Motor adaptation is facilitated by sleep-associated modulation of beta oscillations

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Motor adaptation reflects the ability of the sensorimotor system in the brain to flexibly deal with changes in the environment to generate effective motor behaviour. How and whether sleep contributes to the consolidation of motor adaptation remains elusive. In this study, a new motor task was employed which utilizes a highly automatized motor skill to explore the effect of sleep on motor adaptation. We hypothesized that sleep-mediated beta band (13-30Hz) desynchronization would enhance motor adaptation performance. Healthy human experts in typing on the regular computer keyboard, were trained to type on a vertically mirrored keyboard while we recorded electroencephalography (EEG). Their typing performance was assessed after either a full night of sleep with polysomnography, or a similar period of daytime wakefulness. We show that motor adaptation performance improved after overnight sleep but not after daytime wakefulness. Beta oscillatory power as well as the spectral slope of the EEG (1-45Hz) were reduced during mirrored typing compared to regular typing. Notably, sleep caused an even further decrease in the power of beta oscillations. Additionally, overnight changes in the EEG spectral slope during mirrored typing was associated with the overnight changes in adaptive performance. Finally, an increase in fast sleep spindle density (13-15Hz) during the night following motor adaptation training, predicted successful motor adaptation. These findings suggest that sleep plays a crucial role in modulating neural activity and its impact on motor functions. Therefore, our results may be useful for directing and monitoring the effectiveness of rehabilitation interventions.

1. Introduction

The remarkable plasticity of the sensorimotor system of the human brain enables us to adjust automatized movements, according to sensory error signals, to meet the demands of a new environment, a process known as motor adaptation (Bastian, 2008; Krakauer et al., 2019). While sleep is known to play a role in general motor learning such that it supports learning of new motor skills, whether and how sleep supports motor adaptation remains poorly understood (for a review see: King et al., 2017).

Motor adaptation requires a flexible adjustment of automatized motor skills. Animal as well as human findings have shown that these adjustments are reflected by changes in the activity of beta (13-30Hz) oscillations (Darch et al., 2020; Jahani et al., 2020). Specifically, beta band has been linked to sensorimotor processing in the cortex (Hosaka et al., 2016; Spitzer and Haegens, 2017). Parkinson's patients, who suffer from movement-related problems, show a correlation between an elevated beta band power and the severity of their symptoms (McCarhty et al., 2011; Little and Brown, 2014). The decrease in beta power prior to movements has been suggested to reflect an increased adaptive drive (Darch et al., 2020).

While sleep has been associated with successful consolidation of general motor skills, its meaning for consolidating adapted motor skills is less clear. On the one hand, there is evidence arguing for sleep enhancing motor adaptation performance following sleep (Albouy et al., 2013; Bothe et al., 2019, 2020; Hoedlmoser et al., 2015; Plihal & Born, 1997). Additionally, sleep spindles, a hallmark of sleep-associated memory consolidation, have been shown to increase in density following motor adaptation (Bothe et al., 2020; Solano et al., 2022). On the other hand, sleep-associated enhancement of motor adaptation has not been consistently replicated with one study even presenting evidence for sleep preserving original motor skills and decreasing motor adaptation (Doyon et al., 2009; Debas et al., 2010; Thürer et al., 2018).

Thus, the objective of this study is two-fold: (1) to determine whether sleep facilitates the consolidation of motor adaptation and (2) whether it does so via modulating beta oscillations while performing the motor adaptation task. Hence, we recorded EEG activity during motor adaptation to measure the change in the power of beta band as a function of sleep. We designed a new motor adaptation task leveraging already automatized motor skills, i.e., touch-typing on a computer keyboard. During motor adaptation, participants had to learn to touch-type words on a vertically mirrored keyboard (Fig. 1). We utilized multivariate decoding methods to examine the effects of sleep on motor adaptation. Comparing motor adaptation performance, beta band power and aperiodic activity between a sleep and an awake group allowed us to examine the function of sleep for motor adaptation (for pre-registered analyses see https://osf.io/jfdv6).

2. Results

2.1 Overnight sleep improves behaviour in a fine-motor adaptation task

33 male experts in touch-typing on the regular keyboard were divided into a sleep (N=16) and an awake (N=17) group. Both groups commenced with a typing session on the regular keyboard and then started the motor adaptation training by typing on the mirrored keyboard (Fig. 1A). Following a retention interval that included either overnight sleep (8h) or a similar period of daytime wakefulness participants were tested on the regular and mirrored keyboard, respectively. Each trial started with a fixation cross for 1.5s. After that a word appeared above the fixation cross that the participants had to type as fast and as accurately as possible (Fig. 1B). As the behavioural dependent variable, we calculated performance on the word level by relating typing accuracy (amount of correctly pressed keys per word) to typing speed measured in seconds (performance = typing accuracy / typing speed). For more information on the experimental paradigm, the word lists, and the structure of the mirrored keyboard see Fig. S1A-B and Table S1.

To test whether motor adaptation is consolidated during sleep, a 2x2 mixed non-parametric test on mirrored typing performance (Fig. 1C) with a within-subject factor *Time* (before vs. after retention), and a between-subjects factor *Group* (Sleep vs. Wake) revealed a main effect of *Time* ($ATS(1) = 22.61$, $p < 0.001$, $RTE_{pre} = 0.45$, $RTE_{post} = 0.55$) as typing performance was higher after the retention than before the retention for both groups. There was no main effect of *Group* ($ATS(1) = 1.71$, $p = 0.19$, $RTE_{Wake} = 0.44$, $RTE_{post} = 0.57$). However, there was a significant interaction of *Group x Time* ($ATS(1) = 7.04$, $p = 0.007$, $RTE_{preWake} = 0.42$, $RTE_{postWake} = 0.46$, $RTE_{preSL} = 0.49$, $RTE_{post} = 0.64$) as the performance improved significantly after nocturnal sleep ($ATS(1) = 25.27$, $p_{bonf} < 0.001$, $RTE_{pre} = 0.42$, $RTE_{post} = 0.58$) but not after daytime wakefulness ($ATS(1) = 1.63$, $p_{bonf} = 0.4$, $RTE_{pre} = 0.48$, $RTE_{post} = 0.52$). This finding suggests a positive effect for sleep on motor adaptation. When the regular typing trials were included in the statistical model, the results confirmed that sleep-dependent positive effects were specific to mirrored typing with no interference with regular typing performance and no effect of wakefulness on performance in both typing conditions (Fig. S1C).

To assess whether sleep-dependent adaptation was transient or rather sustained throughout the whole testing session, we measured performance on a trial-by-trial basis (word-per-word) during mirrored typing in the pre- and post-retention sessions (Fig. 1D). Our results revealed that the highest difference in motor adaptation performance between the sleep and the wake group was in the first eight trials (of approximately 30 trials) after the retention interval (cluster-based permutation analysis of independent samples t-tests; trials 1-2: $\sum t(31) = 6.91$, $p = 0.03$, $d= 0.56$; trials 6-8: $\sum t(31) = 5.49$, $p = 0.023$, $d = 0.94$). Note the decline in performance in the wake group immediately after retention and the absence of this effect in the sleep group. We found no difference in regular typing performance after sleep (Fig. S1D-E).

