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Maintaining vs. enhancing motor sequence memories: Respective roles of striatal and hippocampal systems

Genevieve Albouy [a,b], Stuart Fogel [a,b,c], Bradley R. King [a,b], Samuel Laventure [a,b], Habib Benali [d], Avi Karni [e], Julie Carrier [a,b,f], Edwin M. Robertson [g], Julien Doyon [a,b,*]

[a] Functional Neuroimaging Unit, C.R.I.U.G.M., Montreal, QC, Canada
[b] Psychology Department, University of Montreal, Montreal, QC, Canada
[c] Brain & Mind Institute, Department of Psychology, Western University, London, ON, Canada
[d] Unité Mixte de Recherche-S 678, Institut National de la Santé et de la Recherche Médicale/University of Paris 6, Centre Hospitalier Universitaire Pitié-Salpêtrière, Paris, France
[e] Laboratory for Human Brain & Learning, Sagol Department of Neurobiology & E.J. Safra Brain Research Center, University of Haifa, Haifa, Israel
[f] Centre of Advanced Research in Sleep Medicine, Hôpital du Sacré-Coeur de Montreal, Montreal, QC, Canada
[g] Harvard Center for Noninvasive Brain Stimulation, Harvard Medical School and Beth Israel Deaconess Medical Center, Neurology Department, Boston, MA, USA

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ABSTRACT

It is now accepted that hippocampal- and striatal-dependent memory systems do not act independently, but rather interact during both memory acquisition and consolidation. However, the respective functional roles of the hippocampus and the striatum in these processes remain unknown. Here, functional magnetic resonance imaging (fMRI) was used in a daytime sleep/wake protocol to investigate this knowledge gap. Using a protocol developed earlier in our lab (Albouy et al., 2013a), the manipulation of an explicit sequential finger-tapping task, allowed us to isolate allocentric (spatial) and egocentric (motor) representations of the sequence, which were supported by distinct hippocampo- and striato-cortical networks, respectively. Importantly, a sleep-dependent performance enhancement emerged for the hippocampal-dependent memory trace, whereas performance was maintained for the striatal-dependent memory trace, irrespective of the sleep condition. Regression analyses indicated that the interaction between these two systems influenced subsequent performance improvements. While striatal activity was negatively correlated with performance enhancement after both sleep and wakefulness in the allocentric representation, hippocampal activity was positively related to performance improvement for the egocentric representation, but only if sleep was allowed after training. Our results provide the first direct evidence of a functional dissociation in consolidation processes whereby memory stabilization seems supported by the striatum in a time-dependent manner whereas memory enhancement seems linked to hippocampal activity and sleep-dependent processes.

Introduction

Memory in humans has historically been classified into two independent systems thought to be anatomically and functionally dissociated. Declarative memory was described to rely on the integrity of the medial temporal lobe, including the hippocampus in particular, whereas procedural memory was predominantly associated with striatal activity (Squire and Zola, 1996). In the past decade, this dichotomist model has been surpassed by more interactive views proposing that memory systems do not act independently, but rather interact (Poldrack and Packard, 2003; Poldrack and Rodriguez, 2004). The concept of reciprocal interactions between memory systems has been supported by a series of recent behavioral studies showing interference between declarative and procedural learning, suggesting that these memory systems share common neural networks (Brown and Robertson, 2007a,b; Cohen and Robertson, 2011; Keisler and Shadmehr, 2010; see Robertson, 2012 for a review). Furthermore, in the framework of procedural memory, neuroimaging investigations of functional activation and connectivity associated to motor sequence learning have revealed that both the cortico-striato-cerebellar (e.g., Coynel et al., 2010; Debas et al., 2010, 2014; Doyon et al., 2002; Tzvi et al., 2014; see Doyon et al., 2009; Doyon and Benali, 2005; Doyon et al., 2003; Doyon and Ungerleider, 2002 for reviews) and hippocampo-cortical networks (Albouy et al., 2008, 2012, 2013c; see Albouy et al., 2013b for a review) are not only involved in the acquisition, but also in the consolidation of motor sequence memories. However, the respective roles of the striatum and the hippocampus in motor sequence learning and their respective link with subsequent sleep-related changes in performance, an indicator of memory consolidation, remain unclear.

* Corresponding author at: Functional Neuroimaging Unit, C.R.I.U.G.M., 4565, Queen-Mary, Montreal, Quebec H3W 1W5, Canada. Fax: +1 514 340 3530.
E-mail address: julien.doyon@umontreal.ca (J. Doyon).
URL:E-mail addresses:E-mail address: http://doyon.criugm.qc.ca (J. Doyon).

