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Resting-state connectivity predicts visuo-motor skill learning

Aurélie L. Manuel[a,*], Adrian G. Guggisberg[a,b], Raphaël Thézé[a], Francesco Turri[b], Armin Schnider[a,b]

[a] Laboratory of Cognitive Neurorehabilitation, Department of Clinical Neurosciences, University Hospital of Geneva and University of Geneva, 1206, Geneva, Switzerland
[b] Division of Neurorehabilitation, Department of Clinical Neurosciences, University Hospital of Geneva and University of Geneva, 1206, Geneva, Switzerland

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ABSTRACT

Spontaneous brain activity at rest is highly organized even when the brain is not explicitly engaged in a task. Functional connectivity (FC) in the alpha frequency band (α, 8–12 Hz) during rest is associated with improved performance on various cognitive and motor tasks. In this study we explored how FC is associated with visuo-motor skill learning and offline consolidation. We tested two hypotheses by which resting-state FC might achieve its impact on behavior: preparing the brain for an upcoming task or consolidating training gains. Twenty-four healthy participants were assigned to one of two groups: The experimental group (n = 12) performed a computerized mirror-drawing task. The control group (n = 12) performed a similar task but with concordant cursor direction. High-density 156-channel resting-state EEG was recorded before and after learning. Subjects were tested for offline consolidation 24h later. The Experimental group improved during training and showed offline consolidation. Increased α-FC between the left superior parietal cortex and the rest of the brain before training and decreased α-FC in the same region after training predicted learning. Resting-state FC following training did not predict offline consolidation and none of these effects were present in controls. These findings indicate that resting-state alpha-band FC is primarily implicated in providing optimal neural resources for upcoming tasks.

Introduction

The human brain spontaneously produces electromagnetic activity even when a subject performs no specific task. In particular, oscillations in the alpha frequency band (α), that is, about 8–12 Hz, can be observed during wakefulness without engaging in any task. Spontaneous brain activity is highly organized and coherent within specific neuroanatomical systems (Damoiseaux et al., 2006; Fox et al., 2005; Greicius et al., 2003) and accounts for the majority of the brain's energy cost (Raichle and Mintun, 2006). Synchronization of oscillations between different brain regions at rest reflects communication (i.e. functional connectivity, FC) between brain regions (Fries, 2005) and correlates with better behavioral performance on various cognitive and motor tasks in healthy humans (Fox et al., 2007; Guggisberg et al., 2015; Hipp et al., 2011; Sadaghiani et al., 2015). This has been shown in particular for alpha rhythms which are the main carrier for phase synchronization during resting-state (Dubovik et al., 2013; Guggisberg et al., 2008, 2015; Hillebrand et al., 2012; Rizk et al., 2013). The precise role of these oscillations is unknown.

There are currently two hypotheses on how resting-state FC might impact behavior (Deco et al., 2011; Harmelech and Malach, 2013; Miall and Robertson, 2006; Raichle and Snyder, 2007; Sadaghiani and Kleinschmidt, 2013). First, it might optimize the availability of neural resources and prepare for neural processing during tasks. Brain activity immediately *before* a task was found to influence behavioral performance as well as the magnitude of neural responses during the task (Britz and Michel, 2011; Sadaghiani and Kleinschmidt, 2013). Evidence for this possibility has been provided in particular for neural oscillations in the alpha frequency band in visual perception. Amplitude, phase, and synchronization of alpha oscillations at stimulus onset influenced subsequent perception of visual stimuli (Busch et al., 2009; Ergenoglu et al., 2004; Hanslmayr et al., 2005, 2007; Mathewson et al., 2009; van Dijk et al., 2008). However, the role of longer periods of rest on subsequent task processing and learning has so far not been explored.

A second hypothesis posits that resting-state communication *after* learning contributes to consolidation of training gains. This is true for sleep-related neural consolidation processes (Diekelmann et al., 2009; Gais et al., 2002; Huber et al., 2004; Maquet et al., 2000; Robertson et al.,

* Corresponding author. Aurélie Manuel Stocker, Brain & Mind Centre, The University of Sydney, 94 Mallett Street, Camperdown, NSW 2050, Australia
E-mail address: aurelie.manuelstocker@sydney.edu.au (A.L. Manuel).

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2004; Stickgold, 2005; Walker et al., 2002). However, the role of resting-state processes during wakefulness for consolidation is less clear. Memory consolidation has also been reported during awake resting periods (Cohen et al., 2005; Press et al., 2005), although behavioral gains have been less consistent.

Alpha and beta rhythms have been shown to modulate after motor learning (Deeny et al., 2009; Gentili et al., 2015; Mehrkanoon et al., 2016; Wu et al., 2014). Wu et al. (2014) used electroencephalography (EEG) and reported that increased FC in the beta-band in left parietal-motor areas during task predicted improvements in a pursuit rotor task. Gentili et al. (2015) found a reduction of alpha-band FC in frontal regions after training on a motor adaptation task. So far studies investigated network changes by comparing changes in resting-states before vs. during, or before vs. after motor-skill learning task (Albert et al., 2009a; Gregory et al., 2014; Sami et al., 2014; Vahdat et al., 2011; Wu et al., 2014). It remains unknown how alpha-band FC before task influences motor skill learning and how it is related to offline consolidation.

