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Enhancing early consolidation of human episodic memory by theta EEG neurofeedback

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ABSTRACT

Consolidation of newly formed memories is readily disrupted, but can it be enhanced? Given the prominent role of hippocampal theta oscillations in memory formation and retrieval, we hypothesized that upregulating theta power during early stages of consolidation might benefit memory stability and persistence. We used EEG neurofeedback to enable participants to selectively increase theta power in their EEG spectra following episodic memory encoding, while other participants engaged in low beta-focused neurofeedback or passively viewed a neutral nature movie. Free recall assessments immediately following the interventions, 24 h later and 7 d later all indicated benefit to memory of theta neurofeedback, relative to low beta neurofeedback or passive movie-viewing control conditions. The degree of benefit to memory was correlated with the extent of theta power modulation, but not with other spectral changes. Theta enhancement may provide optimal conditions for stabilization of new hippocampus-dependent memories.

1. Introduction

The initial formation of a memory trace is followed by a time interval during which that trace may become consolidated (Dudai, 2004, 2012). Such consolidation has been demonstrated to be vital for the persistence of all types of long-term memory (McGaugh, 2000; Rasch & Born, 2013). Early stages of consolidation involve the stabilization of structural and functional synaptic and other neural changes engendered by a learning event (Bailey, Kandel, & Harris, 2015; Redondo & Morris, 2011). Pharmacological interventions such as post-learning administration of protein synthesis inhibitors block synaptic consolidation, while other substances can potentiate synaptic consolidation (Rosenberg et al., 2014). Finding non-invasive interventions that might benefit consolidation in humans, especially of declarative memory for facts and events, seems to be a desideratum. A novel method of optimizing consolidation is suggested by findings regarding the important role of brain oscillations, especially theta rhythms, in mnemonic processes (Burke et al., 2014; Fell & Axmacher, 2011; Hsieh & Ranganath, 2014). This raises the possibility that post-learning theta rhythm modulation might be a method of promoting consolidation. In recent research (Reiner, Rozengurt, & Barnea, 2014; Rozengurt, Barnea, Uchida, & Levy, 2016), we found significantly greater post-training procedural memory performance following neurofeedback (NFB) in a group of participants who selectively increased theta power, compared to participants who selectively increased low beta power, or passive controls. In addition, as in sleep consolidation studies (Rasch & Born, 2013), theta NFB led not only to protection of learning from decay, but to offline improvement relative to best prior performance. Since the initial stages of procedural memory involve hippocampal mechanisms (Albouy, King, Maquet, & Doyon, 2013), we set out to investigate whether similar theta EEG NFB enhancement of early consolidation would be found for episodic memory.

Healthy young adult participants viewed 30 object pictures, each presented for 3 s, and performed an immediate free recall test, repeating the process twice more to establish a learning curve. Participants then engaged in NFB modulation of theta power, or in one of two control conditions: low beta NFB (an active control condition matching the experience of engaging in NFB procedures), or movie viewing (a passive control condition modelling how memory would be affected under ecological activity conditions), all for 30 min. All participants then took the fourth recall test. Two additional follow-up recall tests were administered: 24 h later, to determine the interaction of NFB training and sleep on consolidation, and 1 w later, to assess the stability of consolidation effects engendered by NFB. We found notable subsequent memory benefits for the Theta NFB group at all three assessment points relative to the active and passive control conditions. Such theta NFB effects on this episodic memory task suggest that theta enhancement may provide a method for potentiating hippocampus-

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dependent memory.

2. Materials and methods

2.1. Participants

75 volunteers (45 females; mean age 29.6 y, SD 7.1 y) took part in the study in return for payment and/or academic requirement credit. They reported no history of psychiatric or neurological disorders, nor chronic use of medication. All participants reported having a minimum of 6 h of nocturnal sleep in the night before and during the week of the experiment, and no physiological sleep disruptions. Informed consent was obtained from all participants for a protocol approved by the Institutional Review Board of the Interdisciplinary Center Herzliya. The 75 participants were randomly assigned to Theta group (17 F, 8 M, mean age 30.9 y, SD 7.7 y), (low) Beta active control group (14 F, 11 M, mean age 28.6 y, SD 7.0 y), or Movie passive control group (14 F, 11 M, mean age 28.8 y, SD 6.5 y).

