Variable training but not sleep improves consolidation of motor adaptation

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Abstract

Motor memory is an important learning feature. How its consolidation depends on sleep is still unsolved. Some motor tasks were previously shown to depend on sleep to some extent, whereas pure non-hippocampal dependent motor tasks, like motor adaptation, might not. However, recent research suggests that training schedules might affect the sleep dependency of motor adaptation tasks. This study investigated whether sleep differentially impacts memory consolidation on a motor adaptation task dependent on the training schedule. Healthy men were trained with their dominant right hand on a force field adaptation task and re-tested after an 11-h consolidation period either involving overnight sleep (Sleep group) or daytime wakefulness (Wake group). The Retest session comprised a Posttest and a Transfer test to the left hand. Half of the subjects in each group trained the adaptation to different force field magnitudes in a blocked schedule with low inter-trial variability (Sleep-Blocked; Wake-Blocked), the other half in a random schedule with high variability (Sleep-Random; Wake-Random). EEG records during task performance and overnight polysomnography was obtained. Consistent with the notion that sleep generally does not benefit motor adaptation, memory performance did not differ between Wake and Sleep groups, although Posttest performance specifically correlated with sleep spindles nesting in slow wave upstates. Increased, inter-trial variability at Training produced better performance at the Posttest and Transfer test. This improvement appeared to result from the participants' increased ability to use feedback for ongoing movement corrections, and correlated with EEG alpha power over the left parietal cortex during the task.

Keywords: sensorimotor learning, sleep dependent memory, motor memory consolidation, force field adaptation, EEG

Significance statement

This study confirms that consolidation of motor adaptation and generalization to the non-dominant hand benefits from training with higher trial-to-trial variability. The consolidation success was independent of sleep, even if training was scheduled with different amounts of variability. Consolidation benefits of variable training were linked to effective feedback corrections during the ongoing movement and correlated with synchronous activity in the parietal cortex of the trained hemisphere.

Introduction

The influence of post-learning sleep on motor memory consolidation has been frequently investigated (King et al., 2017). However, the literature shows an inconsistent picture with studies supporting (e.g. Plihal & Born, 1997; Fischer et al. 2002, Albouy et al., 2013) and not supporting (e.g. Donchin et al., 2002; Rickard et al., 2008) sleep dependent motor memory consolidation. Many studies, hence, point to a more complex relationship between specific factors of motor tasks and sleep (Adi-Japha and Karni, 2016; but also see Rickard and Pan, 2017). In a recent qualitative literature review, King et al. (2017) identified that motor benefits or stabilizations due to sleep can be seen in explicit sequence learning tasks, specific variants of implicit sequence learning tasks, and specific visuomotor adaptation tasks, with all of these tasks involving hippocampal function to a certain extent. On the other side, it has been suggested that specific non-hippocampal-mediated tasks, like motor adaptation to dynamic perturbations (e.g. force field adaptation; Shadmehr and Mussa-Ivaldi, 1994), reflect a motor memory process that is purely time- but not sleep-dependent (Donchin et al. 2002), although those results, to the best of our knowledge, have not been confirmed so far.

Beyond sleep's dependency on specific task aspects, the effects might also depend on the specific training schedule. Several studies showed that motor training under highly unstable conditions, compared to more stable conditions, enhances posttest and transfer performance, suggesting that depending on the training schedule different memory systems are involved (e.g. Shea and Morgan, 1979; Magill and Hall, 1990; Lage et al., 2015). Furthermore, it has been assumed that specifically benefits after variable training

depend on sleep (King et al., 2017). This assumption is derived from a study investigating imaginary training which showed that variable but not constant mental training of a motor task leads to sleep dependent memory improvements (Debarnot et al., 2015). Moreover, other studies revealed that hippocampal dependency of a motor task changes with the schedule and the amount of training (Dick et al., 2003; Martel et al., 2007; Merbah and Meulemans, 2011).

In this study, we assessed the effects of sleep on memory for a force field adaptation task. Specifically, we were interested whether effects of sleep might express depending on the variability of different force fields used during training. For this purpose, subjects were examined either in more stable or highly unstable training conditions, and retested after periods of sleep or wakefulness with the same arm. Since previous work from our lab showed sleep dependent consolidation effects for contralateral transfer (Witt et al., 2010), we also examined transfer performance on the contralateral hand. We recorded EEG correlates during training, intervening sleep, and during retest, and also aimed to characterize the role of online feedback mechanisms in mediating improvements during movement execution.

Materials and Methods

Participants

Forty-eight healthy, male participants recruited from the local university campus were included in the study (age 24.27 ± 0.45 yrs.). All participants were native German speakers with normal or corrected to normal vision and were tested for right-handedness by the Edinburgh handedness inventory (Oldfield, 1971). They reported not to nap habitually or have any sleep disorders and did not take any medication at the time of the experiments. Participants followed a normal sleep–wake rhythm and reported no night shifts during the 6 weeks before the experiment. Participants were instructed to keep a regular sleep schedule, abstain from caffeine- and alcohol-containing drinks for at least 2 days before and on the days of the experiments. Experimental task and task-protocol were new to the participants. All participants provided written informed consent and the study was approved by the ethics committees of the Karlsruhe Institute of Technology and the University of Tübingen.

Apparatus and motor adaptation task

Apparatus and task stem from a previous study (see Thürer et al. 2017, for a detailed description). Participants performed point-to-point reaching movements at a robotic manipulandum (Kinarm End-Point Lab, BKIN Technologies, Kingston, Canada; Figure 1A). The manipulandum sampled position of the handle and forces exerted on the handle at 1000 Hz. Participants' grasped the handle and their forearm was supported by an air-sled system which enabled low friction movements. The task goal was to move a cursor on a screen – controlled via the robot handle – into a target circle (Figure 1B). To prevent movement anticipation, each trial started with a fixation cross and the highlight-duration of this fixation cross varied randomly between 0.8 and 1.5 s. When the fixation cross changed its shape to a target circle, subjects were allowed to start their movement (no fast reaction times were required). After reaching the target, the manipulandum actively guided subjects' hands back to the center point and provided the beginning of the next trial. In total, six targets were arranged on a circle with a diameter of 20 cm surrounding the center target. The target order was pseudo-randomized so that in every block (containing 6 movements) every target highlighted just once. In addition, within each group the target order was different for every single subject so that the mean target direction and the mean force field magnitude across all subjects was identical of each specific trial.

The manipulandum can produce forces via the handle towards subjects' hands. In this study, we implemented three types of trials. In null field trials, no forces were produced and subjects performed movements under unperturbed conditions. In force field trials, the motors of the manipulandum were turned on and produced a velocity-dependent curl force field in clockwise direction with three different viscosity magnitudes of 10, 15, and 20 Ns/m. In force channel trials, the manipulandum produced a virtual force channel from start to target so that the subjects were only able to move along this path directly into the target (Figure 1C). In every single trial, visual feedback about the movement time was given to ensure similar movement times across trials and subjects (< 450 ms: too slow; > 550 ms: too fast).

Offline calculations of dependent variables on the behavioral level were performed using MATLAB R2015b (MathWorks Inc., Natick, MA, United States). For null field and force field trials, we computed the

motor error by using the enclosed area (EA) between subjects' hand path and the vector joining start and target (Figure 1C, left). This parameter was averaged over 30 trials for the Baseline, First Training Trials, Last Training Trials, Posttest, and Transfer. To quantify motor performance in force channel trials, we calculated a force field compensation factor (FFCF; Figure 1C, right) by means of the linear regression of the measured and the ideal perpendicular force profile (Joiner and Smith, 2008) and averaged this across each 6 force channel trials. As subjects do not receive error-feedback in these trials, this parameter reflects mainly movement prediction and, thus, feedforward mechanisms (Scheidt et al., 2000). From now on, the term motor error will refer to the enclosed area and the term motor prediction will refer to the force field compensation factor.

Design and Procedures

This study compares the effects of random (unstable) vs. blocked (stable) training on motor adaptation and consolidation processes during wake vs. sleep. In a between-groups design, participants were randomly assigned to four equal sized groups (n = 12) of comparable age (range 18–30 yrs; $p > 0.45$, for one-way ANOVA between groups) with altered training conditions and retention periods taken place either in the night or during the day. All participants trained with their dominant right hand the motor adaptation task. The task was either trained in a random trial sequence (Random group) or in three randomized blocks, each containing a consistent field magnitude (Blocked group). Participants trained either in the morning (9 am; Figure 1D) and were retested in the evening (8 pm; Wake-Random, WR; Wake-Blocked, WB) or, vice versa, trained in the evening and were retested the following morning after a night of sleep (Sleep-Random, SR; Sleep-Blocked, SB). The retention period between Training and Retest sessions was about 11 hours for all groups. The Wake participants spent their awake time following their usual daily activity and Sleep participants went home after Training to sleep there with polysomnographic home recordings. Retest session contained a Posttest and Transfer test, quantifying the motor performance of participants using their right (Posttest) and left (Transfer) hand (Figure 1D).