2.2. Central beta power during adaptation decreased following nocturnal sleep.

We then sought to characterize the changes in central beta power as a function of sleep. We investigated changes in beta power between the typing sessions before (REG1 and MIR3) and after the retention (REG2 and MIR4). We divided each session into 10s segments with five seconds of overlap, then transformed the signal to the frequency domain and removed the 1/f aperiodic component from the EEG signal to look exclusively at brain oscillations. A 2x2x2 mixed non-parametric test with within-subject factors *Keyboard,* and *Time*, and a between-subjects factor *Group* (Fig. 2A) revealed that central beta power during mirrored typing was marginally lower than that during regular typing ($ATS(1) = 2.90$, $p = 0.09$, $RTE_{REG} = 0.51$, $RTE_{MIR} = 0.49$). Interestingly, however, the decrease in beta power from regular to mirrored typing becomes significant when looking at the global power averaged over all EEG electrodes (Fig. S2A). Moreover, beta power was lower after retention as compared to before retention ($ATS(1) = 4.51$, $p = 0.01$, $RTE_{pre} = 0.52$, $RTE_{post} = 0.48$) and was lower in the sleep group as compared to the wake group ($ATS(1) = 4.54$, $p = 0.033$, $RTE_{Wake} = 0.6$, $RTE_{Sleep} = 0.4$). Crucially, however, there was a significant interaction *Group x Time* ($ATS(1) = 19.6$, $p < 0.001$, $RTE_{pre\_S} = 0.51$, $RTE_{pre\_W} = 0.49$, $RTE_{post\_S} = 0.51$, $RTE_{post\_W} = 0.49$) as central beta power decreased after nocturnal sleep ($ATS(1) = 31.38$, $p_{bonf} < 0.001$, $RTE_{pre} = 0.56$, $RTE_{post} = 0.44$) but did not change following a period of daytime wakefulness ($ATS(1) = 1.13$, $p_{bonf} = 0.58$, $RTE_{pre} = 0.49$, $RTE_{post} = 0.51$). There was no interaction *Group x Time x Keyboard* ($ATS(1) = 0.93$, $p = 0.33$, $RTE_{REGpre\_S} = 0.45$, $RTE_{MIRpre\_S} = 0.44$, $RTE_{REGpost\_S} = 0.35$, $RTE_{MIRpost\_S} = 0.34$, $RTE_{REGpre\_W} = 0.59$, $RTE_{MIRpre\_W} = 0.57$, $RTE_{REGpost\_W} = 0.64$, $RTE_{MIRpost\_W} = 0.58$). This result suggests that beta power during motor adaptation might be influenced by sleep. Contrary to our hypothesis, however, the difference in central beta power from pre- to post-sleep did not correlate with the change in performance in the adaptation task (Fig. S2B). Fig. S2C-I demonstrate the temporal aspects of the decrease in beta power after sleep observed in Fig 2A.

To investigate whether mirrored and regular typing becomes more similar as a function of sleep, we employed multivariate decoding on the time-frequency data to differentiate between regular and mirrored typing before and after the retention. We predicted that sleep-associated consolidation results in neural patterns becoming more similar between mirrored and regular typing. Consequently, we expected decoding performance to decrease following sleep but not following wakefulness. We performed frequency decoding on the central electrodes (C3 and C4) and on 600ms epochs centred on keypresses. The highest decoding performance, in general, was observed in the beta frequency range (Fig. S3A) demonstrating that beta power contributed the most to differentiating between regular and mirrored typing. Crucially, decoding performance in the beta range (> 18Hz) dropped significantly after sleep

(Fig. 2B; -0.3s – 0.1s, cluster-based analysis with 5000 permutations, alpha = 0.025 for two-sided dependent sample t-test: $\sum t(15) = -5905.22$, $p = 0.008$, $d = -0.83$) but not after wakefulness (Fig. S3B-C), showing that beta power became more similar between regular and mirrored typing after sleep. This suggests that sleep-associated consolidation processes incorporate the adaptation task (mirrored typing) into existing memory networks of the automatized task (regular typing). Similarly, we used time-frequency decoding to classify correct vs. incorrect mirrored typing trials before and after retention. Our results revealed a decrease in decoding performance in the high beta region after sleep around -1.1s – 0.9s relative to keypresses (Fig. 2C; cluster-based analysis with 5000 permutations, alpha = 0.025 for two-sided dependent sample t-test: ∑t(15) = -2803.67, p = 0.006, d = -1.103) but not after wakefulness (Fig. S3D), pointing towards the modulation of beta activity by sleep. Fig. S3E shows the decoding performance before and after sleep separately. Fig. S3F-K demonstrate time-series decoding as well as Frequency decoding performed on all EEG electrodes.

2.3. NREM stage 2 fast sleep spindle density predicts motor adaptation

We then wanted to investigate whether sleep spindles predict the consolidation of motor adaptation. Precisely, we asked whether the change in fast spindle density from the baseline night to the experimental night correlates with the change in adaptive performance. As it has been shown that spindles are modulated over learning-related areas (Cox et al., 2014; Petzka et al., 2022), we focused on central fast spindle densities (averaged over C3 and C4) in correspondence to our beta power analysis. We found a positive correlation between the change in fast spindle density during NREM stage 2 (N2) sleep from the baseline night to the experimental night, and performance gains on the mirrored keyboard from pre- to post-sleep (Fig 3A; $r(14) = 0.58$, $p = 0.03$). Cluster-based permutation analysis on spearman correlations across electrodes (10000 permutations, alpha = 0.025 for two-sided dependent sample t-test) demonstrated that this correlation was significant over a cluster of 10 electrodes (Fig. 3B; all electrodes except O2; $\sum t(15) = 33.32$, $p < 0.001$, $d = 0.29$). This correlation was still significant when measured over both N2 and N3 stages, i.e., NREM (Fig. S4A-B; $r(14) = 0.5$, $p = 0.047$) but was not significant in NREM stage 3 (N3) sleep (Fig. S4C-D; $r(14) = 0.41$, $p = 0.11$). There was no correlation between N2 fast spindle density and beta power change (Fig. S4E). Further, Fig. S4F-G, demonstrates our registered analysis regarding the role for beta oscillations during REM sleep in mediating sleep's effect on motor adaptation. Contrary to our hypothesis, REM density and REM beta power did not change from the adaptation to the experimental night, suggesting no influence of motor adaptation on beta power during subsequent REM sleep.

2.4. The spectral slope of EEG signals predicts motor adaptation.

Finally, we performed an exploratory analysis to investigate a putative link between the spectral slope of the EEG signal and motor adaptation. The power of the electrophysiological signal decays exponentially as a function of frequency (Freeman et al., 2003; He, 2014). The slope of this decay, i.e., the spectral slope, has been suggested to reflect the excitation-inhibition ratio in the cortex with a steeper slope indicating more inhibitory contribution to the signal and vice versa (Gao et al., 2017; Lombardi et al., 2017). Excitation-inhibition balance in the brain is crucial for adaptation as well as memory processing (Deneve et al., 2017; Barron, 2021). Therefore, we sought to characterise the changes in the spectral slope during motor adaptation. Typing sessions were segmented into 10s segments with five seconds of overlap. A 2x2x2 mixed non-parametric test with the slope of the 1-45Hz EEG signal averaged over all electrodes as the dependent variable and two within-subject factors *Keyboard (REG vs. MIR),* and *Time (Pre- vs. Post-retention)*, and a between-subjects factor *Group (Wake vs. Sleep)* revealed a main effect of *Keyboard* as the slope was steeper during mirrored typing as compared to regular typing (Fig. 4A, $ATS(1) = 6.77, p = 0.009, RTE_{REG} = 0.53, RTE_{MIR} = 0.47$) suggesting an increased inhibitory process during motor adaptation. There were no effects of *Time* ($ATS(1) = 2.73, p = 0.1, RTE_{pre} = 0.52, RTE_{post} = 0.48$), or *Group* ($ATS(1) = 0.17, p = 0.68, RTE_{Wake} = 0.52, RTE_{Sleep} = 0.48$). There were also no significant interactions *Time x Group* ($ATS(1) = 1.62, p = 0.2, RTE_{pre\_S} = 0.52, RTE_{pre\_W} = 0.54, RTE_{post\_S} = 0.44, RTE_{post\_W} = 0.51$), *Keyboard x Time* ($ATS(1) = 1.6, p = 0.2, RTE_{pre\_REG} = 0.54, RTE_{pre\_MIR} = 0.51, RTE_{post\_REG} = 0.51, RTE_{post\_W} = 0.44$), nor *Keyboard x Time x Group* ($ATS(1) = 0.009, p = 0.92, RTE_{REGpre\_S} = 0.53, RTE_{MIRpre\_S} = 0.51, RTE_{REGpost\_S} = 0.47, RTE_{MIRpost\_S} = 0.41, RTE_{REGpre\_W} = 0.54, RTE_{MIRpre\_W} = 0.51, RTE_{REGpost\_W} = 0.55, RTE_{MIRpost\_W} = 0.48$). Moreover, the change in the spectral slope between the pre-sleep mirrored typing session (MIR3) and the post-sleep mirrored typing session (MIR4) predicted the change in adaptive performance MIR4-MIR3 (Fig. 4B; $r(14) = 0.57, p = 0.02$). In the wake group, however, the changes in the spectral slope mediated by a period of wakefulness did not predict performance change (Fig. S4H). These results demonstrate that the switch from regular to mirrored typing is reflected in changes in the EEG slope and suggest a link between sleep-dependent effects on motor adaptation and the changes in the spectral slope of the EEG after sleep.