2.2. Experimental design

After random assignment to one of the three experimental groups, participants were prepared for EEG recording. Resting baseline EEG was recorded for 4 min. Participants were given task instructions and viewed 30 object pictures (e.g., spoon, door, leaf, hammer, bus) each presented for 3 s, followed by a free recall test which took approximately 5 min. Next, participants viewed the 30 objects again in a different random order, followed by a second recall test, which was followed by a third study-test cycle. Participants then engaged in NFB for a period of 30 min (three 10-min sessions with short rest breaks) in the two NFB groups, or 30 min of neutral nature movie viewing in the passive control group. Following the NFB/movie viewing session, participants took the fourth recall test. 24 h after the initial session, participants took the fifth recall text, via a phone call (~50% of the participants) or by returning to the lab. This follow-up recall test was intended to determine the interaction of NFB training and sleep on consolidation of episodic memory. One week after the initial session, participants took the sixth and final recall test (via phone call or in lab, as before), intended to assess the stability of episodic memory consolidation effects engendered by NFB. Six participants did not complete the post-1-week free recall test (3 participants from the Beta experimental group, and 3 participants from the Theta experimental group). Participants were unaware of the goals of the experiment.

2.3. Neurofeedback protocol

NFB was performed and recorded using 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. 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 and relative EEG spectral power for each bandwidth was calculated using fast Fourier analysis, with the following parameters: epoch duration of 4096 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). For the recording of resting stage baseline, all participants sat quietly with their eyes open for 4 min. The Fz electrode was employed to provide real-time NFB, as in our previous studies (Reiner et al., 2014; Rozengurt et al., 2016), and in accordance with additional studies (Egner & Gruzelier, 2003, 2004). Notably, as frontal midline theta has been implicated in episodic memory encoding and retrieval processes (Hsieh & Ranganath, 2014), this was seemingly the optimal location for both conditions in this task. 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 ratio (i.e., theta/low beta or low beta/theta). A horizontal criterion line was presented overlying the bar, representing the goal band power ratio level. Participants were instructed to keep the bar above the criterion line as much as possible. It was explained to them that bar height is determined by the character of their EEG, and that they must learn to control it by maintaining whatever mental state provides them with positive feedback.

To directly contrast the two active NFB conditions, we provided participants with real-time feedback based on their theta/low beta ratio, as is common in clinical application of NFB in putative treatment of attention deficits (e.g., Bluschke, Broschwitz, Kohl, Roessner, & Beste, 2016; Van Doren et al., 2017). Theta group participants received positive feedback for increasing theta/low beta ratio; Beta group participants received positive feedback for increasing their low beta/theta ratio. Positive bar rise feedback was only provided if in addition to increasing their target band-power ratio (theta/low beta or low beta/theta), participants did not increase high beta power (to minimize motion artifacts). Initially, the WINEEG software automatically adjusted the threshold to be 90% of the participant's mean target band-power ratio during the first 2 min of the NFB session. Participants generally improve in their ability to increase target band power ratio, so this adjustment continued dynamically until the end of the NFB session (Ros et al., 2013). Band power measures for the electrophysiological and psychophysiological analyses were averaged across the entire 30 min NFB session for the Fz electrode. 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), to be subjected to analyses of variance (ANOVA) to characterize group differences as well as relationships between frequency change and episodic memory performance. The non-NFB control group ("Movie group") had their EEG recorded passively at baseline and during movie viewing using a BioSemi Active Two system (BioSemi, Amsterdam, The Netherlands) from 64 electrodes mounted in an elastic cap according to the extended 10–20 system. The on-line filter settings of the EEG amplifiers were 0.16–100 Hz. EEG was continuously sampled at 2048 Hz. The BioSemi system enables very high precision EEG recording, and was used in this group since the proprietary interface with NFB software was not required. For offline analysis, 19 electrodes corresponding to those comprising the Mitsar montage were selected, and the data was downsampled to 256 Hz and converted to the WinEEG format, which was used for all further offline pre-processing and analysis as described above.

