be possible to do so in future studies using transcranial alternating current stimulation, which may be able to cause band power changes while maintaining participant mental passivity.

A number of limitations of this study should be mentioned. We did not have the opportunity to objectively monitor participants' posttraining sleep behaviors, and so our ability to analyze the effects of NFB on MSL in interaction with a night's sleep was limited to self-report of fulfilling the criterion of a minimum of 6 h of sleep. In future studies, this should be confirmed using actigraphy. Additionally, it is possible that NFB might be made more effective in modulating learning by the use of dynamic ramping up of the criterion for positive feedback throughout NFB, rather than the use of the initial baseline band power as the threshold during the entire training session, as we did in the current experiment. Another limitation of the study is that, in our attempt to control movement-related activity by withholding positive feedback when high beta was increased along with target theta or low beta, we could not determine for each individual participant which specific frequencies characterized their two beta bands. That may have resulted in inclusion of such motor-related activity for some beta group participants, and may have made it differentially difficult for beta group participants to selectively achieve their beta increase goals. Individual band-frequency tailoring (as done for alpha power by Escolano, Navarro-Gil, Garcia-Campayo, Congedo, & Minguez, 2014) may enable better specificity in future studies.

Previous research implies that immediate posttraining MSL is likely to strengthen its spatial representation component rather than its motor process component. This is suggested by the study of Albouy, Fogel and colleagues (2013), who compared postnap gains in performance of the motor sequence with the hand in the original downward orientation versus flipping the hand so that fingers face upward, and found that the nap benefited the allocentric extrinsic (spatial) but not the egocentric intrinsic (motor) representation. Relatedly, Albouy, Fogel and colleagues (2013) also propose that sleep preserves rather than enhances the striatal aspects of MSL, while enhancing the hippocampal aspects of MSL, and this may be the case in theta NFB effects as well. This fits with the proposal of Hsieh and Ranganath (2014) that frontal midline theta oscillations are preferentially involved in the maintenance of temporal order information; in this case, the relevant representation is the spatio-temporal sequence of finger positions to be followed in performance of the task.

Another interesting comparison of this NFB protocol with nap consolidation studies is in the long-term effects of the intervention. Korman and colleagues (2007) found that, although a nap led to improved MSL performance 8 h after training relative to waking, after a subsequent night's sleep, nap and no-nap groups displayed equivalent offline gains in performance relative to posttraining baseline. In the current study, theta NFB yielded larger offline

performance gains when those were assessed immediately after NFB, and unlike the finding of Korman and colleagues (2007), those differential gains persevered even after a night's sleep (though the further added difference between theta and beta NFB groups was not statistically significant). Furthermore, later assessment (7 days after training) indicated additional improvement in the theta group but decline in the beta group. This may indicate that the mechanisms involved in NFB consolidation and nap consolidation are different, and therefore interact differently with subsequent sleep influences on consolidation. Further investigation is required to determine whether NFB also differs from nap/sleep effects on MSL consolidation in other factors, such as protection of new learning from interference by subsequent competitive training (Korman et al., 2007).

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