3. Discussion

In this study, we employed a novel paradigm, which exploits the extensive training that the participants received on typing on computer keyboards throughout their lives, to leverage a fine-motor adaptation task where participants adapt to typing on a vertically mirrored keyboard (Fig. 1A-B). We measured the typing performance on the regular and the vertically mirrored keyboard before and after a retention period that included either 8h of nocturnal sleep or a similar period of daytime wakefulness.

Our results demonstrated that sleep consolidated the performance in the adaptation task, i.e., typing on the mirrored keyboard (Fig 1C). Overnight sleep contributed to stabilizing the levels of performance that the participants reached at the end of the training session, protecting their performance from a transient drop that was observed after a period of wakefulness (Fig 1D). Beneficial sleep-dependent effects on motor adaptation had no interference with the automatized, and more relevant, skill of typing on the regular keyboard (Fig. S1C-F).

Although the performance in the sleep group was generally higher than that of the wake group throughout the testing session (MIR4), the strongest difference between the group appeared in the early phase of testing (approximately the first 10 trials) suggesting that the effects of sleep on motor adaptation are mostly transient. This notion might explain why several previous studies could not detect any sleep effects on motor adaptation, as they might have been attenuated when averaging performance levels over entire sessions.

Our EEG results demonstrate a change in movement-related brain activity following nocturnal sleep (Fig 2). By specifically targeting central electrodes (C3 and C4), which presumably captures activity in motor regions, we observed a decrease in central beta (13-30Hz) power during mirrored typing as compared to regular typing (Fig. 2A). Using time-frequency decoding, we showed that movement-related beta power was highest in classifying regular vs. mirrored typing trials (Fig. S3A). Crucially, beta decoding performance dropped significantly after sleep (Fig. 2B). This decrease in classification was mirrored by a general decrease in beta power after sleep that was observed during mirrored as well as regular typing trials (Fig. 2A). These results might suggest a role for sleep in motor adaptation consolidation that putatively aim at incorporating movement representations of the mirrored typing (adaptation task) within networks the well-established networks of the automatized task (regular typing). (Bastian, 2008). Additionally, as beta power decreased during regular typing after sleep, it is plausible that sleep influences not only motor adaptation but also the de-adaptation process, i.e., going back to the automatized process (regular typing) after adaptation training (Davidson & Wolpert, 2004).

These results describe, for the first time to our knowledge, an interaction between sleep and beta power in which sleep promotes a general decrease in movement-related beta power to optimize motor performance. Therefore, our results are in line with the notion that beta band activity serves to maintain the status quo while preventing flexible behaviour (Engel and Fries, 2010) and thereby corroborating previous findings showing that the decrease of beta power reflects adaptative motor behaviour (Darch et al., 2020).

Previous work has shown that changes in beta oscillations correlate with fluctuations in the activity of GABAergic interneurons (Baumgarten et al., 2016; Jensen et al., 2005; Rossiter et al., 2014; Stagg, 2014) which might provide an explanation why the decrease in beta reflects successful motor adaptation. Jensen and colleagues (2005) demonstrated a correlation between the increase in GABA-mediated inhibition and the increase in the power of beta oscillations. Therefore, it is plausible that the drop in the power of beta oscillations reflect the release of inhibition, i.e., dis-inhibition, of cortical activity. This dis-inhibition might be potentially useful to cope with the increase in cognitive load during motor adaptation (Schmitz, 2022).

The notion of sleep-mediated dis-inhibition to the benefit of (de-)adaptation was further examined by measuring the difference in the slope of the EEG signal during regular typing and mirrored typing sessions. Recently, Gao and colleagues (2017) employed a computational model of excitatory and inhibitory cortical circuits to demonstrate that a steeper spectral slope reflects the recruitment of more inhibitory neuronal populations and vice versa. Our results showed that the spectral slope of the EEG signal becomes steeper during the motor adaptation task (i.e., mirrored typing) as compared to the original task (i.e., regular typing; Fig. 4) suggesting more inhibitory activity at the early stages of adaptation. Importantly, the flattening of the slope during mirrored typing trials after sleep which correlated with the enhanced adaptative performance (Fig. 4B) suggests, in agreement with the beta power results, the release of inhibition in the cortex to the benefit of motor adaptation. The change in slope after a period of wakefulness did not correlate with performance (Fig. S4G) further corroborate the beneficial role of sleep as a modulator of cortical inhibition in the context of motor adaptation.

The increase in cortical inhibition has been shown to be crucial for continual learning as well as for protecting overlapping memories from interfering with each other (Barron, 2021; Barron et al., 2016; Koolschijn et al., 2019). Following the initial learning phase, sleep promotes such inhibition in the cortex to facilitate memory consolidation (Bridi et al., 2020; Niethard et al., 2017). Our results suggest that this inhibition might be mediated by the increase in the density of NREM stage 2 fast sleep spindles (13-15Hz) from the baseline night to the experimental night which correlated with performance gains in the adaptation task from pre- to post-sleep (Fig. 3). Indeed, sleep spindles have been shown to promote inhibition in the cortex (for a review see: Fernandez and Luthi, 2019) and increase in number after motor adaptation training (Solano et al., 2021, 2022). Following sleep, hippocampus-mediated dis-inhibition of neocortical circuits during the retrieval phase facilitates memory recall (Koolschijn et al., 2020).

According to such a model of cortical dynamics, the initial increase of the slope during motor adaptation that we observed, would serve memory encoding while protecting overlapping memories from interference. During the following sleep period, sleep spindles would regulate the process of excitation-inhibition balance to support consolidation. Finally, during recall the release of inhibition would be essential for the efficient switching between different memories, i.e., typing strategies.

Together, our results highlight periodic (beta power) and aperiodic (spectral slope) EEG parameters as potential markers for sleep-dependent motor adaptation. Further, our findings describe a regulatory role for sleep spindles in motor adaptation. This model is in line with recent theories of memory consolidation which suggest that the interchange between intervals of periodic activity (manifested by the appearance of sleep spindles) and aperiodic activity observed during spindle refractory periods during sleep is crucial for memory consolidation processes (Antony et al., 2018; Helfrich et al., 2021). Future work should aim to elucidate on the specific contributions of periodic and aperiodic activity to sleep-dependent memory processes.

3.1. Limitations: Our study has a few limitations; first is that we cannot rule out the existence of a motor-learning component in our task. Participants had to perform a series of six five finger movements to type the six different words on the mirrored keyboard and therefore, they might have just learned to perform these six motor sequences of five finger movements to type the words instead of adapting their movements according to previous knowledge. However, since we recruited experts in touch-typing, participants must have had to first inhibit a specific and very strong motor plan before they were able to perform the new adaptation task. Therefore, even if the task is somewhat contaminated by traces of motor learning activity, the prevailing behaviour in such a task would still be the adaptation of fine-motor skills.

Another limitation of our study is the observed difference in beta power between the sleep and the wake group at baseline (testing). Since the participants were randomly assigned to the groups, we would assume that the effects would be constant for everybody, then baseline scores won't affect the observed changes. Instead, we expect this difference to be due to circadian influences on beta band activity. That is, the differences in the time of day where training and testing took place might have affected the observed beta power values. Indeed, a previous study has shown that beta activity during pre-movement desynchronization periods increased from morning to afternoon, while that during post-movement rebound periods remained steady throughout the day (Wilson et al., 2014). Although the drop in beta power that we observed might have been influenced by circadian variations, the fact that we did not observe any significant change in beta power in the wake group suggests that the decrease in beta power is sleep-specific and not just a mere circadian effect.