2.4. Statistical analysis

NFB effects were examined by repeated measures ANOVA (Figs. 1,

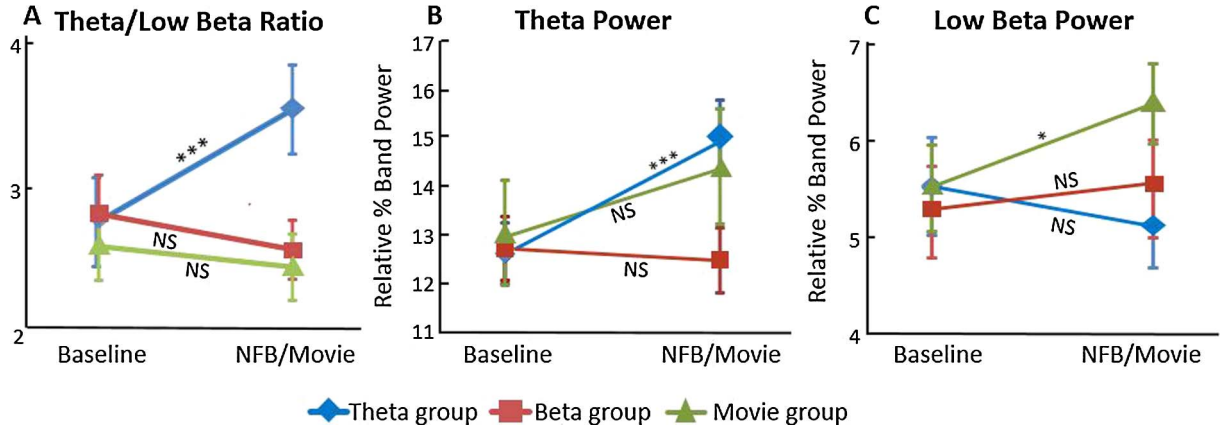

Fig. 1. NFB modulation of (A) EEG theta/low beta ratio, (B) theta power, and (C) low beta power. *P*-values are provided for group differences in these metrics between baseline and NFB/movie means. Error bars indicate ± SEM; *, $P < .05$; ***, $P < .001$; NS, non-significant.

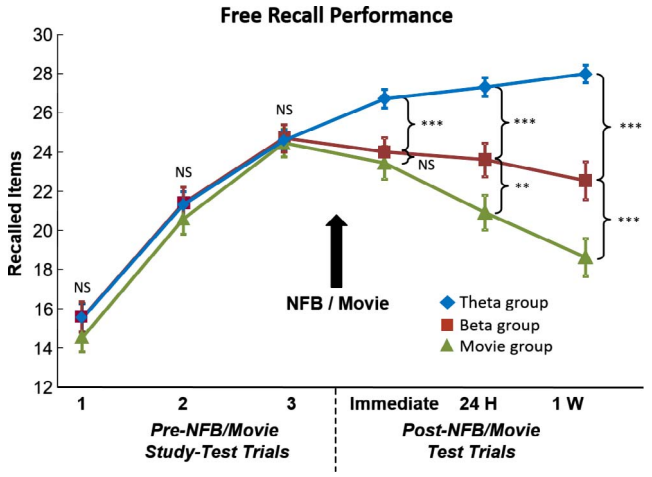

Fig. 2. Free recall scores during each stage of the experiment, for Theta NFB, low Beta NFB, and Movie groups. Error bars indicate ± SEM; NS, non-significant; **, $P < .01$; ***, $P < .001$.

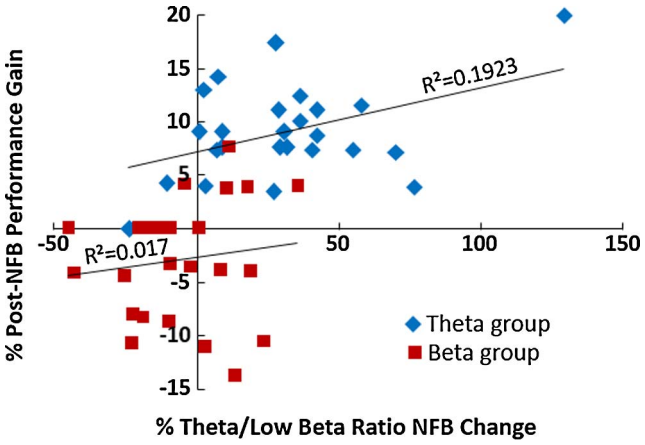

Fig. 4. Percent performance improvement immediately following NFB compared to immediate pre-NFB training measures, as a function of the degree of change in theta/low beta ratio for all NFB participants across Theta and Beta groups ($n = 50$).

2, 5, 6) and regression analyses (Figs. 3 and 4). Data are presented as percent band-power values or, when mentioned, as band-power ratios. All statistically significant analyses were set at $p < .05$, error bars represent SEM, and n represent number of participants. Statistical calculations were performed with SPSS software.

3. Results

3.1. NFB modulation of EEG power ratio

As described in the Methods, feedback was given to both Theta and Beta groups using theta/low beta ratio, which therefore provides a synoptic index of modulatory success across NFB groups, and a parallel indication of incidental frequency band change during movie viewing

