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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,