Finally, it is important to mention that we have deviated from the pre-registered analyses by adding our exploratory analysis of the EEG slope (Fig. 4). However, we were motivated by the growing evidence linking the EEG spectral slope with changes in cognitive functions (Waschke et al.,2021; Hohn et al., 2022), and consciousness levels (Lendner et al., 2020). We opted for adding this exploratory analysis to our study to provide more information regarding the dynamics of excitation and inhibition in the cortex and their role in mediating adaptive processes in the brain.

3.2. Conclusion: In summary, we provided strong evidence for the role for sleep in the adaptation of highly automatized fine-motor skills. Our results describe several changes in cortical oscillatory as well as aperiodic activity following overnight sleep, that go in the same direction as the beneficial sleep-dependent influence on adaptive behaviour. We propose a positive effect of sleep on motor adaptation that manifested through promoting the context-specific release of cortical inhibition. Moreover, sleep facilitated the integration between the newly learned adaptation task in the already existing motor memory networks while protecting these two overlapping memory traces from interference. The mechanisms by which sleep promotes cortical dis-inhibition and protects memory interference need to be addressed in future studies.

4. Methods

4.1 Participants: 33 healthy human male subjects (age range 19-29 years, mean = 25 ± 4 years; sleep group n=16, wake group n = 17), were tested in a randomised, between-subjects design. All participants were experts in touch typing (250 correct keypresses/minute). The decision of the typing criterion assumes that experts in touch-typing are able to type at least 50 five-letter words per minute (Inhoff, 1991). Selection criteria were being male, right-handed, German-speaking, with no history of severe organic and/or mental illness, no sleep disorders (i.e., Pittsburgh Sleep Quality Index Global Score > 5, Buysse et al., 1989), no signs of mood disorders (i.e., Self-Rated Anxiety Scale Raw Score < 36 and Self-Rated Depression Scale Raw Score < 40, no unusual bedtimes and/or extreme chronotype. Participants received ECTS (European Credit Transfer System) points and were informed about the aspects of the project in detail. They gave their written informed consent before the beginning of the study and the ethics committee of Salzburg University approved the experiment.

4.2. Experimental design:

4.2.1. Protocol: To assess fine-motor adaptation, we created a paradigm where participants had to type 18 five-letter, German words on the regular computer keyboard (REG) as well as on a vertically mirrored keyboard (MIR) as rapidly and as accurately as possible. The mirrored keyboard was basically a regular keyboard with the output of the keys vertically mirrored. Sleep-wake rhythm was monitored via wrist actigraphy starting three days prior to the first laboratory visit and for the whole duration of the experiment. Subjective sleep/wake rhythm and sleep quality was also collected via sleep logs. After the entrance examination (day 1), participants in the sleep group slept for a baseline night on day 4 in the laboratory. The training session took place either in the evening (08:00pm - 11:00pm) of the 6th day for the sleep group, or in the morning (09:00am - 12:00pm) of the 4th day for the wake group. A retention period that included either 8h of sleep during the night at habitual bedtime (11:00pm to 07:00am) for the sleep group (testing starts at 09:00am) or a period of daytime wakefulness (approximately 8h) for the wake group (testing at 05:00pm to 07:00pm), preceded the testing session. We monitored vigilance via visual psychomotor vigilance task (PVT; Hoedlmoser et al., 2011; adapted from Dinges & Powell, 1985) before and after the training period as well as after the retention interval.

4.2.2. Training and testing sessions procedure: Following their arrival at the laboratory, participants were informed about the experimental procedure and then set up with the EEG electrodes. They had to type 18 German words composed of 17 different letters (A, C, D, E, F, H, I, K, L, M, N, O, P, R, S, T, U). Importantly, participants had to touch type and could not look at the keyboard while typing as it was hidden under a wooden block. Words had to be typed bimanually: two-to-three letters with the left/right hand. The training day started with the first regular typing session (REG1) which consisted of four three-minute blocks of typing on a regular keyboard separated by 15s breaks. During these typing-blocks, participants had to type all the 18 words – 4x3min: 18 words). After a ten-minute break, participants were trained on typing a subsample of the words (*List 1;* six words composed of eight different letters: A, E, K, L, M, N, P, R) on a vertically mirrored keyboard. On the mirrored keyboard, participants had to learn to perform the same sequence of movements but with the other hand. The mirrored typing part consisted of three sessions (MIR1-MIR3). Each session was composed of four three-minute blocks separated by 15s breaks summing up to a total of twelve three-minute blocks of training on the mirrored keyboard. During MIR1-MIR2, the structure of the mirrored keyboard was displayed at the bottom of the screen to aid the learning process. For MIR3, however, participant had to type without any aid. Following training, participants spent a retention interval of either 8h daytime wakefulness or 8h overnight sleep before proceeding with the second experimental session. This second session consisted of two three-minute blocks of regular typing (REG2 – 2x3min; 18 words) followed by two three-minute mirrored typing blocks (MIR4-MIR5 2x3min). MIR4 contains the six words that we used in the training (MIR1-MIR3) while MIR5 contains another 12 words that were typed only on the regular keyboard. Six of the 12 words presented during MIR5 consisted of the same letter as the trained words (*List 2*; A, E, K, L, M, N, P, R). The other six words were composed of nine different letters (*List 3;* C, D, F, H, I, O, S, T, U) which were not practiced on the mirrored keyboard in the training session before retention. For more information on the lists, see Table S1.

4.2.3. Trial structure: Participants were instructed to type each word as accurately and as fast as possible. Each trial started with a fixation cross (1.5s; cf. Figure 1B), after that a word appeared above the fixation cross. For the trial to end, participants had to press the five keys regardless of whether they were correct. The time taken to type the five letters was computed starting from the first button press until the fifth. There was no time limit for the trials. Participants received immediate feedback as they saw the letter they typed on the screen; however, they had no option to change it. The task was designed in that way to measure both typing accuracy and speed.

4.3. Behavioural analysis: The behavioural estimate of performance was the product of dividing typing accuracy (ratio of correct letters per five-letter word) by typing speed (time in seconds required to type five letters). For Fig. 1C performance was averaged over all words in the session resulting in a single performance value per session per subject. For Fig. 1D, on the other hand, values indicate performance for each word in the session.

4.4 EEG acquisition: EEG was recorded using a 32-channel Neuroscan system (Scan 4.3.3 Software, Neuroscan Inc.; Charlotte, USA) with 500Hz sampling rate and channel Cz as online reference. We used a simplified montage with 11 EEG electrodes (F3, F4, Fz, C3, C4, Cz, P3, P4, Pz, O1, and O2). Eye movements were recorded via one vertical and one horizontal electrooculogram (EOG) channels, and muscle activity via a bipolar submental electromyogram (EMG) channel. Ground electrode was placed at AFz location. Impedances were kept below 5kΩ.

4.5. Sleep staging and spindle detection:

4.5.1 Staging: sleep was scored semi-automatically on the basis of 30s epochs via an algorithm developed by the Siesta group (Somnolyzer 24×7; The SIESTA Group Schlafanalyse GmbH., Vienna, Austria; Anderer et al., 2005; Anderer et al., 2010) following the criteria of the American Academy of Sleep Medicine (AASM, American Academy of Sleep Medicine & Iber, 2007).

4.5.2 Sleep spindle detection: We detected sleep spindles using the automatic SIESTA algorithm (ASK analyser, The Siesta Group Schlafanalyse GmbH., Vienna, Austria, Gruber et al., 2015). First, we referenced all electrodes to the average of both mastoids before filtering the signal between 0.1 and 40 Hz and resampling it to 128Hz. The algorithm first filters the raw data between 11 and 16 Hz before detecting spindle events using the criteria described in Schimicek et al. (1994). Only events with an amplitude >12µv and duration between 500ms and 3000ms were considered. The detected spindles were compared to a template generated based on the visual scoring of experts on 8730 minutes of PSG data from 189 healthy participants and 90 participants with sleep disorders via Linear discriminant analysis (LDA). Only events with an LDA score of 1.7 or higher corresponding to 98% specificity were considered (for more details see: Anderer et al., 2005). Sleep spindles that occurred during N2 and N3 sleep were included. The frequency of each spindle event was defined using period-amplitude analysis of the band-pass filtered signal in the time domain, and spindles were subdivided into slow (11-13 Hz) and fast (13-15Hz) spindles (Schabus et al., 2007). The density of fast spindles was estimated as the number of events per minute of N2, N3, or both (NREM).