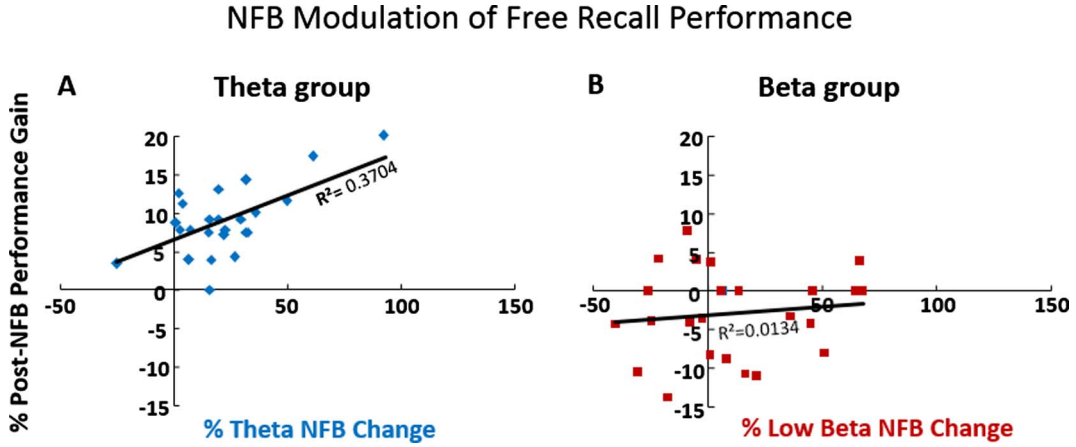

Fig. 3. Percent performance immediately improvement following NFB compared to immediate pre-NFB training measures, as a function of the degree of change in (A) theta power during NFB compared to baseline, for $n = 25$ participants of the Theta group; and in (B) low beta power during NFB compared to baseline, for $n = 25$ participants of the Beta group.

in the passive control condition. For theta/low beta ratio (Fig. 1a), repeated measures ANOVAs, with factors of group (Theta, Beta, Movie) and stage (resting baseline, NFB/movie), indicated no main effect of stage, $F_{(1,72)} = 1.57$, $p = .21$, no main effect of group, $F_{(2,72)} = 1.43$, $p = .25$, but a significant group X stage interaction, $F_{(2,72)} = 10.86$, $p < .001$. We examined the interaction by conducting separate repeated measures ANOVAs for each group, with theta/low beta ratio change as the dependent variable. This revealed that theta/low beta ratio increased (+27.9%) significantly in the Theta group, $F_{(1,24)} = 18.83$, $p < .001$, but decreased (−4.3%) non-significantly in the Beta group, $F_{(1,24)} = 2.59$, $p = 0.12$, and in the Movie group (−5.7%), $F_{(1,24)} = 0.67$. These group differences were not a function of initial variance in EEG band power, as baseline theta/low beta ratio did not significantly differ between groups, $F_{(2,72)} = 0.07$.

We further examined the effects of the intervention on each band separately in the three experimental groups. For theta power (Fig. 1b), group differences in baseline power were not significant, $F_{(2,72)} < 1.0$. Regarding the changes during NFB, repeated-measures ANOVA with factors of stage (repeated) and group (between-Ss) yielded a significant main effect of stage, $F_{(1,\ 72)} = 10.64$, $p < 0.01$, no main effect of group, $F_{(2,\ 72)} < 1.0$, and a significant group X stage interaction, $F_{(2,\ 72)} = 4.47$, $p < 0.02$. We examined the interaction by conducting repeated measures ANOVA for each group separately, which revealed that the difference between baseline and NFB theta power was significant for the Theta group (+16.2%), $F_{(1,\ 24)} = 19.64$, $p < 0.001$, but not for the Beta group (−1.8%), $F < 1.0$, nor for the Movie group (+9.5%), $F_{(1,\ 24)} = 3.58$, $p = 0.07$.

For low beta power (Fig. 1c), group differences in baseline power were similarly not significant, $F_{(2,72)} < 1.0$. Regarding the changes during NFB, repeated-measures ANOVA indicated that the main effect of stage was not significant, $F_{(1,\ 72)} = 1.63$, $p = .20$, nor was the main effect of group, $F_{(2,\ 72)} < 1.0$, but there was a significant group X stage interaction, $F_{(2,\ 72)} = 4.07$, $p < .05$. We examined the interaction by conducting repeated measures ANOVA for each group separately, which revealed that for the Theta group, the difference between baseline and NFB low beta power (−8.0%) was not significant, $F_{(1,\ 24)} = 1.93$, $p = .18$, nor was it significant for the Beta group (+4.3%), $F_{(1,\ 24)} < 1.0$. In contrast, in the Movie group low beta power increase (+13.7%) was significant, $F_{(1,\ 24)} = 6.50$, $p < .02$. The Beta group might have experienced difficulty in upregulating low beta power since, as noted above, we implemented control of movement-related activity by withholding positive feedback for target low beta when high beta was increased along with it. In contrast, the movie group was unconstrained, and attention paid to the movie could yield increased low beta as observed. We addressed the Beta group's modulation difficulties in additional analyses reported below.

3.2. NFB effects on episodic memory improvement

NFB/movie effects on free recall performance for the three experimental groups are presented in Fig. 2. We first determined by one-way ANOVAs that performance (expressed as number of correctly recalled items) in each of the initial, pre-NFB/movie study-test trials did not differ significantly between groups, all Fs < 1.0. This indicates that later effects of NFB cannot be attributed to prior group differences in baseline memory ability or initial learning.