Before Training, participants were mounted with a task-EEG and familiarized themselves with the motor adaptation task. During Familiarization, participants performed 144 null field trials with their right hand. Before Training and Posttest, participants were tested on possible confounding effects of subjective sleepiness (Stanford Sleepiness Scale, SSS; Hoddes et al., 1973), mood (Positive Affect Negative Affect Scale, PANAS; Krohne et al., 1996; Watson et al., 1988), and objective vigilance (5-min psychomotor vigilance task, PVT; Roach et al., 2006).

Then, participants performed a Baseline measurement using 30 null field trials and 6 additional force channel trials. Training contained 144 force field trials followed by 6 consecutive force channel trials. All participants trained force field trials split into three force field magnitudes (10, 15 and 20 Ns/m) with a mean force field magnitude of 15 Ns/m over all trials. Random and Blocked groups trained the magnitudes under different training schedules that manipulate the training variability of those groups: the Random group trained all trials with force field magnitude switching from trial to trial in a pseudo-random order (unstable); the Blocked groups trained three trial blocks, each containing 48 trials with consistent force field magnitude, with force field magnitude switching only between the blocks. The block order was counterbalanced across participants of each group. The Wake group participants ended the Training session with unmounting of the task-EEG and were given instructions for the daytime until arrival for the Retest session in the evening; the Sleep group participants, however, were additionally prepared for the sleep-EEG and received instruction for the overnight home-polysomnography recording until the next day. The Sleep group started the Retest session with the unmounting of the sleep-EEG.

The Retest session was the same for all participants. Thereby, all participants performed a Posttest of the task with 6 force channel trials, 30 force field trials, and 6 force channel trials. All force field trials were fixed at the mean force field magnitude of the Training (15 Ns/m). Posttest was followed by a Transfer test. Transfer test had the same protocol as Posttest and participants performed the behavioral task with the non-dominant left hand. Note that the force field direction in the Transfer test was still clockwise.

Task-EEG

To record the EEG during task performance we used the actiCHamp system with 32 active-electrodes and used the BrainVision PyCorder V1.0.6 for data recordings (Hard- and software from Brain Products, Gilching, Germany). The task-EEG was synchronized with the manipulandum via a direct link and the data was sampled at 1000 Hz. Electrodes were mounted on subjects' heads with a cap and 29 electrodes were used for the recording of cortical activity using the international 10-10 system (Fp1, Fp2, F7, F3, Fz, F4, F8, FC5, FC1, FC2, FC6, T7, C3, Cz, C4, T8, CP5, CP1, CP2, CP6, P7, P3, Pz, P4, P8, TP10, O1, Oz, O2). The remaining three electrodes were used to record horizontal and vertical eye movements. Electrode Cz was used as the reference and Fpz as the ground electrode. The impedances of the electrodes were kept below 10 kΩ.

Offline EEG analyses were done using MATLAB R2015b (MathWorks Inc., Natick, MA, United States) and EEGLAB 13.5.4b (Delorme and Makeig, 2004). Raw data of the task-EEG was filtered first by a FIR high-pass filter with a cut-off frequency of 0.5 Hz and then by a FIR low-pass filter with a cut-off frequency of 281.25 Hz. Line noise was removed using the cleanline plugin for EEGLAB. Channels strongly affected by artifacts were removed by visual inspection and the missing channels restored using a spherical interpolation. Electrodes were re-referenced to the average reference and channel location Cz was reconstructed and appended to the data. Then, EEG data was epoched into segments of 8.5 s ranging from 6 s before to 2.5 s after trial start. Principle component analysis (PCA) was performed to compress the data to 99.9 % of the variance and, thus, deal with the reduced rank due to interpolation. Then, infomax independent component analysis (ICA; Makeig et al., 1996) was performed on the principle components. To detect bad ICA components, the components were evaluated in the spectral, spatial and temporal domain. Components showing distinct artifacts were rejected and the data was re-transformed into the channel domain.

We calculated the percentage power in the frequency domain for subsequent statistical comparisons. For this, we used complex Morlet wavelets for the frequency decomposition. We decomposed the data into 40 frequency bins ranging from 2 to 100 Hz in logarithmic space with 5 to 19 wavelet cycles changing as a

206 function of frequency. The decomposed data was averaged over 30 trials and squared, resulting in the
207 average power for: Baseline, First Training Trials, Last Training Trials, Posttest, and Transfer. Then, power
208 was normalized according to the average reference period 250 ms before the highlighting of a fixation cross
209 and the event-related desynchronization / synchronization (ERD / ERS) was calculated (Pfurtscheller and
210 Lopes da Silva, 1999).

211 Data was averaged in the frequency domain into specific frequency bands: theta (4-7 Hz), alpha (8-
212 13 Hz), beta (14-30 Hz), and gamma (30-45 Hz). The data was also compressed in the time-domain by
213 averaging to two time windows: movement planning (-0.4 s to 0 s) and movement execution (0 s to 0.4 s),
214 where 0 s indicates the trial start.

215

216 **Polysomnography and sleep-EEG analyses**

217 Standard polysomnography was assessed using a home recording system (Somnoscreen Plus,
218 Somnomedics, Randersacker, Germany) including electroencephalography (EEG) at locations F3, F4, Fz,
219 C3, C4, Cz, P3, P4, Pz (International 10–20 system), electrooculography (EOG) sites around the eyes,
220 electromyography (EMG) with electrodes placed at each musculus mentalis as well as the two electrodes at
221 each mastoids behind the ear. Fpz served as the ground electrode and Cz as the original reference. Data was
222 digitized at 256 Hz and down-sampled to 128 Hz to facilitate computation. Offline manual sleep scoring
223 and automatic basic sleep-EEG analysis was performed using the open-source toolbox SpiSOP (Weber,
224 2016, http://www.spisop.org, SpiSOP, RRID:SCR_015673). Data of two participants (one from the
225 Blocked, one from Random group) were excluded for these analyses due to technical failures (n = 22).
226 Scoring was performed by an experienced rater according to standard criteria (Rechtschaffen and Kales,
227 1968) and was blind to the participant's conditions. Sleep-EEG analyses, apart from sleep scoring, were
228 performed on EEG channels re-referenced to the average signals from the mastoids. Sleep-EEG parameters
229 were detected using standard settings of SpiSOP (Weber, 2016) based on analyses described in (Wang et
230 al., 2017) and briefly described in the following.

231 *Power spectral analyses of sleep EEG.* Power spectra were calculated separately for Stage 2, SWS,
232 non-REM and REM sleep on consecutive artifact-free 10 s intervals of non-REM sleep, which overlapped
233 in time by 9 s. Each interval was tapered by a single Hanning-adapted window (1 s tails follow Hanning
234 window, the other 8 s are 1) before applying Fast Fourier Transformation that resulted in interval power
235 spectra with a frequency resolution of 0.1 Hz. Power spectra were then averaged across all blocks (Welch's
236 method) and normalized by the effective noise bandwidth to obtain power spectral density estimates for the
237 whole data. Mean power density in the following frequency bands was determined: slow-wave activity (0.5–
238 4 Hz), theta (4–8 Hz), spindles (9–15 Hz), alpha (8–12 Hz), slow spindles (9–12 Hz) and fast spindles (12–
239 15 Hz), and beta (15–30 Hz), and log transformed (decibel) prior to statistical testing.

240 *Slow waves.* For the identification of slow waves, the signal in each channel during non-REM sleep
241 epochs was filtered between 0.5 and 3.5 Hz. Next, all intervals of time with consecutive positive-to-negative
242 zero crossings were marked as putative slow waves if their durations corresponded to a frequency between
243 0.5 and 1.11 Hz (zero crossings marked beginning and end of slow oscillation), yet these were excluded in
244 case their amplitude was >1000 mV (as these were considered artifacts) or when both negative and positive
245 half-wave amplitudes lay between −15 and +10 mV. A slow wave was identified if its negative half-wave
246 peak potential was lower than the mean negative half-wave peak of all putatively detected slow oscillations
247 in the respective EEG channel, and also only if the amplitude of the positive half-wave peak was larger than
248 the mean positive half-wave amplitude of all other putatively detected slow waves within this channel. For
249 each participant and channel, the number of slow oscillations, their density (per min non-REM sleep), mean
250 amplitude, and slopes (down slope, the ratio between value of the negative half-wave peak and the time to
251 the initial zero crossing, up slope, the ratio between absolute value of the negative half-wave peak and the
252 time to the next zero crossing) were calculated.

253 *Sleep spindles*. For each EEG channel, the signal during non-REM epochs was filtered in a 2-Hz
254 frequency band centered to the visually determined corresponding power peak (12 to 15 Hz range, 13.32 ±
255 0.11) in the non-REM power spectrum of each participant. Then, using a sliding window with a size of 0.2
256 s, the root mean square was computed, and the resulting signal was smoothed in the same window with a

moving average. A sleep spindle was detected when the smoothed RMS signal exceeded an individual amplitude threshold by 1.5 standard deviations of the filtered signal in this channel at least once and for 0.5 to 3 s. The threshold crossings marked the beginning and end of each spindle and quantified their duration. Sleep spindle amplitude was defined by the voltage difference between the largest trough and the largest peak. Spindles were excluded for amplitudes >200 mV. We focused the analysis on fast spindles only as slow spindles power peaks could not clearly identified in too many participants. For each participant and channel's absolute spindle counts, spindle density (per min non-REM sleep), mean amplitude, average oscillatory frequency and duration were calculated.