4.6. EEG data pre-processing: EEG data were pre-processed using the EEGLab toolbox (v14.1.1b) in Matlab (v2019a). Raw data were notch-filtered at 50Hz to remove line noise using the CleanLine toolbox in EEGLab, high-pass-filtered at 0.1 Hz, and then referenced to an average reference. Epoched data were automatically inspected for artefacts and bad epochs with large amplitude fluctuations (above 1000uv) were removed.

4.7. Time-frequency analysis: Time-frequency analyses were performed in Fieldtrip (Oostenveld et al., 2011). Spectral power was estimated using multitaper fast Fourier transform (FFT) with discrete prolate spheroidal sequences (DPSS) tapers. We used frequency smoothing of 0.4Hz from 0.1Hz to 45Hz in 0.5Hz steps and 100ms temporal steps fitting 5 cycles per time window. We used large epochs of 10s to avoid data contamination due to edge artifacts. To separate periodic and aperiodic components of the EEG signal, we used the irregular resampling auto-spectral analysis (IRASA, Wen & Liu 2016) implementation in fieldtrip. The spectral slope of the EEG signal was estimated by calculating the slope of the fractal component in the signal in the log-log (log frequency, log power) space. We choose a broadband range for slope estimations, i.e., 1-45Hz, as a compromise to get the best possible representation of the signal without including any noise in the estimation due to line noise or line-noise-removal procedure.

4.8. Multi-variate pattern analysis (MVPA): This analysis was done using the MVPA-Light toolbox (Treder, 2020). An LDA classifier was trained to distinguish between regular and mirrored typing trials or between correct and incorrect mirrored typing trials based on either time locked data or time-frequency data. The pre-processing procedure was the same as previous. In addition, EEG signal was z-scored, and we used a K-fold cross-validation method (K=five, two repetitions). We report the area under the curve (auc) parameter, as it is less sensitive than the accuracy parameter to class imbalances.

4.9. Statistical analysis: Robust statistical analysis was performed using rank-based non-parametric tests as implemented in the *nparLD* package (Ngouchi et al., 2012) available in R (v4.1.2). It reports ANOVA-type statistics (ATS), p-values (alpha = 0.05, two-sided), as well as relative treatment effects (RTE) as effect sizes. RTE values represent the probability of the values from the whole dataset being smaller than a randomly chosen observation from the respective group. The higher the RTE value of one condition means a higher probability that a randomly chosen value from that condition is larger than that randomly drawn from the whole dataset, and vice versa. We performed post-hoc tests via the '*NparLD*' function with Bonferroni's correction for multiple comparisons. For all time-series analyses, non-parametric permutation statistics were performed as implemented in Fieldtrip (Maris and Oostenveld, 2007). Two-sided (un)paired-sample t-tests were computed with a Monte Carlo procedure over 5000 permutations (cluster-alpha = 0.05 and critical alpha = 0.025). The sum of the t-values (∑t) is reported, as well as Cohen's d effect sizes calculated over all possible permutations. For correlations, we used Pearson's correlation in case of normally distributed data and Spearman as indicated by the Shapiro-Wilk test. For the topographical plots, Spearman's method was applied whenever the normality assumption was violated in at least 1 electrode. Rho and p-values are reported; in case of multiple correlations, correction was done using Monte-Carlo procedure with 10000 permutations as implemented in fieldtrip.

