NeuroImage 102 (2014) 666–673

Contents lists available at ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/ynimg

Full Length Articles

Resting state connectivity immediately following learning correlates with subsequent sleep-dependent enhancement of motor task performance☆

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ARTICLE INFO

Article history:
Accepted 22 August 2014
Available online 28 August 2014

Keywords:
Sleep
Motor learning
Memory consolidation
Resting state
Functional connectivity MRI
Procedural memory

ABSTRACT

There is ongoing debate concerning the functions of resting-state brain activity. Prior work demonstrates that memory encoding enhances subsequent resting-state functional connectivity within task-relevant networks and that these changes predict better recognition. Here, we used functional connectivity MRI (fcMRI) to examine whether task-induced changes in resting-state connectivity correlate with performance improvement after sleep. In two separate sessions, resting-state scans were acquired before and after participants performed a motor task. In one session participants trained on the motor sequence task (MST), a well-established probe of sleep-dependent memory consolidation, and were tested the next day, after a night of sleep. In the other session they performed a motor control task (MCT) that minimized learning. In an accompanying behavioral control study, participants trained on the MST and were tested after either a night of sleep or an equivalent interval of daytime wake. Both the fcMRI and the sleep control groups showed significant improvement of MST performance, while the wake control group did not. In the fcMRI group, increased connectivity in bilateral motor cortex following MST training correlated with this next-day improvement. This increased connectivity did not appear to reflect initial learning since it did not correlate with learning during training and was not greater after MST training than MCT performance. Instead, we hypothesize that this increased connectivity processed the new memories for sleep-dependent consolidation. Our findings demonstrate that physiological processes immediately after learning correlate with sleep-dependent performance improvement and suggest that the wakeful resting brain prepares memories of recent experiences for later consolidation during sleep.

Introduction

When not actively engaged in an external task, the human brain sustains a high level of spontaneous activity that is synchronized within distinct networks (Smith et al., 2009). Recent studies support a role for this wakeful resting state activity in memory processing. Resting state activity in motor networks is modulated after motor learning, but not after movement *per se* (Albert et al., 2009; Vahdat et al., 2011). Moreover, both increased resting state functional connectivity in task-relevant networks (Stevens et al., 2010; Tambini et al., 2010) and a 'replay' of stimulus-specific neural activity (Deuker et al., 2013) during wakeful rest periods that follow memory encoding predict better recognition (i.e., fewer items forgotten). These findings suggest that resting state activity in task-relevant neural networks after learning contributes to the retention of declarative memories. In the present study we examined whether the modulation of resting state activity by procedural motor learning correlates with subsequent performance *enhancement* that is known to depend on sleep.

Following active encoding, memory consolidation proceeds off-line, during both wake and sleep, without requiring conscious intent, effort or awareness (Stickgold and Walker, 2007). Not all memories last, however; some rapidly fade. For a memory to be retained for subsequent sleep-dependent consolidation it must be selected for retention and further

☆ Abbreviated title: The resting brain supports memory consolidation.

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http://dx.doi.org/10.1016/j.neuroimage.2014.08.044
1053-8119/

processing during the intervening wake period (Stickgold and Walker, 2013). We hypothesized that this selection for subsequent sleep-dependent consolidation would be reflected in the modulation of activity in task-relevant brain networks immediately after learning as measured by functional connectivity MRI (fcMRI). To test this, we used a procedural motor learning task and examined the relations between changes in motor network connectivity following learning and improved performance after a night of sleep.

We acquired resting state scans of healthy young participants before and after performing a finger-tapping task. In one scanning session, participants were trained on the finger-tapping motor sequence task (MST, Karni et al., 1998; Walker et al., 2002) a simple motor procedural learning task that is known to undergo sleep-dependent consolidation (Albouy et al., 2013; Kuriyama et al., 2004; Nishida and Walker, 2007; Walker et al., 2002, 2003a,b). Significant improvement of MST performance occurs after sleep but not after an equivalent period of wake and correlates both with the amount of stage 2 NREM sleep (Walker et al., 2002) and the number and density of sleep spindles (Albouy et al., 2013; Barakat et al., 2011; Nishida and Walker, 2007). (In a separate behavioral control study, we confirmed that MST improvement depended on sleep rather than the mere passage of time.) During a control scanning session, participants performed a paced motor control task (MCT) that involves approximately the same number of finger movements as the MST but is externally paced and employs a simpler sequence to minimize learning. We first identified differential changes in resting state activity within the motor network due to learning during MST training vs. movement during MCT performance. To test our primary hypothesis, we examined whether changes in motor network functional connectivity following MST training correlated with sleep-dependent improvement in performance measured the next day.