Sleep spindles co-occurring with slow wave upstates. To explore if spindles co-occurring with slow waves possess altered properties and associations with behavior, we identified slow waves that had at least one detected sleep spindle from the lowest trough (down state) to +0.5 seconds after the next positive-to-negative zero crossing (i.e., the slow wave upstate). Only the first spindle with the shortest delay to the down state was considered. Then properties of these co-occurring sleep spindles and slow waves were determined as mentioned above. In addition, the mean delay to the down state as well as the standard deviation of the delay were calculated.

For an exploratory analysis of standard and fine-tuned sleep EEG parameters and their associations with memory consolidation, power density, slow wave and spindle parameters (e.g. density) were averaged per electrode. Pz was excluded from analysis since it went bad in 4 sleep subjects with otherwise good sleep EEG.

Statistical analysis

We used independent t-tests and mixed model ANOVAs with the within factors time (First Training Trials, Last Training Trials), retention (Last Training Trials, Posttest; Last Training Trials, Transfer), and the between factors sleep (Sleep, Wake) and training (Random, Blocked) to test differences in the motor error (EA) and motor prediction (FFCF).

Statistical analysis of task-EEG in terms of a possible sleep effect were done using cluster-based statistics corrected by the maximum permuted cluster values. Therefore, mixed model ANOVAs with factors retention (Last Training Trials, Posttest; Last Training Trials, Transfer) and sleep (Sleep, Wake) were performed for every frequency band during movement planning and execution. Clusters were computed on the channel level according to p-values of the ANOVAs and the summed F-value for each cluster was stored as the observed statistic. Then, permutation testing was done using 1000 iterations. For each iteration, data was shuffled across both dimensions (retention, sleep), ANOVA was computed, and the maximum cluster value was stored. P-values were defined as the account of maximum permutation clusters exceeding the observed statistic divided by the number of iterations.

Furthermore, we tried to reproduce previous findings from our lab (Thürer et al., 2017), targeting the neural basis for the benefits of variable training. Accordingly, independent t-tests between training groups (Random, Blocked) were performed to test alpha band power differences during Posttest and Transfer. In addition, motor error differences between Posttest and Last Training Trials (Training-to-Posttest) and Transfer and Last Training Trials (Training-to-Transfer) were computed for each subject on the behavioral level and correlated with the EEG data during Training using Spearman correlations.

Likewise, to find potential correlates of consolidation success within sleep parameters, we performed an explorative analysis across both Sleep groups using Spearman correlations between behavioral changes over the retention period and all sleep parameters (i.e., total sleep time [TST]; sleep onset delay; duration and percentage of TST sleep in stages like Wake after sleep onset, Stage 1, Stage 2, SWS, non-REM [i.e. SWS+Stage 2]; Power and energy density of each sleep stage in the prominent frequency bands; parameters of slow waves, sleep spindles and their co-occurrence during the slow-wave upstates). Due to the explorative nature in the absence of a behavioral sleep effect we did not corrected these correlations for multiple comparisons.

Threshold for statistical significance was set to $p = 0.05$. Multiple comparisons were either corrected by the maximum statistic (permutation test) or by the False Discovery Rate (FDR; Benjamini and Hochberg,

1995). In the case of FDR, p-values in this study represent the FDR corrected p-value (Benjamini and Yekutieli, 2001).

Results

Behavioral results

All groups adapted to the dynamic force fields and decreased their motor error (quantified by the enclosed area, EA) during Training (Figure 2A,B, $F(1,44) = 143.05$, $p < 0.001$, $pEta^2 = 0.765$, for ANOVA with factor time (First Training Trials, Last Training Trials)) independent of Sleep/Wake conditions ($F(1,44) = 0.06$, $p = 0.801$, $pEta^2 = 0.001$) or Blocked/Random training conditions ($F(1,44) = 1.95$, $p = 0.169$, $pEta^2 = 0.042$). The Blocked groups adapted faster during Training than the Random groups (time*training, $F(1,44) = 4.50$, $p = 0.040$, $pEta^2 = 0.093$; time*sleep, $F(1,44) = 1.29$, $p = 0.262$, $pEta^2 = 0.028$, for mixed ANOVA with factors training (Blocked, Random), sleep (Sleep, Wake), and time (First Training Trials, Last Training Trials)). Faster learning was confirmed by FDR corrected *post-hoc t*-tests on Last Training Trials between Random and Blocked groups ($t(46) = 3.96$, $p = 0.002$, $d = 1.144$).

Random and Blocked groups started with similar Posttest performance (Figure 2A,B), showing that the retention from the Last Training Trials (11 hours earlier) to Posttest was worse for the Blocked compared to the Random groups (Figure 2B, retention*training, $F(1,44) = 6.95$, $p = 0.012$, $pEta^2 = 0.136$, for mixed ANOVA with factors retention (Last Training Trials, Posttest) and training (Blocked, Random)), but independent of sleep (retention*sleep, $F(1,44) = 1.68$, $p = 0.201$, $pEta^2 = 0.037$). A descriptive benefit of Sleep over Wake among the Blocked groups only from the Last Training Trials to Posttest (Figure 2B) was not statistically supported (retention*sleep or retention*sleep*training, $F(1,44) = 1.44$, $p = 0.237$, $pEta^2 = 0.032$, for mixed ANOVA with factors retention (Last Training Trials, Posttest), training (Blocked, Random) and sleep (Sleep, Wake)). The benefit of Random over Blocked training manifested quickly during the Posttest from the 5th trial onwards (Figure 2C). This benefit is also confirmed by Pearson correlation analyses showing that training success (i.e., lower motor error at the end of Training) was inversely related to retention success (percentage of Posttest error related to last Training error, $r = -.78$, $p < 0.001$, $n = 48$)

with this effect weaker in the Random (r = -0.51, p = 0.01, n = 24) than in the Blocked groups (r = -0.86, p < 0.001, n = 24; p = 0.018, z = 2.36, for the difference using Fisher r-to-z transformation). However, training success in general was moderately predictive and positively correlated with the overall Posttest performance for all groups (r = 0.29, p = 0.044, n = 48; for any group r is within 0.167–0.35). This suggests, though initial Training performance might benefit from a blocked training schedule, motor memory retention benefit from a randomized training schedule. These processes were unaffected by sleep.

We further investigated if memory consolidation also enhanced the generalization from the dominant hand (during Training) to the non-dominant (Transfer). As expected, all groups performed worse during Transfer testing as compared to the Last Training Trials, even after averaging across all 30 Transfer trials ($F(1,44)$ = 483.56, p < 0.001, $pEta^2$ = 0.917). In addition, initial Transfer performance of all groups was worse compared to the initial Training performance (First Training Trials; Figure 2). This lower initial performance during contralateral transfer learning indicates that participants expected the force field in the opposite direction as during Training (relying on an internal rather than an external representation). This is also supported by the motor prediction (force field compensation factor, FFCF) showing similar force field predictions in the initial Transfer trials for the Blocked and Random groups (Blocked: -15.64 %, SD 16.61 %; Random: -15.62 %, SD 17.85 %, negative sign indicates that participants expected the opposite force field direction). Motor error in Transfer test was lower in the Random than in the Blocked groups (retention*training, $F(1,44)$ = 16.57, p < 0.001, $pEta^2$ = 0.274, for mixed ANOVA with factors retention (Last Training Trials, Transfer) and training (Blocked, Random)) and this effect manifested immediately after the first Transfer trial (Figure 2A,D). Transfer learning effects were independent of sleep (retention*sleep, $F(1,44)$ = 0.11, p = 0.742, $pEta^2$ = 0.002) and not strongly predictive by training success (for all groups r = 0.12, p = 0.42, n = 48; Random group r = 0.14, p = 0.54, n = 24; Blocked group r = 0.395, p = 0.056, n = 24). Likewise, Posttest performance had no strong correlation to Transfer performance (r = 0.27, p = 0.072, n = 48). However, transfer learning was strongly influenced by motor memory retention, that is, improvements over the retention period from Last Training Trials to Posttest were associated with improvements from Last Training Trials to Transfer (r = 0.84, p < 0.001, n = 48), an association that was

weaker for the Random ($r = 0.48$, $p = 0.024$, $n = 24$) than for the Blocked groups ($r = 0.88$, $p < 0.001$, $n = 24$; $p = 0.007$, $z = 2.72$, for the difference between correlation coefficients after Fisher r-to-z transformation). This suggests that, in general, an enhanced consolidation from Training to Posttest is strongly connected to an enhanced Training to Transfer consolidation but transfer learning was less hampered by motor memory consolidation after random than after blocked training.