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Insights into the possible contributions of the hippocampus and striatum in procedural memory consolidation can be inferred based upon behavioral studies that explored the consolidation processes underlying different representations of a motor sequence. Motor sequence learning has indeed been described to encompass two distinct components: (1) a "goal representation" of the sequence built under spatial, allocentric coordinates and (2) a "movement representation" mediated through egocentric, motor coordinates (Albouy et al., 2013a; Cohen et al., 2005). Interestingly, it has consistently been shown that consolidation of the allocentric (spatial) and egocentric (motor) representations of the sequence depends differently on sleep, suggesting that distinct systems enhance these two different aspects of the memory trace: while consolidation of the spatial representation of the sequence is enhanced following a period of nocturnal (Cohen et al., 2005; Witt et al., 2010) or diurnal (Albouy et al., 2013a) sleep, consolidation of the motor representation does not seem to depend on sleep (Albouy et al., 2013a; Cohen et al., 2005; Hallgato et al., 2013). At the cerebral level, it has been shown that activity in the hippocampus is particularly linked to sleep-dependent consolidation, whereas striatal activity seems to develop in a time-dependent manner (Albouy et al., 2008, 2013c; but see Debas et al., 2010). Based on these series of evidence, it is thus tempting to speculate that the hippocampus and the striatum support, respectively, the allocentric (spatial) and egocentric (motor) representations of a motor sequence during the learning process. Interestingly, these assumptions are in line with evidence that the hippocampus and the striatum are critical for allocentric- and egocentric-response-based navigation strategies, respectively (Bohbot et al., 2007; Doeller et al., 2008; Iaria et al., 2003). Altogether, we thus argue that the hippocampus and related cortical areas such as parieto-frontal cortices, as well as the associative cerebellum (Grafton et al., 1998; Hikosaka et al., 2002; Hikosaka et al., 1999; Nakahara et al., 2001) participate in the creation of an allocentric map of the sequence that is further processed during a subsequent sleep period. In parallel, we propose that the striatum and related cortices including motor areas, as well as the sensorimotor cerebellum (Bischoff-Grethe et al., 2004; Grafton et al., 1998, 2002; Hikosaka et al., 2002; Hikosaka et al., 1999; Romei et al., 2009) support the egocentric, motor representation of the sequence and ensure the long-term stabilization of this memory trace (Doyon et al., 2009) in a time- rather than sleep-dependent manner. However, this explanation remains speculative, as the neural correlates of such dissociation in motor sequence memory consolidation have not yet been explored.

The aim of the present study was twofold. First, we tested, for the first time, the hypothesis that hippocampo- and striato-cortical areas would support the spatial and motor representations of a motor sequence, respectively. The second aim of the study was to disentangle the role of the hippocampus and the striatum in sleep-related motor sequence memory consolidation processes. Thus, this study, which is an fMRI extension of our previous behavioral study (Albouy et al., 2013a), was designed to isolate the two memory traces encompassing the allocentric (spatial) and egocentric (motor) representations of a learned motor sequence. We hypothesized that these traces do not only differentially depend on hippocampal and striatal activity, respectively, but that the underlying consolidation processes are differentially influenced by sleep. After training on an explicit sequential finger-tapping task (see Fig. 1, Training [T] session), subjects were tested on their ability to produce the motor or spatial representations of the sequence with the same hand, but with the keypad turned upside down (Fig. 1, Representation Test [RT] session). By inverting the keypad, the same finger movements were no longer associated with the identical spatial sequence and vice versa. Accordingly, such a manipulation generated two different sequence representations: an egocentric (EGO) representation that probed movement-based learning (i.e., the same sequence of finger movements resulting in a different spatial sequence) and an allocentric (ALLO) representation that examined spatial-based learning (i.e., the same spatial sequence requiring subjects to produce a different sequence of finger movements). After this test session, participants were either allowed to sleep during a 90-minute interval (NAP), or were asked to stay in quiet wakefulness (NONAP). Subjects in the four experimental groups (ALLONAP, ALLONONAP, EGONAP and EGONONAP) were then retested after a nap/no nap period on the same representation they were trained on (Fig. 1, Representation Retest [RR] session).

We hypothesized that: (1) the allocentric representation of the sequence would be supported by activity in hippocampo-cortical regions, whereas practicing the egocentric representation would recruit striato-motor areas; (2) offline gains in performance would only emerge after sleep for the allocentric, presumably hippocampal-dependent, representation of the sequence, whereas performance would be maintained after both sleep and wakefulness for the egocentric, striatal-dependent representation of the sequence; (3) activity in the hippocampus during learning would predict sleep-dependent gains in performance; and, (4) sleep would reorganize cerebral activity associated with the task in hippocampo-cortical areas for the allocentric representation, whereas the simple passage of time (irrespective of sleep or wake) would reinforce striatal activity for the egocentric representation of the sequence.

Materials and methods

Ethics statement

All participants gave their written informed consent to take part in the study, which was approved by the Research ethics board of the Regroupement en Neuroimagerie du Québec (RNQ). Subjects were compensated for their participation.

Participants

Sixty-two young (mean age: 23 ± 3.4 years, 39 females), right-handed (Oldfield, 1971), healthy volunteers were recruited by local advertisements to participate in the study. Subjects had no history of medical, neurological or psychiatric disease. None of the subjects were taking medications at the time of testing. Also, none received formal training on a musical instrument or as a typist. The quality of their sleep was normal (see Supplemental Results) as assessed by the Pittsburgh Sleep Quality Index questionnaire (Buysse et al., 1989) and the St. Mary Hospital questionnaire (Ellis et al., 1981). All participants were also asked to follow a 4-day constant sleep schedule (according to their own rhythm ± 1 h) before the experiment. Compliance to the schedule was assessed using both sleep diaries and wrist actigraphy measures (Actiwatch AW2, Bio-Lynx scientific equipment Inc., Montreal, Canada).

Of the 62 participants recruited for the study, seven subjects were discarded from the analyses. Five subjects were judged as outliers based upon their performance (as it was slower than the average of the sample of subjects by more than 2 standard deviations) during all the practice sessions (one subject in the ALLONONAP and one in the EGONONAP group) or during the representation test session only (two subjects in the ALLONAP and one in the EGONAP group). One subject in the ALLONAP group was excluded because of technical problems (wrong position of the hand on the keyboard) during the representation retest session. Finally, one subject in the ALLONONAP group was also excluded because he spent more than 5 min in stage 2 sleep during the NONAP period despite experimenter's supervision. Consequently, a total of 55 subjects were included in the analyses: 13 subjects in the ALLONAP group (mean age: 24.5 ± 2.9 years, 7 females), 13 in the ALLONONAP group (mean age: 24.9 ± 3.7 years, 8 females), 14 in the EGONAP group (mean age: 23 ± 3.3 years, 9 females) and 15 in the EGONONAP group (mean age: 24 ± 3.8 years, 10 females).