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6. Figures

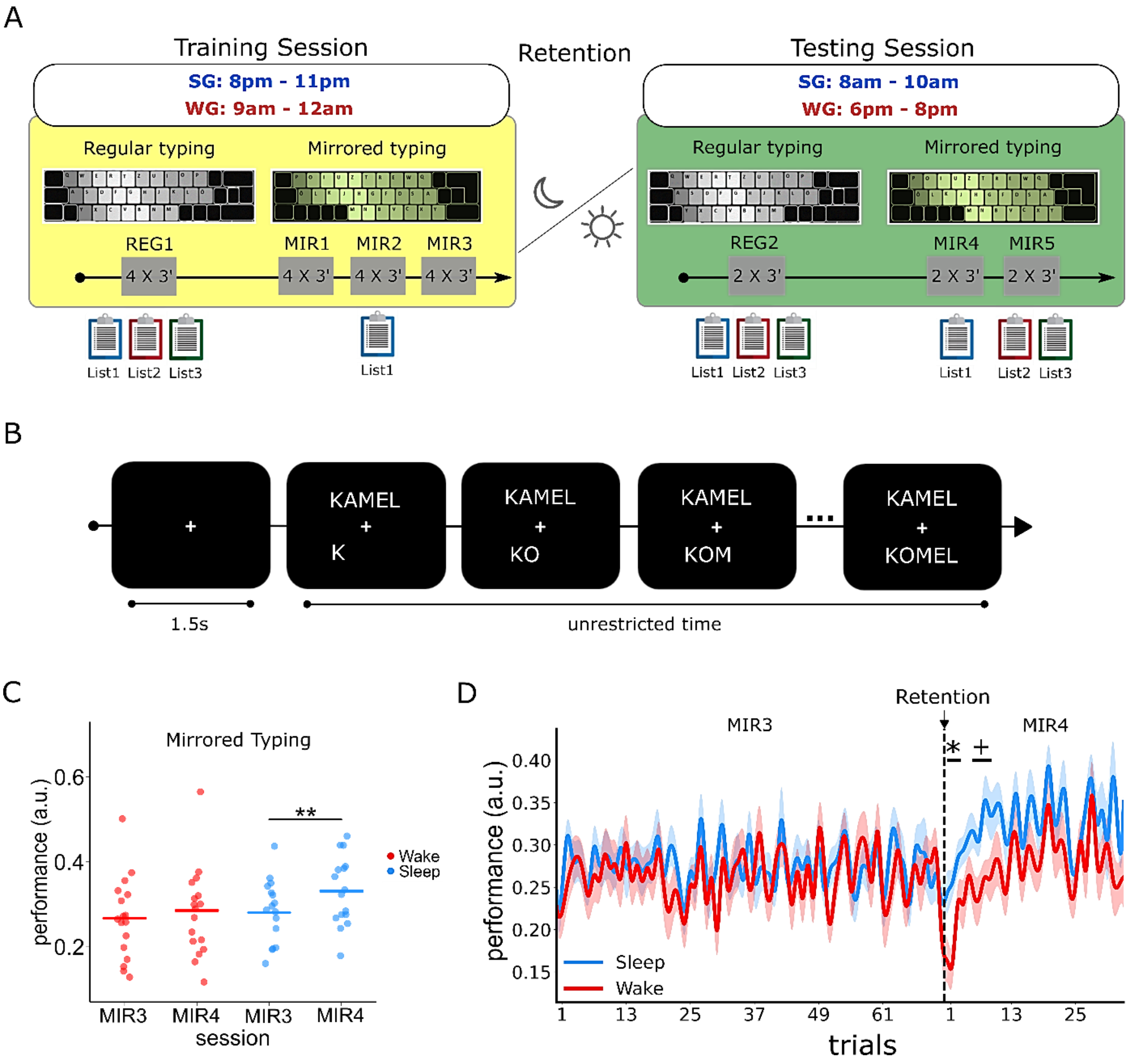


Figure 1. Experimental design and behavioural results. 33 human male experts in touch-typing on the computer keyboard were invited to participate in the experiment after passing the initial screening (see section 4.1). Participants were divided into a sleep (n=16) and a wake (n=17) group. A) (Left)The training part started with four typing blocks of three minutes each on the regular keyboard (REG1) separated by short pauses. Participants typed 18 German five-letter words. After a 15-minute break the mirrored typing session started with three mirrored typing sessions (MIR1, MIR2, and MIR3) which consisted of four three-minute typing blocks. Note that during REG1 participants typed all 18 words while in MIR1, 2 and 3 participants typed only a subset of the words (List1, six words). The retention interval contained either 8h of nocturnal sleep at habitual bedtimes or a similar period of daytime wakefulness. (Right) The testing part of the experiment started with a regular typing session (REG2) which consists of two typing blocks of three minutes. After a 5-minute break, participants performed two mirrored typing blocks (MIR4 & MIR5). In MIR4 participants typed the words in List1, while in MIR5 they typed the rest of the 18 words (12 words; List2 and List3). B) Typing trial structure. The trials started with a fixation cross for 1.5 seconds, then a word appeared on the screen above the fixation cross. The word remained on the screen until the participant typed five letter regardless of whether they were correct. Participants received immediate feedback by seeing the letters they typed below the fixation cross. However, participants did not have the option to correct what they typed. There were no time constraints for typing, as the trials ended when participants typed five letters regardless of whether they were correct. C-D) Behavioural results**.** C) Typing performance on the mirrored keyboard before and after the retention interval averaged over each session. Typing performance on the mirrored keyboard improved significantly only after sleep (MIR3 to MIR4). There was no significant change after wakefulness (See Fig. S1C). D) Time-resolved analysis of performance in a trial-by-trial manner revealed that sleep maintained the same level of behavioural performance that was achieved at the end of the training session and protected performance from a transient drop that was observed in the early phase of the testing session for the wake group. REG1: Regular typing before retention, + $p < 0.1$, * $p < 0.05$. REG2: Regular typing after retention, MIR3: Mirrored typing before retention, MIR4: Mirrored typing after retention.

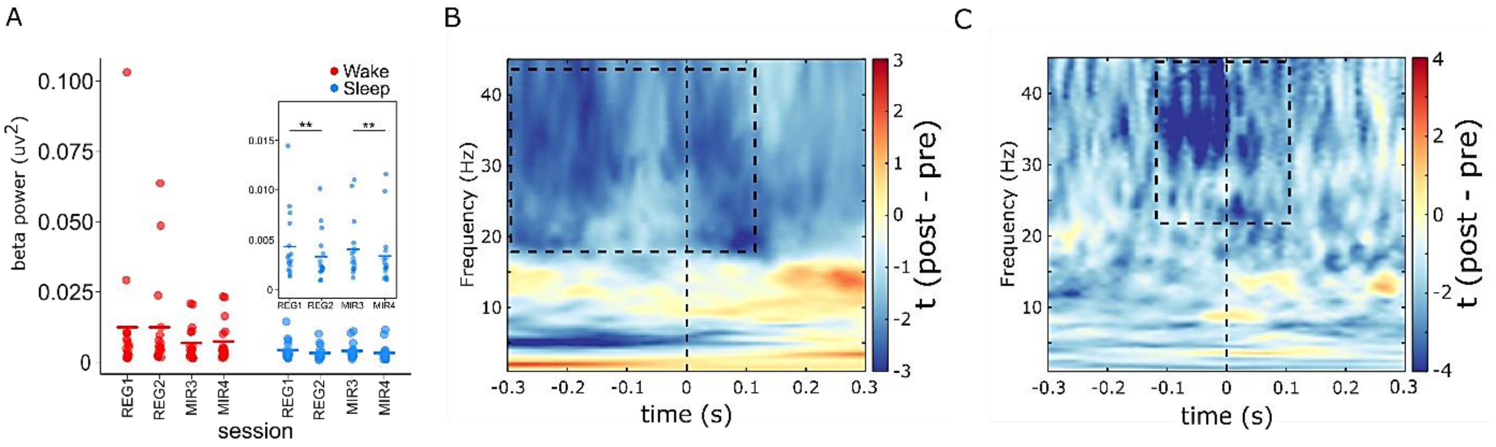


Figure 2. Sleep induced changes in adaptation-related brain activity. A) Beta band power averaged over electrodes C3 an C4 (presumably reflecting activity in motor regions), during regular and mirrored typing before and after retention. Central beta power decreased during mirrored typing and after sleep for both regular and mirrored typing but increased after a period of wakefulness. The box magnifies beta power during mirrored typing for a better illustration of power differences. B) The difference in multivariate time-frequency decoding (REG vs. MIR) on central electrodes (C3 and C4) from pre- to post-sleep (Post-sleep – Pre-sleep). Decoding performance in the beta band decreased after sleep but not after wakefulness. See Fig. S2 and Fig. S3 for separate decoding performance pre and post sleep, and for time-series and frequency decoding for all electrodes. C) The difference in time-frequency decoding between correct vs incorrect mirrored typing trials from before (MIR3) to after (MIR4) sleep (MIR4-MIR3). Note a decrease in decoding performance after sleep in the high beta range (>25Hz). REG1: Regular typing before retention, REG2: Regular typing after retention. MIR3: Mirrored typing before retention, MIR4: Mirrored typing after retention. $^{**}p < 0.001$. Each point in panel A represent one subject and the crossbars represent the mean of the group. Vertical line at zero indicates button press. Dashed boxes indicate significant clusters. Dashed horizontal line in panel A represent chance level.

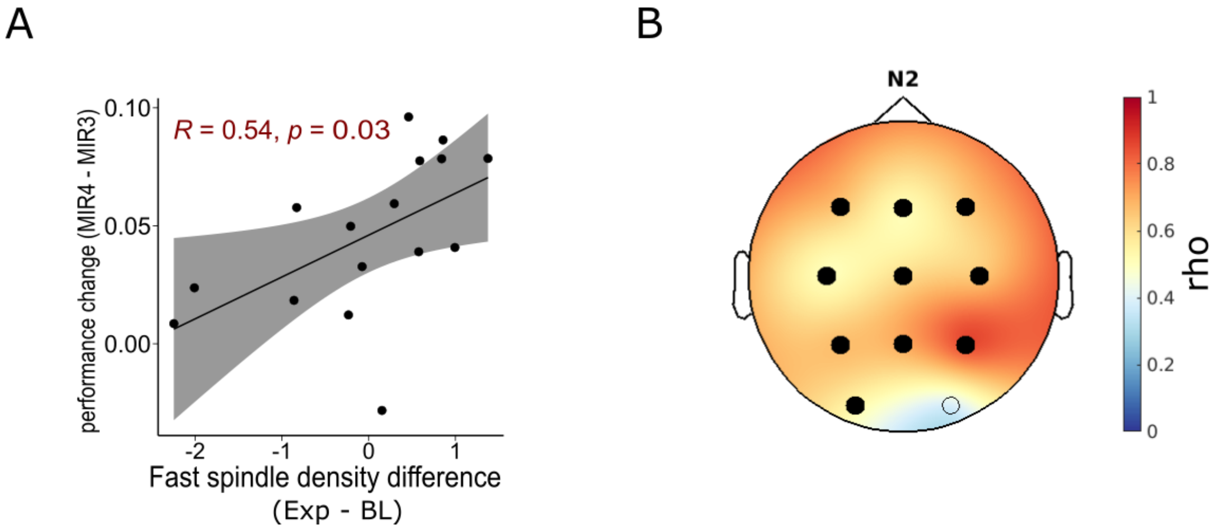


Figure 3. NREM stage 2 fast sleep spindle density predicts motor adaptation. A) The change in the density of central fast sleep spindles (averaged over C3 and C4) during NREM stage 2 sleep from the baseline to the experimental night correlated with overnight performance gains on the mirrored keyboard (MIR4 - MIR3). B) The correlation between fast spindle density and performance gains was significant over a cluster of 10 electrodes (all EEG electrodes except O2). BL: baseline night, Exp: experimental night. R: Pearson's correlation. Rho: Spearman's correlation.