Motor error quantified by EA is affected by both, predictive feedforward and responsive motor feedback. As the feedback responses typically start to compensate for feedforward errors already at 100 ms (Jeannerod, 1988) and the average trial duration across groups was about 550 ms, EA should mostly reflect the feedback responses. Thus, we tested if the observed influences of training conditions also underlie feedforward motor prediction as measured by FFCF. Neither training nor sleep condition influenced motor prediction changes from Training to Posttest (retention*sleep, $F(1,44) = 1.23$, $p = 0.274$, $pEta^2 = 0.027$; retention*training, $F(1,44) = 0.56$, $p = 0.459$, $pEta^2 = 0.013$) or Training to Transfer (retention*sleep, $F(1,44) = 1.37$, $p = 0.249$, $pEta^2 = 0.030$; retention*training, $F(1,44) = 0.41$, $p = 0.524$, $pEta^2 = 0.009$). This suggests that the observed effect here is more affected by late feedback than early feedforward responses.

Task-EEG

Explorative analysis using cluster-based statistics for a possible retention*sleep effect (with retention: Last Training Trials, Posttest; Last Training Trials, Transfer) revealed that cortical activity in all frequency bands were unaffected by Sleep vs. Wake. Thus, we focused on further task-EEG analysis regarding the training conditions (Blocked, Random).

Analysis of a possible training condition effect was restricted to the alpha band power (Figure 3) over parietal areas according to previous work showing a linkage between training effect and force field adaptation only in alpha frequencies (Thürer et al., 2017). Based on these previous findings, we defined a left- and right-hemispheric region of interest (ROIl: CP5, CP1, PZ, P3; ROIr: CP6, CP2, PZ, P4) and found a higher alpha band power for the Random compared to the Blocked groups in the Posttest and a similar effect which did not reach significance in the Transfer test, both during movement execution (Posttest, $t(46)$

385 = -2.22, p = 0.031, d = 0.642, for t-test of ROIl; Transfer, $t(44)$ = -1.85, p = 0.072, d = 0.543, for t-test of
386 ROIr). Increased alpha band values over ROIl from Training to Posttest during movement execution were
387 associated with better task retention success (quantified by a small Training-to-Posttest difference of the
388 motor error; Figure 4) for participants of the Random but not of the Blocked groups (Random, ρ = -0.50, p
389 = 0.031; Blocked, ρ = 0.04, p = 1.0, for Spearman correlations with ρ representing Spearmans rho). This
390 suggests that random training of force fields affects parietal alpha band activity of the Posttest and maybe
391 even of the Transfer test.

392 Furthermore, we explored if the behavioral retention effects (Training-to-Posttest, Training-to-
393 Transfer), are predictable by the alpha band power during Training. Spearman correlations indicate positive
394 but weak associations from Training-to-Posttest for both groups (Random, Blocked), phases (planning,
395 execution), and ROIs (ROIl, ROIr), which did not reach statistical significance (Figure 5; Training-to-
396 Posttest, all ρ for Blocked between 0.22-0.33; all ρ for Random between 0.12-0.18). However, associations
397 of Training-to-Transfer consolidation were strong for Blocked (ρ in all cases between 0.39-0.60) but still
398 weak for Random groups (ρ between 0.04-0.20). These positive correlations for Blocked groups were
399 statistically significant after FDR correction for ROIl (Figure 5; planning, ρ = 0.595, p = 0.025; execution,
400 ρ = 0.550, p = 0.025) but only during trial execution for ROIr (planning, ρ = 0.389, p = 1.0; execution, ρ =
401 0.486, p = 0.050).

402

403 **Sleep EEG**

404 Though sleep during consolidation did not improve the motor performance more than wake-time, we
405 explored which activity during sleep could give an indication of the consolidation processes to happen
406 during the time of sleep. None of the basic sleep stage parameters correlated with consolidation performance
407 (Table 1).

408 Consolidation success was predicted by sleep spindles and their occurrence during up-states of slow
409 waves in a pattern that more sleep spindles during this short time window reflected the improvements from
410 Training to Posttest and Training to Transfer (Table 2). This pattern was most pronounced in the left parietal

411 area (i.e., P3). This was also reflected in the over-representation of slow-wave activity (power density)
412 during Stage 2 sleep (i.e. an indicator of higher a priori changes for sleep spindles and slow waves to occur)
413 was likewise predictive of improvements from Training to Posttest. Also, longer sleep spindles during slow
414 waves (and in general) predicted improvements from Training to Posttest. A less steep decline in oscillation
415 frequency (i.e. less 'chirp' towards lower oscillation frequency) during such spindles predicted worsening
416 from Training to Transfer, and a generally higher sleep spindle oscillation frequency in fronto-central areas
417 was predictive for the deterioration of the motor performance from Training to Posttest. Higher dispersion
418 of sleep spindles locked to the slow wave down state in Cz (SD of the delay to the slow wave down peak)
419 predicted less improvement during Transfer as compared to Training. No other sleep measures reached
420 significant correlation with consolidation measures.
421

422 **Discussion**

423 Our results show that Random and Blocked groups adapted to the force field conditions successfully.
424 Subsequent consolidation was influenced by training conditions but unaffected by intervening sleep.
425 Regarding training conditions, although Training outcome was worse for the Random than Blocked groups,
426 all groups showed a similar motor performance in the Posttest and Random groups showed an even more
427 pronounced motor performance compared to the Blocked groups when tested for transfer on the untrained,
428 non-dominant hand. This improvement expressed itself in reductions in motor error (enclosed area), which
429 is mostly affected by responsive feedback corrections, but not in the measure of motor prediction (force
430 field compensation factor).
431

432 **Sleep does not improve consolidation of force field adaptation**

433 Our behavioral results exclude a substantial profit from sleep on the present motor adaptation task. Task
434 performance and measures of consolidation were independent on whether participants spent awake or asleep
435 during the intervening time between Training and Retest. Thus, our study confirms earlier findings by
436 Donchin et al. (2002) and concurs with some force field studies (Brashers-Krug et al., 1996; Shadmehr and

437 Brashers-Krug, 1997) claiming that consolidation of motor adaptation towards dynamic perturbations is
438 time but not sleep dependent. Previous work suggested that force field adaptation represents a non-
439 hippocampal dependent, implicit memory (Brashers-Krug et al., 1996; Rasch and Born, 2013). Accordingly,
440 our negative findings here agree with the assumption that only hippocampal dependent motor processes
441 benefit from sleep (King et al., 2017). However, research showed that hippocampal damage deteriorates the
442 benefits of unstable training conditions (Merbah and Meulemans, 2011), indicating that a motor task might
443 become hippocampal-dependent - and thus would be expected to become sleep-dependent - when trained
444 under highly unstable conditions (Debarnot et al., 2015; King et al., 2017). However, this view is not
445 supported by our behavioral data showing also now sleep effects for the Random groups. The exact extent
446 to which motor adaptation after variable training becomes hippocampal-dependent is unclear and need to
447 be elaborated in future studies.

448 Despite the lack of a consolidation benefit of sleep over wake retentions, the consolidation success
449 correlated positively with sleep spindle activity during slow-wave upstates. This is at odds with the view
450 that consolidation of motor adaptation learning is completely independent of hippocampal processes,
451 because the coalescence of spindle and slow-wave activity during sleep is thought to benefit consolidation
452 of hippocampal-dependent tasks in particular (Rasch and Born, 2013; Maingret et al., 2016; Khodagholy et
453 al., 2017). Intriguingly, we found task-consolidation-associated alpha activity over parietal brain regions
454 which matches the strong association of sleep-mediated consolidation in the same regions. This concurs
455 with the view that cortical regions that were engaged in learning have a strong local association with spindles
456 and slow waves in subsequent sleep (Pereira et al. 2017) and predict the extent of consolidation (Huber et
457 al. 2004). If such associations are functionally involved in the consolidation process in our data or are merely
458 a reflection of consolidation success of other memories, not tested by our task, is unclear.

459

460 **Variable training leads to consolidation benefits**

461 This study reproduced earlier findings of the contextual interference effect (Schmidt and Lee, 2011; Lage
462 et al., 2015) in that higher training variability led to a decreased motor performance at the end of Training,

but to a performance similar to that of the blocked training groups on the Posttest and to even performance benefits on the Transfer test. As previously reported (Thürer et al., 2017), this gain induced by variable training is only seen in the motor error which is mostly affected by feedback responses. By contrast, motor prediction again did not show this effect. Because subjects do not receive task specific feedback during force channel trials, FFCF is only feedforward dependent (Scheidt et al., 2000; Joiner and Smith, 2008). Therefore, it is likely that the motor benefits of the Random groups were facilitated by feedback corrections during movement execution evoked by the permanent regulation of random, unexpected forces during Training.

Although the Random groups ended their training worse compared to the Blocked groups, their Posttest performance was comparable. This points to unstable training conditions to either prime for better memory consolidation or the formation of memory that is more stable. Also, the generalization to the Transfer test on the left hand was more pronounced in the Random groups. The consistency of this generalization benefit over 30 trials speaks for a stable long-term memory effect. This was confirmed by the significant association of benefits in memory consolidation and the training schedule, that is lower Training performance (in terms of higher motor error) from unstable training also led to better retention performance.