We then examined the impact of NFB/movie intervention on subsequent free recall trials. For the immediate post-NFB/movie test, the Theta group exhibited improved free recall (+8.8%), while decline was observed in the Beta group (−2.9%) and Movie group (−4.2%); these group differences were significant, $F_{(2,72)} = 19.51$, $p < .001$, with Bonferroni-corrected comparisons indicating that the Theta group differed from both other groups, $p < .001$, but that they did not differ from each other, $p = .59$. For the post-24 h test, the Theta group showed further improvement (to +11.2%), in contrast to the other groups that exhibited further performance decline (Beta group: −4.5%, Movie group: −14.7%); these group differences were significant, $F_{(2,72)} = 47.15$, $p < .001$, with the Theta group differing from both other groups, $p < .001$, and the Beta group differing from the Movie group, $p < .01$. Similarly, at post-1 w test, the Theta group exhibited further improvement (to +14.0%), while the other groups exhibited further performance decline (Beta group: to −8.9%, Movie group: to −24.1%), these group differences were significant, $F_{(2,66)} = 73.83$, $p < .001$, with the Theta group differing from both other groups, $p < .001$, and the Beta group differing from the Movie group, $p < .001$. Thus, theta-upregulating NFB had a noticeable impact on episodic memory performance, both immediately and in follow-up testing.

Another perspective on the impact of theta upregulation by NFB on episodic memory is provided by calculating the correlation between the percent target-band power change during NFB and immediate post-NFB memory performance improvement. For the Theta group (Fig. 3a), there was a significant correlation between percent theta change during NFB and the improvement in immediate post-NFB successful recall, Pearson's $r_{(25)} = 0.609$, $p = .001$ (2-tailed), while for the Beta group the relationship was not significant, $r_{(25)} = 0.240$, $p = .249$ (2-tailed), nor was it for the Movie group $r_{(25)} = -0.279$, $p = .177$ (2-tailed). In contrast, the correlation between percent low beta change during NFB and the improvement in immediate post-NFB successful recall for the Beta group (Fig. 3b) was not significant, $r_{(25)} = 0.116$, $p = .581$ (2-tailed); nor was it for the Theta group, $r_{(25)} = -0.052$, $p = .805$ (2-tailed), nor for the Movie group $r_{(25)} = -0.344$, $p = .092$ (2-tailed).

This indication of specificity of theta upregulation on off-line improvement in recall success may also be seen in examination of the correlation between theta/low beta ratio change and improvement in immediate post-NFB successful recall, which for the Theta group was significant, $r_{(25)} = 0.439$, $p = .028$ (2-tailed), while not for the Beta group, $r_{(25)} = 0.130$, $p = .434$ (2-tailed), or the Movie control group $r_{(25)} = 0.064$, $p = .761$ (2-tailed). This relationship is portrayed synoptically in Fig. 4 for the Theta and Beta active intervention groups. Taken together, these correlations clarify that this effect was driven solely by theta upregulation in the Theta group, and that it cannot be attributed to task success or to the experience of positive feedback.

3.3. Analysis of NFB-effective participants' performance

While Theta group participants showed significant NFB modulation of their relative theta band activity and theta/low beta ratio, Beta group participants' low beta band power and theta/low beta ratio during NFB were not significantly different than baseline. This raises the possibility that it was band power regulation success, with the concomitant more positive feedback enjoyed by successful regulators, rather than specifically theta band power that was responsible for the Theta group's superiority in post-intervention free recall. To rule out that possibility, we selected from each NFB group only those participants who increased target band power ratio by at least 5% relative to baseline ($n = 19$ for the Theta group and $n = 13$ for the Beta group; Fig. 5). These Theta group participants exhibited a 29.4% mean increase in target theta power between baseline and NFB, $F_{(1,18)} = 38.95$, $p < .001$, and these Beta group participants exhibited a 14.7% increase in target low beta power, $F_{(1,12)} = 20.69$, $p = .001$. Furthermore, these effects were expressed in NFB changes relative to baseline in theta/low beta ratio, with the Theta group exhibiting an increase of 29.3%, $F_{(1,18)} = 10.49$, $p < .01$, and the Beta group exhibiting a decrease of −14.5% (i.e., a relatively greater increase in low beta than in theta), $F_{(1,12)} = 5.85$, $p = .05$.