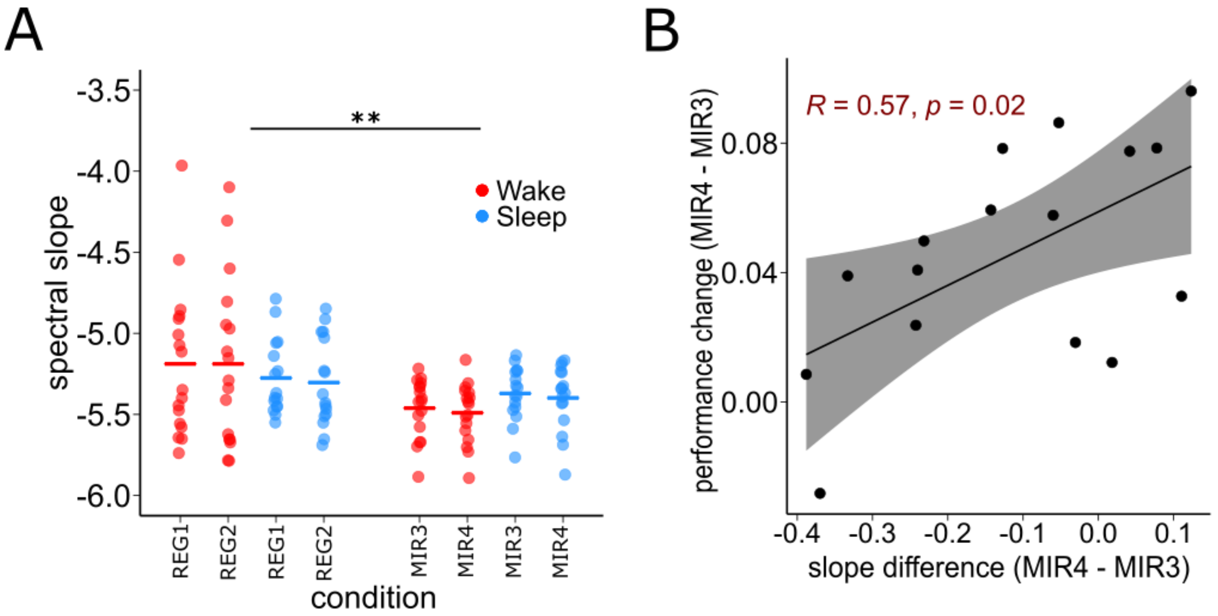
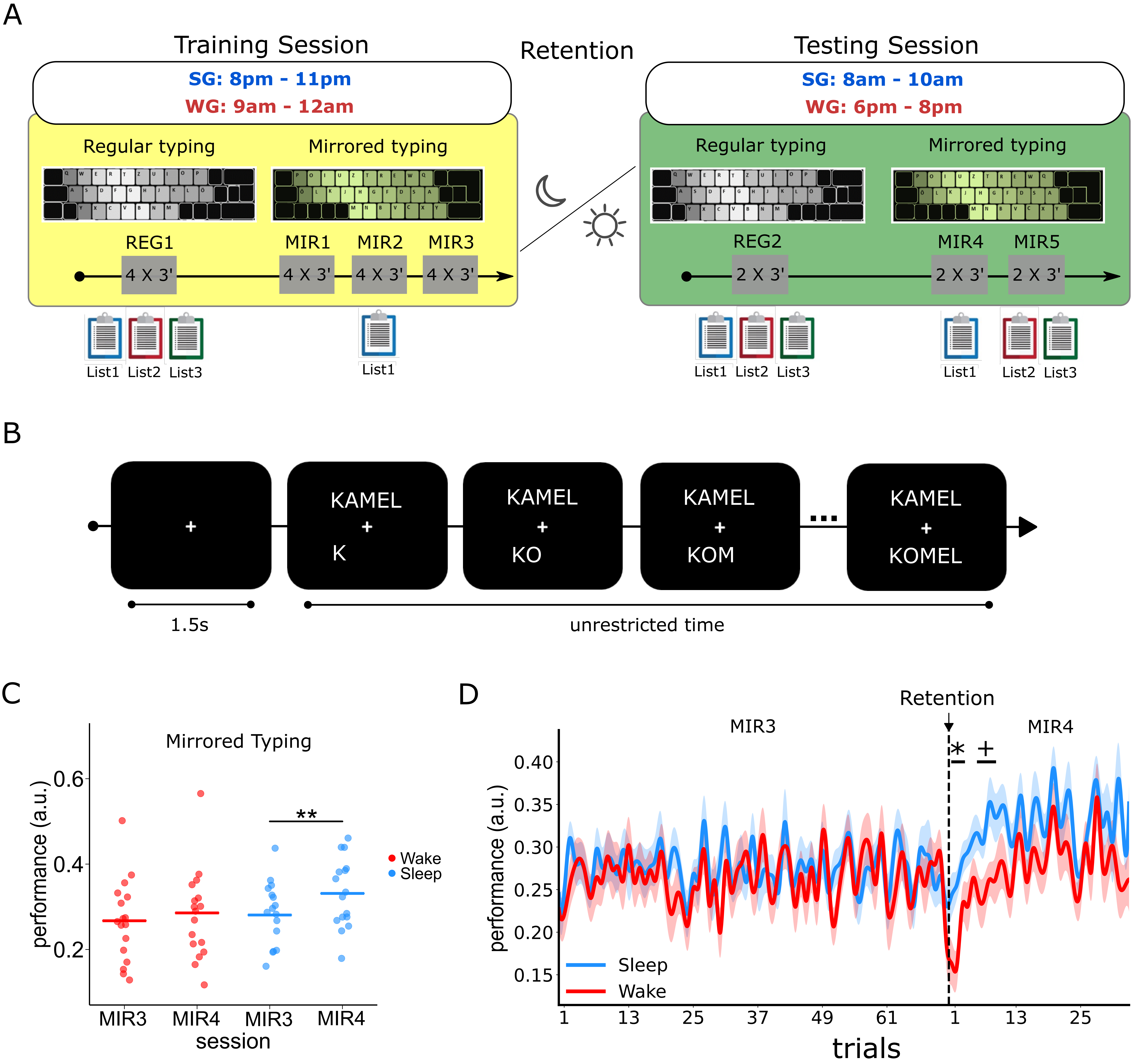
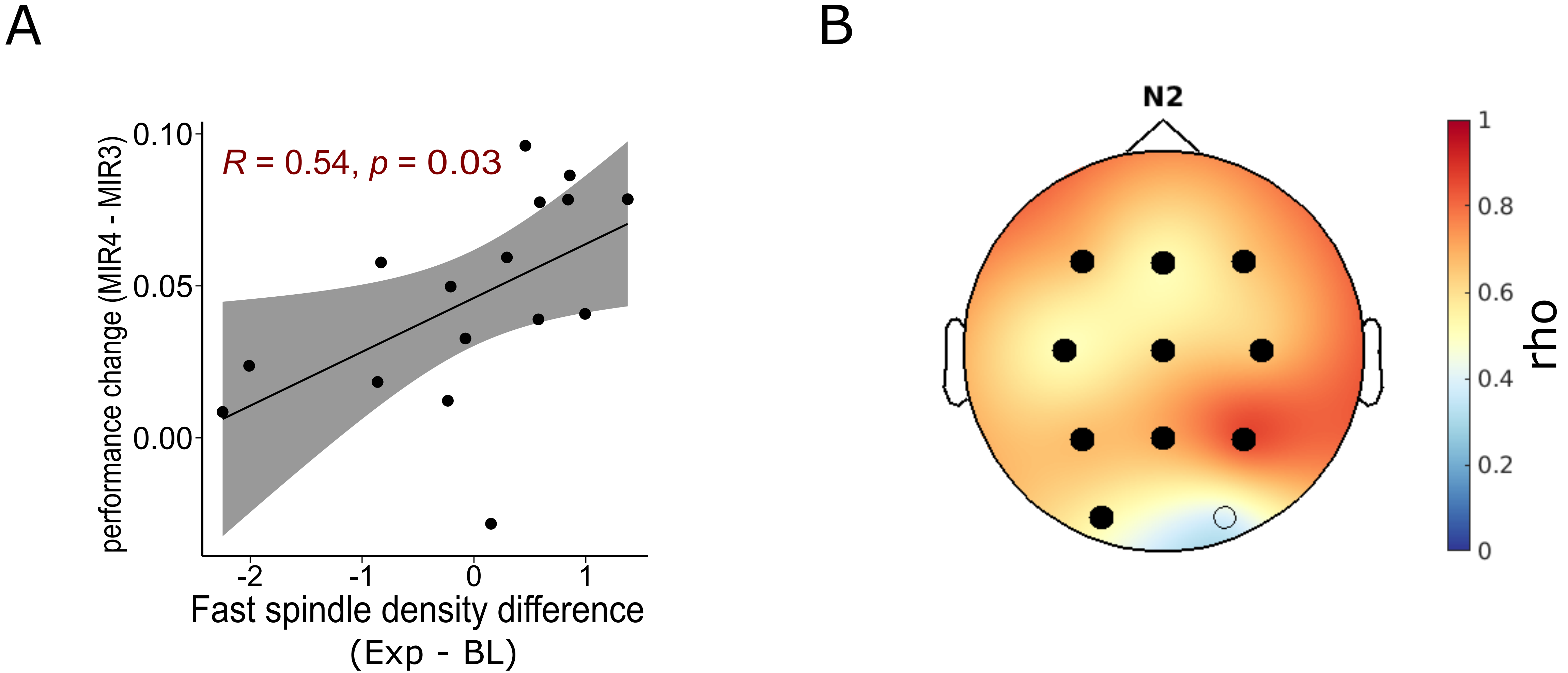
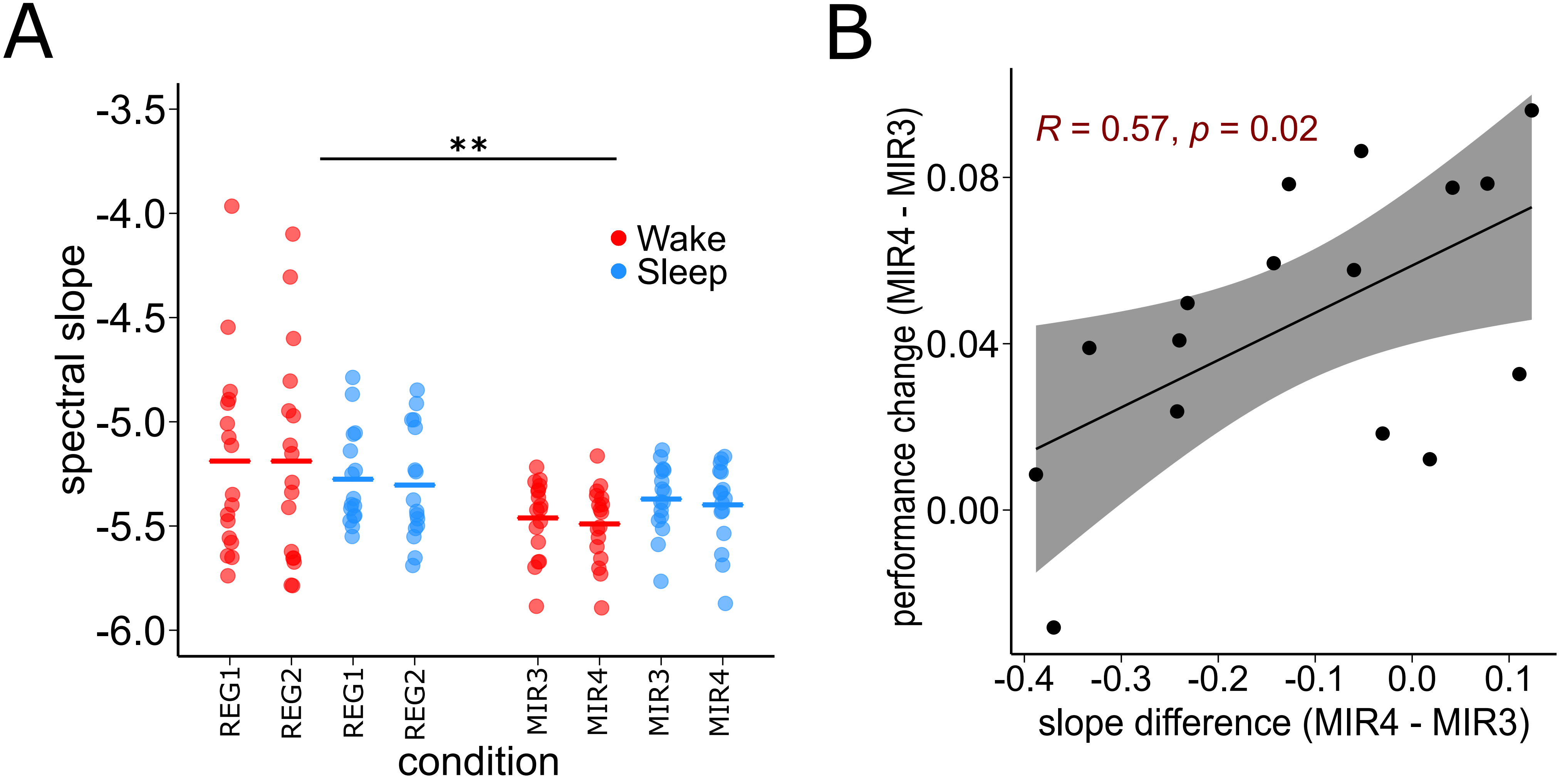