During Transfer testing the participants expected a force field on their left hand that was directed in the opposite direction than force field was during Training of the right hand which explains the initially worse Transfer performance present in all groups when compared to initial Posttest performance. This suggest the generalization did not take place in extrinsic force field transformation but rather in intrinsic, mirror symmetric coordinates, that is, perturbation was expected to come from right on the right hand and from left on the left hand. This agrees with the literature (Shadmehr and Mussa-Ivaldi, 1994) but contradicts the preference of extrinsic coordinates in other studies (Malfait and Ostry, 2004; Stockinger et al., 2017). The divergent findings of coordinate systems in use for generalization are in line with the recent assumption that representations might occur in a mixture of coordinate systems (Berniker et al., 2014; Franklin et al., 2016).

Paradoxically, we do not find an even more decreased initial Transfer performance for Random groups, as would be expected by a more stable intrinsic representation in this group which gives rise to predict the force field in the opposite, 'wrong' direction during Transfer. But the opposite was the case, i.e., the Random groups showed an enhanced Transfer performance compared to the Blocked groups. There are three possible explanations for this outcome:

(1) Generalization was worse for the Random compared to the Blocked groups. Increased motor performance of the Random group might be facilitated by a weaker generalization or consolidation of the generalized memory. However, motor performance quantified by the motor prediction showed similar Transfer performances for all groups, indicating similar generalizations between groups.

(2) Random training favored the formation of a different coordinate system (or mixture of systems; Berniker et al., 2014). The results, however, do not support such explanation as motor predictions were similar between groups. In addition, inspection of single individual data revealed cues for an extrinsic force field representation in only 4 of the 24 participants of the Random groups. This was also the case in 2 of the 24 participants of the Blocked groups.

(3) Random training led to a generally increased ability to use feedback responses. This explanation is supported by the finding that only motor error, which is sensitive to feedback corrections, but not motor prediction showed an increased memory consolidation for the Random groups. In addition, the EEG data shows that parietal but not frontal areas of the brain are involved in the contextual interference effect, with the former known to be specifically implicated in sensory integration (Whitlock, 2017). However, future research should further investigate the influence of variable training on online feedback corrections in motor behavior.

Summarized, variable training leads to benefits in consolidation of a force field adaptation task. This effect is even more prominent when retention is tested on the contralateral hand. We assume that the increased consolidation after highly variable training is facilitated by an increased ability to use online feedback corrections.

Parietal alpha power predicts Transfer performance in the Blocked groups

The EEG during task performance showed that behavioral changes across the consolidation period after Random training are accompanied with a parallel increase (from Training to Posttest) in alpha band power over parietal areas, which concurs with previous findings from our lab (Thürer et al., 2017). In detail, we were able to reproduce here a negative correlation between changes in alpha power over contralateral parietal areas (ROIl) and motor error during movement execution. An increased alpha band power is frequently discussed as a sign of an active inhibition of the underlying cortical region (Klimesch, 2012). Therefore, a negative correlation might indicate that, for Random groups, a more accurate and, thus, better consolidated motor performance comes in parallel with an increased inhibition of parietal areas.

The results also showed that consolidation in this force field adaptation task can be predicted by the alpha power over parietal areas during Training. Blocked but not Random groups showed significant associations between Training-to-Transfer consolidation and the alpha band power. Thus, high parietal alpha power and, thus, inhibition of parietal cortical areas during Training, might favor a weaker consolidation for the Blocked but not for the Random groups. Intriguing questions arising here are whether the greater efficacy of random training specifically results from its ability to counter the disadvantage of increased parietal alpha power during training and whether parietal alpha power is connected to online feedback corrections of the motor system.

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References

Adi-Japha, E., and Karni, A. (2016). Time for considering constraints on procedural memory consolidation processes: Comment on Pan and Rickard (2015) with specific reference to developmental changes. *Psychol Bull*, 142(5), 568–571. https://doi.org/10.1037/bul0000048

Albouy, G., Vandewalle, G., Sterpenich, V., Rauchs, G., Desseilles, M., Balteau, E., … Maquet, P.

(2013). Sleep stabilizes visuomotor adaptation memory: A functional magnetic resonance imaging study. *J Sleep Res*, 22(2), 144–154. https://doi.org/10.1111/j.1365-2869.2012.01059.x

Benjamini, Y., and Hochberg, Y. (1995). Controlling the false discovery rate: a practical and powerful approach to multiple testing. *J R Statist Soc B*, 57(1), 289–300. https://doi.org/10.2307/2346101

Benjamini, Y., and Yekutieli, D. (2001). The control of the false discovery rate in multiple testing under dependency. *Ann Stat*, 29(4), 1165–1188. https://doi.org/10.1214/aos/1013699998

Berniker, M., Franklin, D. W., Flanagan, J. R., Wolpert, D. M., and Kording, K. (2014). Motor learning of novel dynamics is not represented in a single global coordinate system: evaluation of mixed coordinate representations and local learning. *J Neurophysiol*, 111(6), 1165–1182. https://doi.org/10.1152/jn.00493.2013

Brashers-Krug, T., Shadmehr, R., and Bizzi, E. (1996). Consolidation in human motor memory. *Nature*, 382(6588), 252. https://doi.org/10.1038/382252a0

Debarnot, U., Abichou, K., Kalenzaga, S., Sperduti, M., and Piolino, P. (2015). Variable motor imagery training induces sleep memory consolidation and transfer improvements. *Neurobiol Learn Mem*, 119, 85–92. https://doi.org/10.1016/j.nlm.2014.12.010

Delorme, A., and Makeig, S. (2004). EEGLAB: An open source toolbox for analysis of single-trial EEG dynamics including independent component analysis. *J Neurosci Methods*, 134(1), 9–21. https://doi.org/10.1016/j.jneumeth.2003.10.009

Dick, M. B., Hsieh, S., Bricker, J., & Dick-Muehlke, C. (2003). Facilitating acquisition and transfer of a continuous motor task in healthy older adults and patients with Alzheimer's disease. *Neuropsychology*, 17(2), 202–212. https://doi.org/10.1037/0894-4105.17.2.202

Donchin, O., Sawaki, L., Madupu, G., Cohen, L. G., and Shadmehr, R. (2002). Mechanisms influencing acquisition and recall of motor memories. *J Neurophysiol*, 88(4), 2114–2123. https://doi.org/10.1152/jn.00033.2002

Fischer, S., Hallschmid, M., Elsner, A. L., and Born, J. (2002). Sleep forms memory for finger skills. *Proc Natl Acad Sci USA*, 99(18), 11987–11991. https://doi.org/10.1073/pnas.182178199

Franklin, D. W., Batchelor, A. V., and Wolpert, D. M. (2016). The Sensorimotor System Can Sculpt Behaviorally Relevant Representations for Motor Learning. *eNeuro*, 3(4). https://doi.org/10.1523/ENEURO.0070-16.2016

Hoddes, E., Zarcone, V., Smythe, H., Phillips, R., and Dement, W. C. (1973). Quantification of sleepiness: a new approach. *Psychophysiology*, 10(4), 431-436. https://doi.org/10.1111/j.1469-8986.1973.tb00801.x

Huber, R., Ghilardi, M. F., Massimini, M., and Tononi, G. (2004). Local sleep and learning. *Nature*, 430(6995), 78. https:/doi.org/ 10.1038/nature02663

Jeannerod, M. (1988). *The neural and behavioural organization of goal-directed movements*. Oxford, UK: Oxford University Press.

Joiner, W. M., and Smith, M. A. (2008). Long-Term Retention Explained by a Model of Short-Term Learning in the Adaptive Control of Reaching. *J Neurophysiol*, 100(5), 2948–2955. https://doi.org/10.1152/jn.90706.2008

Khodagholy, D., Gelinas, J. N., and Buzsáki, G. (2017). Learning-enhanced coupling between ripple oscillations in association cortices and hippocampus. *Science*, 358(6361), 369-372. https://doi.org/10.1126/science.aan6203

King, B. R., Hoedlmoser, K., Hirschauer, F., Dolfen, N., and Albouy, G. (2017). Sleeping on the motor engram: The multifaceted nature of sleep-related motor memory consolidation. *Neurosci Biobehav Rev*, 80, 1–22. https://doi.org/10.1016/j.neubiorev.2017.04.026

Klimesch, W. (2012). Alpha-band oscillations, attention, and controlled access to stored information. *Trends Cogn Sci*, 16(12), 606-617. https://doi.org/10.1016/j.tics.2012.10.007

Krohne, H. W., Egloff, B., Kohlmann, C.-W., and Tausch, A. (1996). Untersuchungen mit einer deutschen

Version der" Positive and Negative Affect Schedule"(PANAS). *Diagnostica*, 42, 139-156.