The present study aimed to test both hypotheses in a single paradigm of procedural learning (Dayan and Cohen, 2011; Willingham, 1998; Wolpert et al., 2011) in healthy human participants. We explored functional connectivity associated with visuo-motor skill learning in mirror-drawing (Julius and Adi-Japha, 2016; Milner, 1962). This type of task appeals to proprioceptive and visual feedback to control movements, processes presumably relevant to development and learning of a new sport or a musical instrument or “relearning” of motor skills following brain lesions. The mirror-drawing task requires participants to trace a given shape while right-left movements of the mouse are reversed. Unlike sequence learning tasks, performance on the mirror-drawing task generalizes to other tasks, thus constituting a valuable model for studying motor skill learning (Desmottes et al., 2017; Lejeune et al., 2016; Rouleau et al., 2002; Seidler, 2007). Both types of tasks are supported by distinct brain circuits: motor sequence learning is supported by a motor-striato-cerebellar circuit whereas spatial motor-skill learning (e.g. mirror-drawing) is supported by a frontoparietal-striato-cerebellar circuit (Hikosaka et al., 2002). Brain stimulation studies reported modulations in mirror-drawing performance after left parietal (Balslev et al., 2004) or cerebellar stimulation (Doppelmayr et al., 2016). The only study investigating EEG dynamics of mirror-drawing –using a single electrode over participants' forehead– reported a decrease of frontal EEG power during training which correlated with greater overall mirror-drawing performance (Wong et al., 2014).

Up to now, it remains unclear how resting-state FC, and more specifically how alpha-band FC before and after training, is associated with mirror-drawing skills. The aim of the study is to investigate whole brain functional connectivity at rest using high-density EEG to dissociate brain network activity predicting motor-skill learning from those predicting next day offline consolidation.

Methods

Participants

Twenty-four healthy, French-speaking, participants were assigned to the experimental group (Exp Group: $n = 12$, aged 22 ± 4; 7 men; all right-handed) or the control group (Ctrl Group: $n = 12$; aged 23 ± 5; 7 men; all right-handed). Participants provided written informed consent and the study was approved by the Ethics Committee of the Canton of Geneva and conducted according to the Declaration of Helsinki. No participant had a history of psychiatric or neurological illness. There were no gender ($X^2_{(1)} = 0.0$, $p = 1.0$) or age differences between both groups ($t_{(22)} = -0.61$, $p = 0.83$).

Stimuli and procedure

Mirror-drawing task

Stimuli were black-line star shaped figures with eight spikes (34×27 cm, 0.8 cm width). For every trial, a separate star with randomly tilted spikes was used with the constraint that the total length of the line was always similar. Participants in the Exp group performed a computerized classic mirror-drawing task (Milner, 1962) with right-left movements of the mouse reversed as a measure of *motor skill learning*. Participants in the Ctrl group performed a similar task but with concordant direction of cursor movement as a measure of *motor execution*. A blue rectangle indicated where participants were required to start, corresponding to the top spike of the star. Participants were asked to continue on the right hand-side of the start point. The finishing point was in the same blue rectangle as the start. The two variables of interest were the number of errors and the completion time. Errors were calculated as the number of times the participants went beyond– inwards or outwards - the stars' boundary line (Errors). Completion time (Time) was calculated as the time subjects took to complete one star, from the first click in the blue rectangle to the last click in the blue rectangle. Participants were asked to be as accurate and fast as possible, without trading errors for speed or speed for errors. In case of significant deviation of the mouse, i.e. for example a sudden jolt, the trial was terminated by the experimenter and a new star was proposed.

Both groups performed a short 2-min training of their respective tasks to get familiarized. Then, participants performed the task in the morning of the first day for 12 min (Fig. 1A). 24h later, participants came back to the lab to perform the same task for 12 min to test for offline consolidation. Training was determined as the amount of time spent on the task, i.e. 12 min, regardless of how many stars participants performed. Participants were not told they would be tested on this same task the following day, thereby minimizing conscious rehearsal of the task. Participants in the Exp group performed on average (mean ± SD) 9.5 ± 2.5 stars in 12 min on Day1 and 12.3 ± 2.5 stars on Day2. Participants in the Ctrl group performed 25.0 ± 10.1 stars in 12 min on Day1 and 24 ± 10 stars on Day2. Participants filled out a questionnaire addressing use of computer and mouse and frequency of video game playing (as mirror-drawing skills are required for certain types of video games). All participants were regular computer users but naïve with regards to mirror-drawing skills. Furthermore, a questionnaire evaluating sleepiness (Karolinska Sleepiness Scale, KSS) was filled by the participant before each session and the number of hours of sleep before each day was recorded. Participants were asked to stick to their sleeping routine before both days to prevent differences in level of fatigue between both daily sessions.

Statistical analyses

To measure *Learning* we contrasted the first four trials on day 1 (Day 1 BEG) with the last four trials on day 1 (Day 1 END). To measure *Offline consolidation*, we contrasted the last four trials on day 1 (Day 1 END) with the first four trials on day2 (Day 2 BEG) for Errors and Time separately. Two participants in the Exp group performed 7 trials instead of 8 on Day 1; we thus contrasted the first three trials with the last four trials for these two participants. An additional analysis included learning effects on Day2 and contrasted the first four trials on day2 (Day2 BEG) with the last four trials on day2 (Day2 END).

We then performed mixed model repeated-measure ANOVAs for Errors and Time with between-subject factor Group (Exp, Ctrl) and within-subject factor Time of Day (Day 1 BEG, Day 1 END, Day 2 BEG). In case of significant interaction, paired t-tests were performed for each group separately. Greenhouse-Geisser correction was used in cases of violation of sphericity. Effect sizes are reported with the partial eta square ($\eta p2$).

Additionally, we calculated two indexes taking into account the relative percentage of improvement. The *learning index* was calculated for Errors and Time variables separately as ((END-BEG Day1/BEG Day1) *100). Error and Time percentages were then averaged to obtain a single value. The learning index reflects the extent to which their performance improved at the end of Day1 compared to the beginning of Day1.

The *offline consolidation index* was calculated for Errors and Time as ((BEG Day2-END Day1/END Day1)*100); these two percentages were