We then conducted the same analyses of free recall performance comparing these groups as was done for the entire sample (Fig. 6). These analyses revealed that the two groups did not differ in any of the pre-NFB study-test free recall trials, all $Fs < 1.0$. However, these groups differed in percent post-NFB free recall performance change relative to final pre-NFB score at all three test points, all $Fs > 49.5$, all

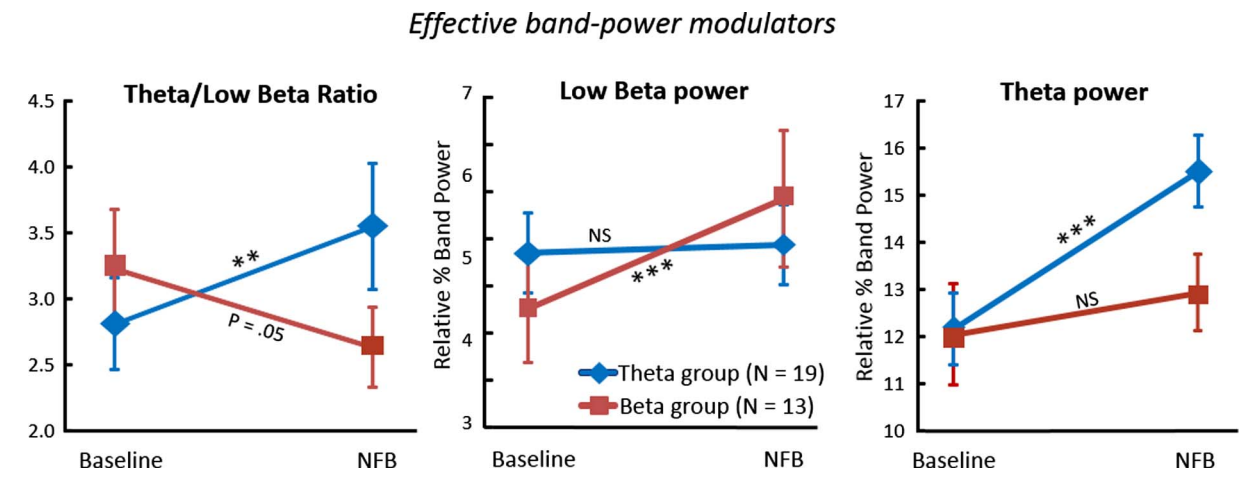

Fig. 5. Group differences in mean theta power, low beta power, and theta/low beta power ratio changes between baseline and NFB, for the sub-group of participants effective in modulating their target band power (n = 19 participants in Theta group, n = 13 participants in Beta group). Error bars indicate ± SEM; **, $P < .01$; ***, $P < .001$; NS, non-significant.

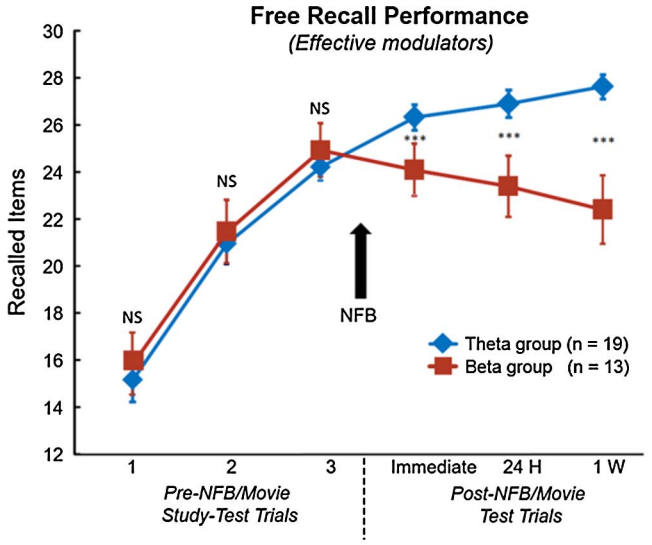

Fig. 6. Free recall scores during each stage of the experiment, for Theta NFB and Beta NFB effective modulator subgroups (n = 19 participants in Theta group, n = 13 participants in Beta group). Error bars indicate ± SEM; NS, non-significant; ***, $P < .001$.

$ps < .001$. Furthermore, there was a significant correlation between percent target-band power upregulation during NFB and percent post-NFB free recall improvement for the Theta effective regulators group, $r_{(19)} = 0.780, p < .001$, but not for the Beta effective regulators group, $r_{(13)} = 0.367, p = .218$. These analyses indicate that the Theta group advantage cannot be attributed to NFB success and its concomitant greater amount of positive feedback in itself, but rather reflects a process specific to theta upregulation.

We employed the Fz electrode to provide real-time feedback for theoretical reasons noted in the Methods section. It might be wondered whether using a different electrode might have yielded different findings. However, in our prior research (Rozengurt et al., 2016), we found a high degree of correlation between theta/beta ratio change yielded by NFB at Fz and the degree of NFB change at other electrodes. We repeated that analysis for the present dataset (Fig. 7), for n = 44 participants for whom we had the raw data available. This revealed a comparable degree of correlation across electrodes (and conceivably, across cortical areas as well, although volume conduction could be responsible for the scalp effects). This indicates that while Fz appears to be a relevant reporting electrode for memory consolidation by NFB, the effects of NFB are global, and other reporting electrodes might function similarly well.