Figure 4. The spectral slope tracks motor adaptation and predicts sleep-mediated improvement in motor adaptation behaviour. A) The slope of the power spectral density averaged over all EEG electrodes, which is a measure for aperiodic activity, became steeper during mirrored typing indicating an increase in inhibitory activity. B) The change in the spectral slope from the pre- to post-sleep mirrored typing sessions correlated with the change in performance in the mirrored typing session from pre- to post-sleep (MIR4 – MIR3). Note that this correlation was significant only in the sleep group (see Fig. S4H). Each point in panel A represent the mean over one subject and the crossbars represent the mean over all subjects. REG1: Regular typing before retention, REG2: Regular typing after retention, MIR3: Mirrored typing before retention, MIR4: Mirrored typing after retention. ** $p < 0.001$.


A
Training Session
SG: 8pm - 11pm
WG: 9am - 12am
Regular typing
Mirrored typing
REG1
MIR1
MIR2
MIR3
4 X 3'
4 X 3'
4 X 3'
4 X 3'
List1 List2 List3
List1
Retention
Testing Session
SG: 8am - 10am
WG: 6pm - 8pm
Regular typing
Mirrored typing
REG2
MIR4
MIR5
2 X 3'
2 X 3'
2 X 3'
List1 List2 List3
List1
List2 List3
B
+
KAMEL + K
KAMEL + KO
KAMEL + KOM
...
KAMEL + KOMEL
1.5s
unrestricted time
C
Mirrored Typing
performance (a.u.)
0.6
0.4
0.2
**
Wake
Sleep
MIR3
MIR4
MIR3
MIR4
session
D
Retention
MIR3
MIR4
*
+
performance (a.u.)
0.40
0.35
0.30
0.25
0.20
0.15
Sleep
Wake
1
13
25
37
49
61
1
13
25
trials

A
beta power (uv^2)
0.100
0.075
0.050
0.025
0
Wake
Sleep
0.015
0.010
0.005
0
**
**
REG1
REG2
MIR3
MIR4
REG1
REG2
MIR3
MIR4
REG1
REG2
MIR3
MIR4
session
B
Frequency (Hz)
40
30
20
10
-0.3
-0.2
-0.1
0
0.1
0.2
0.3
time (s)
3
2
1
0
-1
-2
-3
t (post - pre)
C
Frequency (Hz)
40
30
20
10
-0.3
-0.2
-0.1
0
0.1
0.2
0.3
time (s)
4
2
0
-2
-4
t (post - pre)


A
R = 0.54, p = 0.03
0.10
0.05
0.00
performance change (MIR4 - MIR3)
-2
-1
0
1
Fast spindle density difference
(Exp - BL)
B
N2
1
0.8
0.6
0.4
0.2
0
rho


A
spectral slope
-3.5
-4.0
-4.5
-5.0
-5.5
-6.0
**
● Wake
● Sleep
REG1
REG2
REG1
REG2
MIR3
MIR4
MIR3
MIR4
condition
B
R = 0.57, p = 0.02
performance change (MIR4 - MIR3)
0.08
0.04
0.00
-0.4
-0.3
-0.2
-0.1
0.0
0.1
slope difference (MIR4 - MIR3)