Lage, G. M., Ugrinowitsch, H., Apolinário-Souza, T., Vieira, M. M., Albuquerque, M. R., and Benda, R. N. (2015). Repetition and variation in motor practice: A review of neural correlates. *Neurosci Biobehav Rev*, 57, 132–141. https://doi.org/10.1016/j.neubiorev.2015.08.012

Magill, R. A., and Hall, K. G. (1990). A review of the contextual interference effect in motor skill acquisition. *Hum Mov Sci*, 9(3–5), 241–289. https://doi.org/10.1016/0167-9457(90)90005-X

Maingret, N., Girardeau, G., Todorova, R., Goutierre, M., and Zugaro, M. (2016). Hippocampo-cortical coupling mediates memory consolidation during sleep. *Nat Neurosci*, 19(7), 959. https://doi.org/10.1038/nn.4304

Makeig, S., J. Bell., A., Jung, T.-P., and Sejnowski, T. J. (1996). Independent Component Analysis of Electroencephalographic Data. *Adv Neural Inf Process Syst*, 8, 145–151. https://doi.org/10.1109/ICOSP.2002.1180091

Malfait, N., and Ostry, D. J. (2004). Is interlimb transfer of force-field adaptation a cognitive response to the sudden introduction of load? *J Neurosci*, 24(37), 8084–9. https://doi.org/10.1523/JNEUROSCI.1742-04.2004

Martel, G., Blanchard, J., Mons, N., Gastambide, F., Micheau, J., and Guillou, J. L. (2007). Dynamic interplays between memory systems depend on practice: The hippocampus is not always the first to provide solution. *Neuroscience*, 150(4), 743–753. https://doi.org/10.1016/j.neuroscience.2007.10.004

Merbah, S., and Meulemans, T. (2011). Learning a motor skill: Effects of blocked versus random practice a review. *Psychol Belg*, 51(1), 15–48. https://doi.org/10.5334/pb-51-1-15

Oldfield, R. C. (1971). The assessment and analysis of handedness: The Edinburgh inventory. *Neuropsychologia*, 9(1), 97–113. https://doi.org/10.1016/0028-3932(71)90067-4

Pereira, S. I. R., Beijamini, F., Weber, F. D., Vincenzi, R. A., da Silva, F. A. C., & Louzada, F. M. (2017). Tactile stimulation during sleep alters slow oscillation and spindle densities but not motor skill.

Physiology & behavior, 169, 59-68.

Pfurtscheller, G., and Lopes, F. H. (1999). Event-related EEG / MEG synchronization and desynchronization: basic principles. *Clin Neurophysiol*, 110, 1842–1857. https://doi.org/10.1016/S1388-2457(99)00141-8

Plihal, W., and Born, J. (1997). Effects of early and late nocturnal sleep on declarative and procedural memory. *J Cogn Neurosci*, 9(4), 534–47. https://doi.org/10.1162/jocn.1997.9.4.534

Rasch, B., and Born, J. (2013). About sleep's role in memory. *Physiol Rev*, 93(2), 681–766. https://doi.org/10.1152/Physrev.00032.2012

Rechtschaffen, A., and Kales A. (1968). *A manual of standardized terminology, techniques and scoring system for sleep stages of human subjects*. Washington, DC: Washington Public Health Service, US Government Printing Office.

Rickard, T. C., and Pan, S. C. (2017). Time for considering the possibility that sleep plays no unique role in motor memory consolidation: Reply to Adi-Japha and Karni (2016). *Psychol Bull*, 143(4), 454–458. https://doi.org/10.1037/bul0000094

Rickard, T. C., Cai, D. J., Rieth, C. a, Jones, J., and Ard, M. C. (2008). Sleep does not enhance motor sequence learning. *J Exp Psychol Learn Mem Cogn*, 34(4), 834–842. https://doi.org/2008-08549-010

Roach, G. D., Dawson, D., and Lamond, N. (2006). Can a shorter psychomotor vigilance task be used as a reasonable substitute for the ten-minute psychomotor vigilance task? *Chronobiol Int*, *23*(6), 1379–1387. https://doi.org/10.1080/07420520601067931

Scheidt, R. A., Reinkensmeyer, D. J., Conditt, M. A., Rymer, W. Z., and Mussa-Ivaldi, F. A. (2000). Persistence of motor adaptation during constrained, multi-joint, arm movements. *J Neurophysiol*, 84(2), 853–862. https://doi.org/0022-3077/00

Schmidt, R., and Lee, T. (2011). *Motor Control and Learning: A Behavioral Emphasis*. Champaign, IL: Human Kinetics. https://doi.org/10.1016/0021-9290(88)90286-2

Shadmehr, R., and Brashers-Krug, T. (1997). Functional stages in the formation of human long-term motor memory. *J Neurosci*, 17(1), 409–19. https://doi.org/citeulike-article-id:407791

Shadmehr, R., and Mussa-Ivaldi, F. a. (1994). Adaptive representation of dynamics during learning of a motor task. *J Neurosci*, 14(5), 3208–3224. https://doi.org/8182467

Shea, J. B., and Morgan, R. L. (1979). Contextual interference effects on the acquisition, retention, and transfer of a motor skill. *J Exp Psychol Hum Learn Mem*, 5(2), 179–187. https://doi.org/10.1037/0278-7393.5.2.179

Stockinger, C., Thürer, B., and Stein, T. (2017). Consecutive learning of opposing unimanual motor tasks using the right arm followed by the left arm causes intermanual interference. PLoS ONE, 12(5), 1–20. https://doi.org/10.1371/journal.pone.0176594

Thürer, B., Stockinger, C., Putze, F., Schultz, T., and Stein, T. (2017). Mechanisms within the Parietal Cortex Correlate with the Benefits of Random Practice in Motor Adaptation. *Front Hum Neurosci*, 11, 1–11. https://doi.org/10.3389/fnhum.2017.00403

Watson, D., Clark, L. A., and Tellegen, A. (1988). Development and validation of brief measures of positive and negative affect: the PANAS scales. *J Pers Soc Psychol*, *54*(6), 1063–1070. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/3397865

Weber, F. D. (2016). SpiSOP – Spindles, Slow Oscillations, Power density and fast replication of basic sleep EEG analyses in one tool. Retrieved 2017, from http://www.spisop.org

Whitlock, J. R. (2017). Posterior parietal cortex. *Curr Biol*, 27(14), 691–695. https://doi.org/10.1016/j.cub.2017.06.007

Witt, K., Margraf, N., Bieber, C., Born, J., and Deuschl, G. (2010). Sleep consolidates the effector-independent representation of a motor skill. *Neuroscience*, 171(1), 227–234. https://doi.org/10.1016/j.neuroscience.2010.07.062

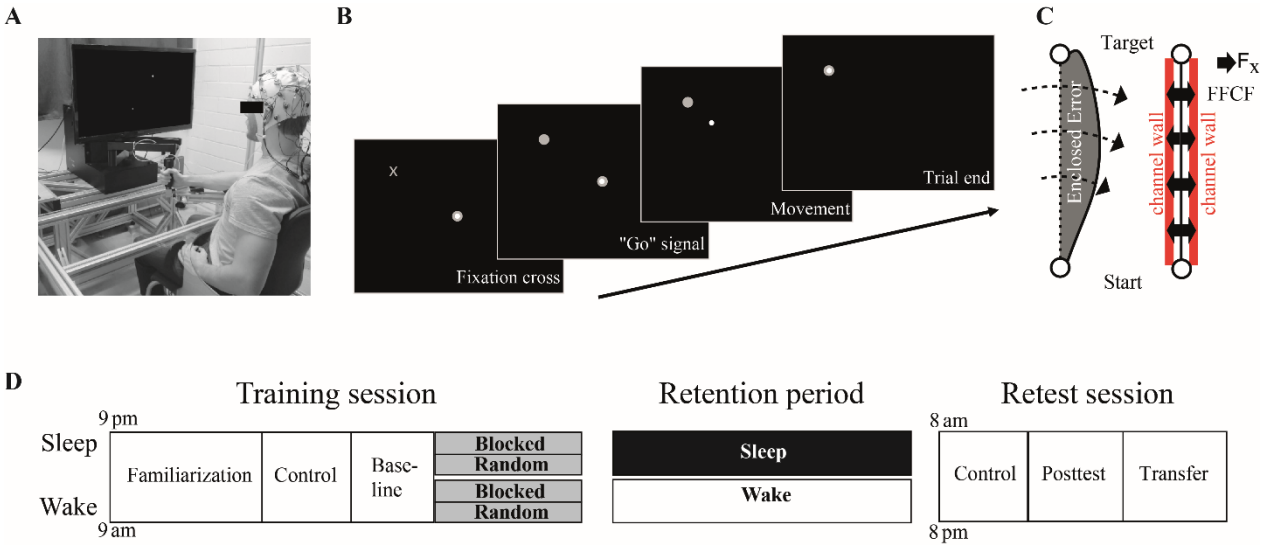

Figure 1: Motor adaptation task and experimental design. **A** The motor adaptation task was instrumented by a robotic manipulandum (Kinarm End-Point Lab, BKIN Technologies) with a custom made low friction air-sled system. The robotic manipulandum can induce force fields to perturb participants' hand movements. During the task, participants' EEG is recorded. **B** Example of one trial from highlighting of the fixation cross to trial termination by reaching the target. **C** Sketch of the parameters quantifying the motor error (enclosed area, EA) and motor prediction (force field compensation factor, FFCF). Enclosed area (left) is defined by the area between the trajectory and the direct line between start and target. Arrows indicate the force field direction. The FFCF (right) is computed using the subject's forces (F_x) directed against virtual channel walls and compared to the ideal force profile to cancel out the perturbation. **D** All participant groups had a Training session to train the motor adaptation task with their dominant right hand including Familiarization phase, Control tests (subjective sleepiness, mood, and vigilance), a Baseline, and the force field Training (gray blocks). After a Retention period, Retest performance was quantified in a Posttest and an additional Transfer test on the left hand. Groups differed in their training and consolidation period. The Random groups trained motor adaptation under highly unstable conditions and the Blocked groups under more stable training conditions. The Wake groups trained in the morning and were retested in the evening and the Sleep groups were trained in the evening and retested the following morning after a night of sleep.