As mentioned in the Materials and Methods section, because of logistical reasons not all participants were able to return to the lab for the 24 h post-NFB/Movie and the 1 w post-NFB/Movie recall tests. We therefore arranged that half of the participants in each group return to the lab, and the other half of each group was tested by telephone. There were no significant differences in performance between participants in these two conditions, both within each NFB/Movie group and across groups, all $Ps > .15$. Data from all participants were therefore collapsed across follow-up test method for all reported analyses.

4. Discussion

In the current study, we demonstrate enhancement of free recall performance by theta NFB implemented between encoding and retrieval stages of an episodic memory task. This benefit seemingly represents a consolidation-related process. This finding resonates with recent reports regarding the importance of early post-encoding activation, asserted to reflect consolidation-related activity, for the persistence of episodic memories (Dudai, Karni, & Born, 2015). Given the immediacy of theta NFB impact on episodic memory, its effects are likely attributable to synaptic consolidation (cellular-molecular processes transpiring shortly after new memory formation) rather than systems consolidation (shifts in the locus of mnemonic indexing from hippocampal to neocortical loci; Dudai et al., 2015), though both processes might have been affected by the intervention.

This study employed an NFB intervention, in which participants engendered the upregulation of target-band power themselves, using on-line feedback. It might therefore be argued that the improvement in free recall performance seen in the Theta group resulted not from physiological processes associated with increased theta power, but to the fact that they were successful in their appointed task, providing them with strong positive feedback that might boost their memory performance. By this account, though, we would expect to find a parallel benefit in the Beta group; in fact, low beta regulation success in the Beta group overall, and even in the more selective sample of successful regulators, was not correlated with subsequent memory benefits. In contrast, there was a very strong correlation between the degree of success in theta enhancement and benefit to memory, specific to the Theta group. Similarly, the Theta group's memory benefit might theoretically be attributed solely to the group differences in the initial suggestions given to participants regarding the strategies they might use to succeed in band power regulation (relaxation for theta and concentration for low beta). However, this would not account for the strong correlation between the degree of theta upregulation and subsequent memory benefit *within* the Theta group.