Methods

Participants

Fifteen young healthy participants enrolled in the fcMRI study and 12 (age 25 ± 2 years, 4 males) successfully completed both scanning sessions and were included in the analyses. Participants endorsed strong right-hand preference (laterality score ≥70) on the modified Edinburgh Handedness Inventory (Oldfield, 1971; White and Ashton, 1976). The 20 participants (age 22 ± 4 years, 7 males) in the behavioral control study provided complete data and were included in the analyses. All participants gave written informed consent and the study was approved by the Partners Human Research Committee.

Procedures

fcMRI study overview

Participants completed two scan sessions in a counter-balanced order one week apart (Fig. 1). Each session began at 3 pm and included two rest scans, one before and one after performing a finger-tapping task with their left-hand while being scanned. During one session, participants trained on the MST and 24 h later, they were tested on the MST in a mock scanner, which replicated the noise and conditions of the original scan. A 24-hour interval was used to avoid possible circadian effects on task performance. During the other session, participants performed the motor control task (MCT), which involved the same finger movements but minimal learning.

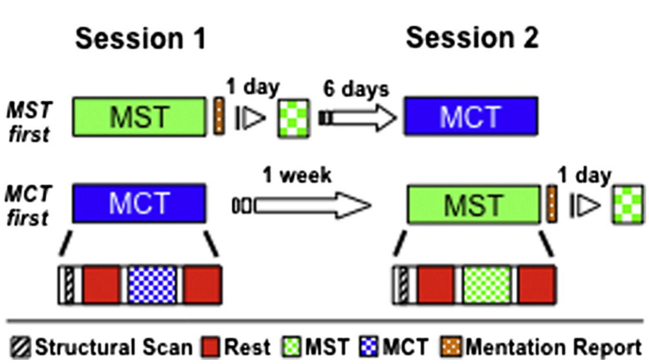

Fig. 1. Experimental protocol for the fcMRI study.

Behavioral control study overview

Participants were pseudorandomly assigned to either the Sleep condition ($n = 11$) or the Wake condition ($n = 9$). Participants trained on the MST and were tested 12 h later. Sleep participants were trained at 9 pm and tested at 9 am the following morning. Wake participants were trained at 9 am and tested at 9 pm after a day of wakefulness. The MST sequence and instructions were identical to the fMRI session, but instead of using a hand mold to respond as they did in fMRI (see below), participants pressed four numerically labeled keys on a standard computer keyboard with the fingers of their left hand. In addition, because participants could look at the labels on the keys, there was no preparatory teaching of the mapping between fingers and keys, nor was there any viewing of the red and green screens in advance of beginning the MST (as described below).

Finger Tapping Motor Sequence Task (MST)

The MST involves pressing four keys with the fingers of the left hand, repeating a five digit sequence (e.g., 4-1-3-2-4) "as quickly and accurately as possible" for 30 s (Walker et al., 2003b). During both the training and test sessions, participants performed twelve 30 s tapping trials each of which was followed by a 30 s break. During tapping trials, the computer screen was green with the numeric sequence displayed at the top, and dots appearing from left to right beneath the sequence with each keystroke. During the breaks, the display was red, and instead of showing the sequence, numbers (displayed as words) counted down the seconds until the next trial. Three seconds before the display turned green again, the words were replaced by flashing dots, which alerted the participant to get ready.

The primary outcome measure was the number of correct sequences per 30 s tapping trial, which reflects the speed and accuracy of performance. Any unfinished sequence at the end of a trial was added to the total, as a fraction of a correct sequence. Next-day improvement was calculated as the percent increase in correct sequences from the last three training trials to the first three test trials, and learning during training was calculated as the percent increase in correct sequences from the first training trial to the average of the last three training trials (Walker et al., 2002).

Motor Control Task (MCT)

The MCT used the same displays as the MST and like the MST it involved pressing four keys with the fingers of the left hand, with twelve 30 s tapping trials alternating with 30 s breaks. It differed from the MST in that during tapping trials, participants repeatedly typed the simple four-digit sequence 1-2-3-4 at a paced rate of 3.3 finger taps per second. As in the MST, the sequence appeared at the top of the screen, but now dots appeared beneath it automatically, indicating the pace of one tap per dot. This pace approximated the total number of finger taps expected in the MST session based on prior work in young healthy participants (Walker et al., 2002).

Preparation and instructions for scanning

To introduce the task design prior to the fMRI sessions, participants viewed three alternations of the green and red displays shown during the motor tasks, but did no actual tapping and were not told which hand they would use or what sequence they would type. The displays were identical to those seen during the task except that X's appeared in place of the sequence and dots appeared beneath the X's at a paced