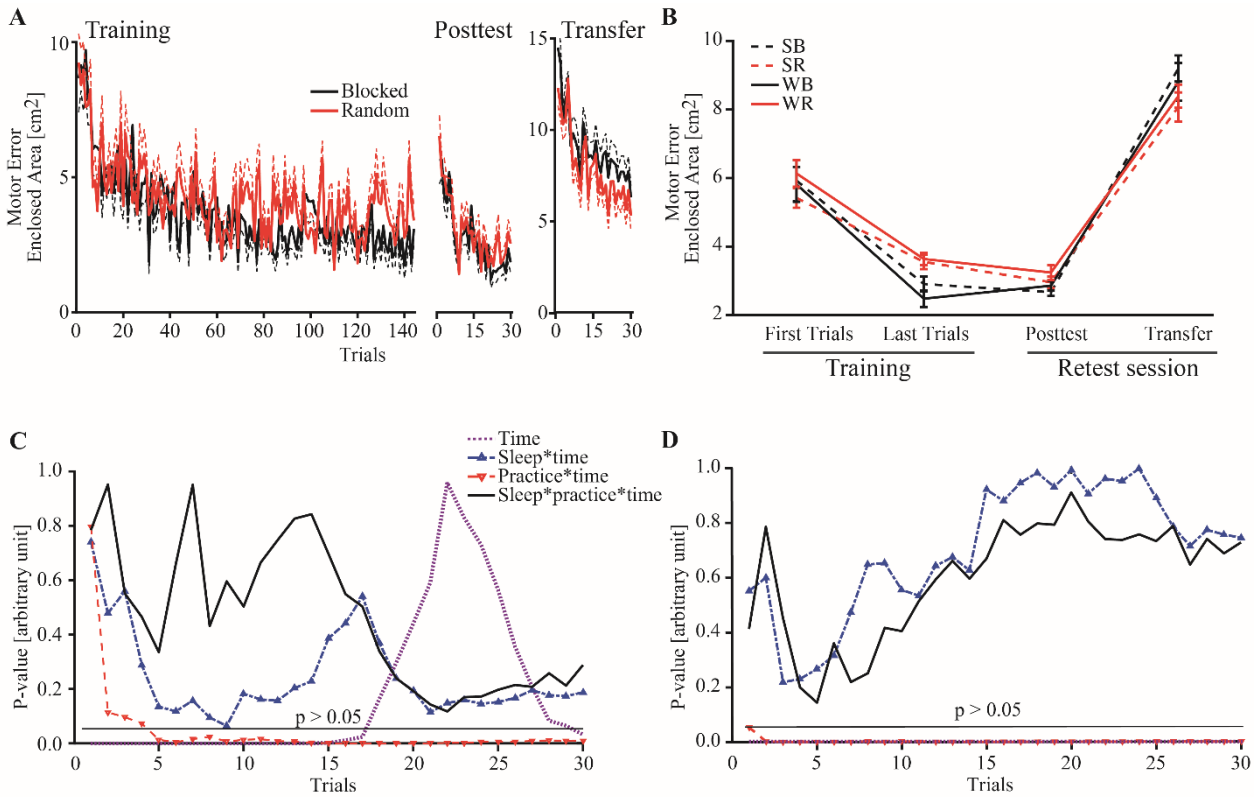

Figure 2: Behavioral results. **A** Progress of the mean (± SEM) motor error (enclosed area, EA) for the Blocked (black) and Random (red) groups during Training (left), Posttest (middle) and Transfer trials (right). **B** Mean (± SEM) motor error across 30 trials for each group during First and Last Training Trials, Posttest and Transfer. SB: Sleep-Blocked, SR: Sleep-Random, WB: Wake-Blocked, WR: Wake-Random. **C** P-values of different factors and interactions of the mixed ANOVAs investigating a consolidation effect from Training to Posttest and **D** Training to Transfer.

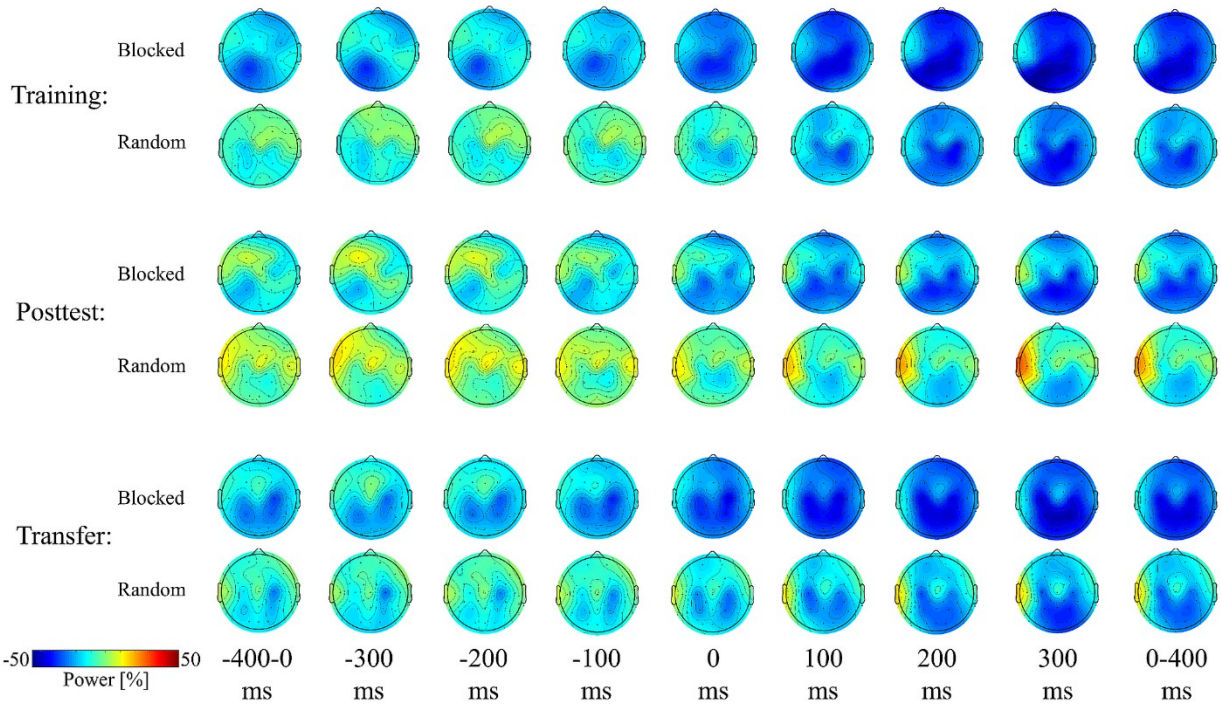

Figure 3: Mean alpha band power. Progress of the mean alpha band power for Blocked and Random groups during the Training session and during the Posttest and Transfer test of the Retest session. Leftmost and rightmost topographies represent the mean power across motor planning (-400-0 ms) and execution (0-400 ms). Other plots represent the topographical power at specific points in time (from -300 to 300 ms).

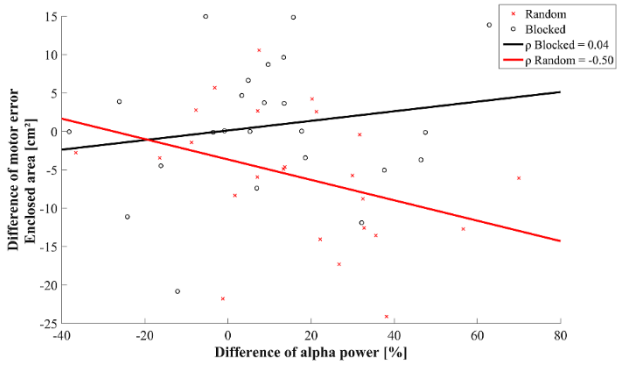

Figure 4: Association between Training-to-Posttest difference for motor error and alpha power. Associations between Training-to-Posttest difference of the motor error (quantified by EA) and alpha power for ROIl (CP5, CP1, Pz, P3) during motor execution were tested using Spearman correlation. Each red cross represents the data of a single participant from the Random group and each black circle of a participant from the Blocked group. Lines represent a basic linear fit (red: Random; black: Blocked) and ρ represent Spearmans rho.