The movie group was included in this study primarily to provide an

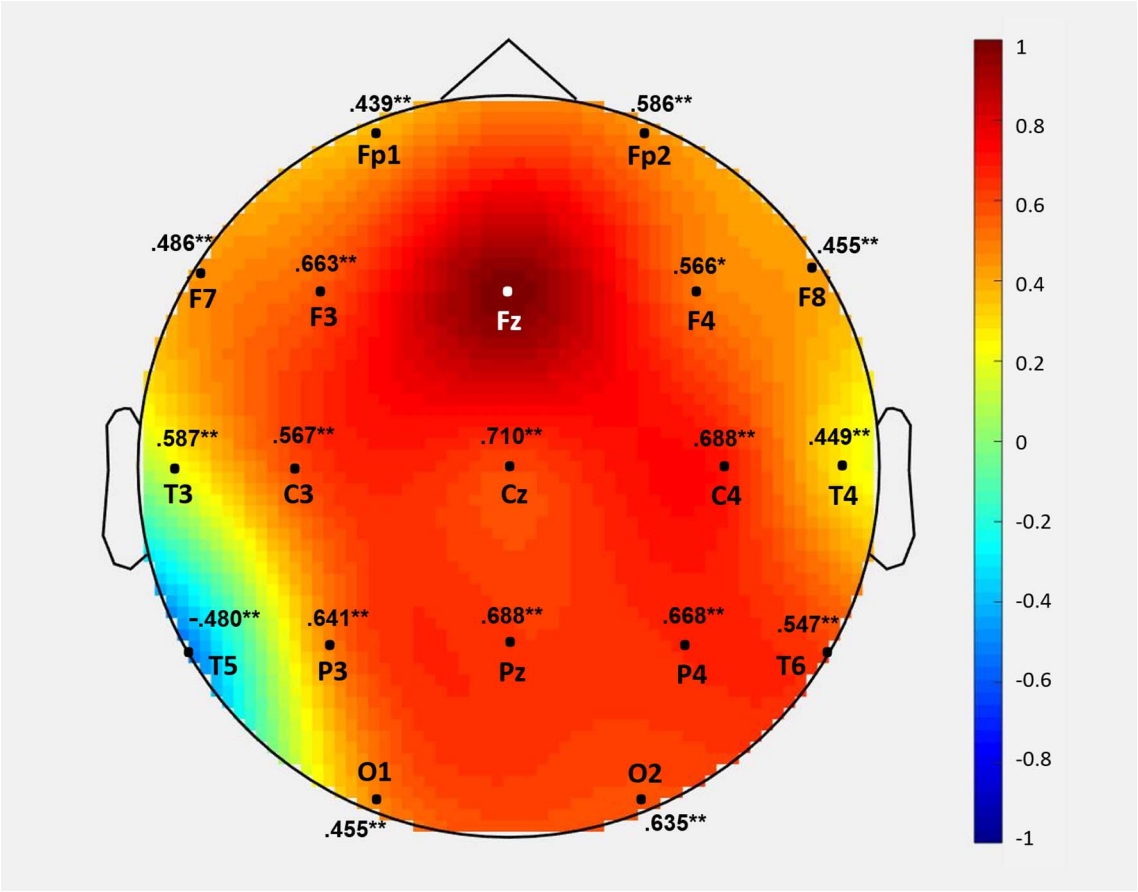

Fig. 7. Pearson's R correlations between NFB theta/beta ratio change at Fz and NFB change at other recording electrodes, for $n = 44$ participants. **, $P < .01$.

indication of what would happen to the memory traces formed in the initial learning trials during a controlled period of ongoing cognitive-perceptual activity, modelling ecological conditions of ongoing experience. The data regarding the Movie group indicates that under the particular conditions of the experiment, without the benefits to memory afforded by theta NFB, recall performance declines over time. While the Beta group did not differ from the Movie group in recall success in the immediate post-intervention test, it is the case that they showed better memory at 24 h and 1 w delay, which is likely attributable to the lesser amount of specific retroactive interference for both NFB groups relative to the movie viewers, which seemingly impacted on later stability of the initial learning. There does not seem to be evidence from these data that low beta NFB provides any specific memory benefits.

We have considered several mechanisms by which theta upregulation might benefit synaptic consolidation (Rozengurt et al., 2016). One possibility is that theta rhythms differentially favor waking replay of firing patterns in neuronal ensembles activated in encoding (Carr, Jadhav, & Frank, 2011; Miller et al., 2013). Relevant to scalp-based NFB as implemented in the current study, cortico-hippocampal theta coherence has been linked to replay strength and subsequent consolidation (Benchenane et al., 2010). Another candidate process in which theta might be facilitatory is the resetting of synapses that have not crossed a threshold for Hebbian plasticity back to baseline activity levels, thus sharpening memory traces by increasing the representational signal-to-noise ratio. Norman and colleagues have proposed a biased competition model, in which cycling between high and low inhibition states associated with different theta phases leads to the strengthening of effective memories by long-term potentiation, and weakening of the competitors by long-term depression (Norman, Newman, & Detre, 2007). The net effect would be reduction of a memory signal-to-noise ratio and better overall memory for target items. Although such biased competition filtering has been associated with sleep consolidation (Albouy et al., 2013), NFB theta potentiation during waking could also enhance such consolidation processes. It is noteworthy that, as in our prior studies of NFB effects on motor sequence learning (Reiner et al., 2014; Rozengurt et al., 2016), theta NFB led not only to preservation but to off-line improvement in recall, which this mechanism might have effected.

It should also be noted that an alternative interpretation of these findings is that rather than reflecting consolidation processes, the benefit exhibited by the Theta group resulted from theta oscillatory activity and/or the mental states engendering it having facilitated retrieval in the immediately following test. That initial boost to retrieval might then in turn have facilitated the subsequent free recall tests. The present data do not allow adjudicating between these interpretations, which might be assessed in future studies in which the initial post-NFB recall test is conducted following a delay of several hours, during which time the acute effects of theta activity state might dissipate.

Relatedly, we have framed these findings in terms of consolidation processes, on the most basic level since the intervention occurs after encoding but before retrieval. The consolidation period in a broad sense is the locus of many memory-related processes: decay, non-specific interference, and forgetting, as well as stabilization and sharpening of representations. Future research should examine to which of these processes theta rhythm modulation might be relevant. For example, combining EEG NFB with real-time fMRI could allow using representational similarity analysis to examine whether the representational patterns of the stimuli at encoding are more strongly represented during neurofeedback in the theta than in the low beta condition.

A number of limitations of this study should be mentioned. NFB success was seemingly challenging for some Beta group participants, as we implemented control of movement-related activity by withholding

positive feedback for target low beta when high beta was increased along with it (Fig. 1c). However, theta NFB effects remained robust when examining effective modulators (Figs. 5 and 6). Additionally, recent research indicates that human hippocampal memory-related theta activity may be focused at lower frequencies (~3 Hz) than the classic theta band (4–8 Hz) we employed (Jacobs, 2013; Lega, Burke, Jacobs, & Kahana, 2016; Pastötter & Bäuml, 2014). Individual band-frequency tailoring (as done for alpha power by Escolano et al., 2014) may enable better specificity.

Our study is the first to indicate that theta rhythm modulation may serve as a method of enhancing early consolidation of episodic memory. Follow-up studies are required to examine the generalizability of the effect to additional aspects of episodic memory and semantic learning, and to explore whether such interventions may provide effective protection from retroactive interference, as would be expected from consolidation enhancement.

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