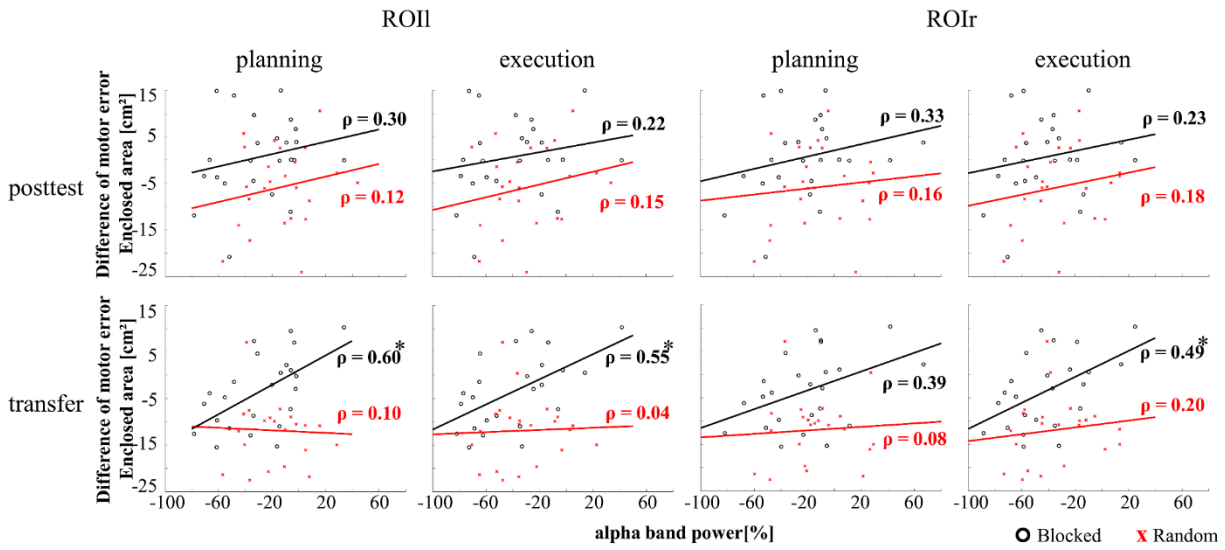

Figure 5: Prediction of motor memory consolidation by alpha power during Training. The predictability of motor memory consolidation (Training-to-Posttest or Training-to-Transfer difference of motor error) is indicated. Each plot represents the data points for each participant of the Blocked (black circle) and Random (red cross) groups together with their groups' linear fit. Asterisks indicate a significant Spearman correlation coefficient after FDR correction. Lines represent basic linear fit whereas ρ represents Spearmans rho.

Table 1

Sleep states and correlations with motor adaptation learning and consolidation

Sleep parameter (n = 22)				Spearman rank correlations with behavior [ρ]				
Stages				Training	Posttest	Transfer	Posttest - Training	Transfer - Training
TST [min]	435.91	±	8.76	-0.219	-0.338	-0.152	0.160	-0.043
Sleep onset [min]	18.56	±	3.70	-0.092	-0.074	-0.011	0.040	0.179
WASO [%]	2.91	±	0.43	-0.238	-0.043	0.207	0.357	0.433*
Stage 1 [%]	7.09	±	0.60	-0.342	-0.329	-0.152	0.123	0.040
Stage 2 [%]	45.23	±	1.52	0.234	0.342	-0.030	-0.174	-0.073
SWS [%]	27.64	±	1.50	0.043	-0.097	0.025	-0.019	-0.082
Non-REM [%]	72.86	±	0.84	0.420	0.281	0.058	-0.377	-0.172
REM [%]	17.14	±	0.71	-0.051	-0.095	-0.152	0.071	-0.158
Sleep spindle power peak	13.32	±	0.11	-0.500*	-0.163	0.072	0.367	0.363

Means ± SEM for the sleep parameters in the left columns. The right columns show Spearman's rank correlation of sleep parameters with behavioral measures of mean motor error (enclosed area) during end of Training, Posttest, Transfer, as well as changes from Training to Retest (Posttest – Training) and Training to Transfer (Transfer – Training). Note that for Posttest – Training and Transfer – Training a negative correlation is indicative of beneficial relation on consolidation success. Given are the total sleep time (TST), sleep onset (with reference to the time of lights off and beginning of first occurrence of stage 1-sleep epoch followed by stage 2-sleep), and time spent awake after sleep onset (WASO), sleep stage 1, sleep stage 2, SWS, non-REM (S2 + SWS) and REM in percentage of total sleep time. In addition, the sleep spindle power peak in the non-REM sleep power spectra of 12–15 Hz frequency range, Significant correlations are in bold, * $p < 0.05$, uncorrected for multiple comparisons.

754 Table 2

755 *Sleep parameters and events and correlations with motor adaptation learning and consolidation*

Sleep parameter (n = 22)			Spearman rank correlations with behavior [ρ]				
Analysis	Property	Elec-trode	Training	Posttest	Transfer	Posttest - Training	Transfer - Training
power density (S2)	(0.5-4 Hz)	P3	0.392	-0.112	0.150	-0.439*	-0.161
power density (REM)	(0.5-4 Hz)	F3	0.467*	0.013	0.362	-0.464*	0.048
spindle	duration	C3	0.536*	-0.075	0.204	-0.517*	-0.093
		C4	0.527*	-0.056	0.209	-0.508*	-0.095
		Cz	0.487*	-0.037	0.179	-0.467*	-0.081
		F4	0.470*	-0.137	0.098	-0.473*	-0.180
		P3	0.466*	-0.081	0.249	-0.481*	-0.049
		P4	0.430*	-0.125	0.277	-0.517*	-0.010
	frequency	C4	-0.544**	-0.138	0.077	0.431*	0.407
		Cz	-0.562**	-0.102	0.020	0.470*	0.360
		F3	-0.558**	-0.172	-0.031	0.434*	0.303
		F4	-0.561**	-0.144	0.063	0.464*	0.411
		Fz	-0.573**	-0.141	0.054	0.449*	0.411
spindle upstate	chirp	C3	-0.348	-0.034	0.255	0.318	0.430*
		C4	-0.276	-0.045	0.270	0.371	0.450*
		P3	-0.187	0.089	0.302	0.315	0.450*
		P4	-0.223	0.072	0.266	0.273	0.439*
	count	C3	0.266	-0.189	-0.316	-0.482*	-0.490*
		C4	0.235	-0.203	-0.407	-0.450*	-0.554**
		Cz	0.248	-0.101	-0.434*	-0.399	-0.582**
		F3	0.442*	0.185	-0.237	-0.400	-0.465*
		Fz	0.413	0.082	-0.268	-0.456*	-0.494*
		P3	0.382	-0.100	-0.379	-0.548**	-0.569**
		P4	0.233	-0.058	-0.397	-0.399	-0.480*
	density	C3	0.268	-0.153	-0.295	-0.469*	-0.481*
		C4	0.255	-0.169	-0.378	-0.452*	-0.529*
		Cz	0.296	-0.146	-0.351	-0.499*	-0.548**

	F3	0.436*	0.158	-0.300	-0.412	-0.513*
	F4	0.404	0.155	-0.098	-0.461*	-0.326
	Fz	0.426*	0.129	-0.258	-0.436*	-0.465*
	P3	0.343	-0.091	-0.368	-0.518*	-0.549**
	P4	0.311	-0.008	-0.318	-0.462*	-0.443*
duration	C3	0.394	-0.198	-0.137	-0.471*	-0.391
	C4	0.471*	-0.299	0.136	-0.599**	-0.139
	Cz	0.455*	-0.231	-0.013	-0.615**	-0.295
	P3	0.369	-0.286	-0.047	-0.505*	-0.252
	P4	0.469*	-0.153	0.016	-0.512*	-0.268
frequency	Fz	-0.525*	-0.103	0.040	0.436*	0.387
SD of slow-wave delay	Cz	-0.225	-0.196	0.302	0.125	0.427*

Exploratory analysis of detailed sleep parameter's relation to consolidation during sleep. The right columns show Spearman's rank correlation of sleep parameters with behavioral measures of mean motor error (enclosed area) during end of Training, Posttest, Transfer, as well as changes from Training to Posttest (Posttest – Training) and Training to Transfer (Transfer – Training). Note that for Posttest – Training and Transfer – Training a negative correlation is indicative of a beneficial relation on consolidation success. Only relations are listed that reached the significant threshold for a relation with changes from either Training to Posttest or from Training to Transfer in any of the electrodes (Pz electrode location was excluded due to reduced sample size). All other measures did not reach significance for relations with these two consolidation measures. Significant correlations are in bold, ** $p < 0.01$, * $p < 0.05$, uncorrected for multiple comparisons.